



Circulating Tumor Cell Collection, Analysis Methods Make Headway in 2019

Jan 07, 2020 | [John Gilmore](#)

NEW YORK – 2019 was a busy year for circulating tumor cell (CTC) capture and detection, as academic and commercial groups continued to develop novel techniques to extract and purify CTCs for diagnosing several cancers, and accelerated their efforts to bring these technologies to the clinic.

Notably, companies are increasingly exploring CTC capture methods alongside circulating tumor DNA (ctDNA) purification and analysis tools to distinguish themselves from the crowded ctDNA detection space and potentially unlock additional liquid biopsy applications.

There is significant interest in non-invasive liquid alternatives to solid tumor biopsies such as using blood or urine to search for CTCs or cfDNA that solid tumors shed into the bloodstream. Proponents of liquid biopsy platforms also argue that they can deliver results faster and require less sample than conventional tumor tissue methods.

Aware of the demand for liquid biopsy methods for research and clinical purposes, the US government put significant support behind development and expansion of these tools in 2019. For example, in September the US [National Cancer Institute](#) announced that it plans to fund research for integrating imaging and liquid biopsies, including measuring CTCs or tumor DNA, to track patient response to cancer therapies and treatment resistance.

Arguably the most attractive feature of CTC analysis is that, unlike cfDNA, when CTCs are extracted the resulting cells can be tested using not just molecular, but also immunologic and functional assays.

"At a technical level, CTCs are a reflection of how invasive the disease is, and how bad the tumor is, since it's measuring the amount of cells in the blood," said Arushi Agarwal, Director in the Precision Medicine Practice at Newton, Massachusetts-based life sciences consulting firm Health Advances. "Whereas ctDNA ... doesn't [necessarily] correlate with the stages of metastasis in the body."

That said, Agarwal, who focuses on liquid biopsy commercialization strategy at Health Advances, noted most liquid biopsy methods have so far lacked the clinical sensitivity and specificity of tissue analyses and are often more expensive than standard tissue biopsies. She also acknowledged that while there was significant pushback against and disappointment with CTC technologies in particular when they first entered in the clinical space, there is now a new wave of interest.

Most CTC efforts still focus on common cancers such as lung and prostate cancer, although companies and research groups have also recently begun to target a wider variety of cancers.

While Agarwal acknowledged that tissue biopsy will most likely remain the gold standard for cancer diagnosis, she highlighted that CTC analysis is clearly finding utility in niches like disease prognosis, minimal residual disease (MRD) monitoring, and companion diagnostics.

"You could use CTCs to monitor drug resistance in lung cancer where you don't want to take a tissue sample every time you want to look for the disease," Agarwal noted. "[Companies] could give patients exactly what they need in a much safer and less invasive way."

Among advancements in the more typical cancer types last year, Singaporean diagnostics firm Biolidics noted [in September](#) that it is working with Hangzhou Normal University to validate its technology to collect CTCs as drug treatment-response biomarkers for late stage lung cancer. Formerly Clearbridge BioMedics, the firm developed the ClearCell FX1 system to isolate and enrich intact CTCs from patient blood samples.

Biolidics also partnered with Japanese diagnostics firm Sysmex to develop a [liquid biopsy-based test](#) on the ClearCell system, as the firm eventually expects to use the technology in companion diagnostics.

In November, University of Toronto researchers [launched a startup called](#) Cellular Analytics to commercialize a microfluidic CTC capture platform called "Cytofind" that measures real-time expression of surface proteins and mRNA content. The researchers aim to use the platform to detect CTCs shed from tumors in the bloodstream and hasten lung cancer drug development.

Meanwhile, other companies with established CTC capture/analysis platforms reached milestones in 2019, setting them up to explore new use cases.

