



Liquid Biopsy Startup C2i Genomics to Launch International Validation Trials for MRD Detection Tech

Jun 12, 2020 | [John Gilmore](#)

NEW YORK – Having recently completed a \$12 million Series [A funding round](#), liquid biopsy spinout C2i Genomics plans to initiate several retrospective and prospective validation trials on its minimal residual disease (MRD) detection platform, MRDetect, with undisclosed clinical centers in the US and Europe over the next year.

The New York-based firm believes MRDetect could be used to help physicians evaluate MRD status in a patient following tumor resection.

Launched as a commercial venture between New York Genome Center (NYGC) and Weill Cornell Medicine researchers in August 2019, C2i is exclusively licensing the technology from the two institutes. The firm raised \$1.2 million in a seed funding round in August, and the academic team behind C2i also received a \$225,000 academic grant from the [Mark Foundation](#) last February to initially commercialize the technology.

In addition to its New York headquarters, C2i has established a research and development team in Israel that is responsible for product development, software engineering, cloud design, and machine learning.

Dan Landau, an assistant professor at Weill Cornell and core faculty member at the NYGC who is also a scientific cofounder of C2i Genomics, explained that MRDetect applies an algorithm to examine the whole genome of a patient's tumor from a resected sample to identify mutation patterns or copy number variations.

Researchers then sequence about 1 ml of a patient's plasma sample using an Illumina sequencer and match the mutation signature in the circulating tumor DNA (ctDNA) to the signature detected in the tumor sample to monitor MRD.

"Because our approach is genome-wide and doesn't aim to saturate all of the available cell-free DNA fragments in the sample, it allows us to use as low as 1 to 2 ml of plasma," Landau explained. "In terms of clinical applicability, your sensitivity is no longer limited by fluctuations in plasma amounts found in the sample or by sampling errors."

In a proof-of-principle study [published](#) earlier this month in *Nature Medicine*, Landau's team showed that MRDetect allowed dynamic tumor burden tracking and post-operative residual disease detection using ctDNA in blood samples from lung adenocarcinoma, colorectal cancer (CRC), and melanoma patients. Clinical sensitivities ranged from 40 to 90 percent while clinical specificities ranged from 92 to 98 percent depending on the cancer type, the amount of copy number alterations, and cancer stage.

By increasing the number of detected single nucleotide variants across the patient's genome, the researchers found that the assay could minimize sampling limitations while predicting tumor frequency in cancer patients as a function of detected sites, mutation load, and sequencing coverage depth using a patient's blood sample.

"Although further validation in large cohort studies is required, these proof-of-principle data highlight the potential of MRDetect to deliver precision stratification of patients for adjuvant therapy, and more broadly, to address the unmet need of informing the complex residual disease therapy decision-making," the study authors noted.

Asaf Zviran, CEO of C2i and first author on the study, noted that the team encountered problems with suppressing background noise and reducing the effects of sequencing errors. Zviran, Landau, and their colleagues therefore developed a method for curbing the effects of these issues while maximizing the platform's clinical sensitivity and specificity.

In light of the study's results, Zviran noted that the team is now building an extensive clinical network of undisclosed US and international cancer centers and launching retrospective and prospective trials on multiple cohorts of cancer patients. The team believes C2i will have access to thousands of plasma samples — potential indications may include lung, colon, bladder, and breast cancers — from international biobanks to help accelerate commercialization of the MRDetect platform for monitoring cancer recurrence.

"One of the huge advantages of using WGS is that there's a very rich dataset," Zviran said. "We've used point mutations, copy number variations, and deletions before, but there are other features not described in the manuscript that can be utilized."

Zviran highlighted that C2i plans to potentially include additional genetic features and improve suppression to remove background noise, thereby improving the platform's signal-to-noise ratio and increasing clinical sensitivity.

C2i has also partnered with California-based [Genomic Testing Cooperative](#) to perform clinical validation studies, results from which Zviran anticipates releasing in early 2021.

As part of the licensing agreement with the NYGC and Weill Cornell, C2i has filed two patents related to MRDetect with the US Patent and Trademark Office.

C2i expects to initially launch a commercial assay for monitoring cancer recurrence in the US and is working with advisors at the US Food and Drug Administration to decide the best regulatory pathway. Zviran also noted that the firm is currently determining its commercial strategy for Europe and other international markets. The company is also still deciding which cancer type it will initially target.

"In principle, [MRDetect] is cancer-agnostic, but we will need to look at it in a case-by-case situation," Zviran noted. "Some of the [cancers] are obvious from the manuscript, [such as] lung and colon cancer, but we'll consider other applications that can be explored with this technology."

While comparing C2i's technology to [Natera's](#) and Archer Dx's [cell-free MRD](#) assays, Zviran argued that MRDetect is a tumor-informed method that is personalized for each individual. Believing that every cancer patient has a different tumor signature or "fingerprint," the team aims to use the unique signal as much as possible while developing the personalized MRD assay for different cancers.

"If you look at clinical oncology today, across solid cancers, [cancer recurrence] information is missing in a lot of clinical decisions we're making," Landau noted. "The MRD challenge is one we take seriously and is a challenge that we believe [our technology] has substantial potential to make an impact on patient care."

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