In March, Epic Sciences' lab received approval from the New York State Department of Health to provide its Oncotype DX AR-V7 Nucleus Detect test for patients with metastatic castration-resistant prostate cancer. The assay uses Epic's CTC platform to identify the presence of AR-V7 protein in these cells' nuclei, which the firm believes can help predict which patients are likely to respond to specific forms of cancer treatment.

Epic has since been able to explore new potential applications for its technology. The San Diego-based firm announced [in April, for example](#), that pharmaceutical company BeiGene is using its homologous recombination deficiency assay, which measures chromosomal instability in CTCs in an ongoing Phase II clinical trial with patients to assess response to the investigational PARP inhibitor paramiparib in metastatic, castration-resistant prostate cancer patients.

Receiving multiple grants from the National Institutes of Health in early 2019, startup Biofluidica [launched three different clinical studies](#) to look at exosomes, cfDNA, and rare cells in patients' bloodstreams. The San Diego-based firm's technology uses a microfluidic chip with sinusoidal-shaped channels containing specific antibodies that bind to different CTCs.

While clinically validating its technology for a variety of cancers, startup Biofluidica is also targeting [acute lymphoblastic leukemia](#), hoping to adapt its approach for MRD detection. Biofluidica Cofounder Steven Soper believes the two-module platform will translate well to clinical hematology because of its use of blood samples rather than bone marrow aspirates.

UK-based medical diagnostics firm Angle made strides last year in applying its [Parsortix cell-sorting system](#) with Hybrid Capture Enrich Amplification and Detection (HyCEAD) Zplex molecular analysis tech to

detect ovarian cancers. After running a blood sample through the Parsortix cell-capture system, researchers harvest CTCs into a storage buffer and launch the HyCEAD process, which combines PCR amplification and chemiluminescent detection.

Agarwal noted that despite promising new applications, detecting extremely low concentrations of tumor cells in a small amount of a patient's liquid sample remains a challenge. As a result, regardless of the clinical niche, companies are also continuing to try to optimize the cell capture process to ensure that samples have enough "critical mass" to produce useful downstream analyses.

Among new approaches popping up last year is one from Irvine, California-based nRichDx, which said that it [aims to carve a space](#) in the liquid biopsy field by providing a platform that collects a variety of sample types including cfDNA and CTCs.

Meanwhile, Akadeum Life Sciences' microbubble technology isolates CTCs for different types of downstream analysis. The Ann Arbor, Michigan-based [startup partnered](#) with Agilent to develop a novel method of isolating target molecules for downstream analytical workflows, later completing a \$4 million [Series A financing](#) round in December.

In a [proof-of-concept study](#) published in July in Science Advances, UCLA researchers also described a method combining antibody-based CTC and disulfide cleavage-driven CTC release to efficiently and quickly purify the cells for downstream molecular analysis. Labeling the platform "Click Chip," the team believes it could use the tool to identify genetic rearrangements to evaluate treatment responses and disease progression in lung cancer.

That many of the new platforms being explored combine CTCs with other targets like ctDNA or exosomes may reflect growing recognition in the field that these various compartments have unique, and potentially additive value.

Agarwal noted that some groups, for example, are now trying to use ctDNA to initially detect a cancer in a patient, followed by CTC and additional tools for monitoring the patient's response to treatment.

CTCs may eventually be viewed as more useful than ctDNA approaches for certain applications that have garnered more attention in recent years, she added. "If you're trying to develop ... tools for monitoring, [you want] to tailor what you're offering to target the biggest population and ones with the biggest need for the application," Agarwal said. "CTCs can open up opportunities to look at different markers, such as protein biomarkers, cell-surface markers, RNA expression, fusion transcripts, and possibly unlock other technologies for genomic analysis."

Still, challenges remain. Agarwal argued that until the sensitivity and specificity of CTC analysis methods matches that of ctDNA-based tools, their cost will remain high and may continue to hinder adoption into the clinic. That said, she believes that CTC tools will eventually find their role in oncology practice.

"At the end of the day, it's really about how companies can demonstrate [their tool's] clinical utility," she noted.

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