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C2i Genomics raises $12M series A to bring whole genome pattern recognition to liquid biopsy

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Whole genome sequencing is not part of treating patients in practice – or even involved in most clinical trials of drug candidates. But C2i Genomics Inc. is working to make that a reality. It applies pattern recognition to whole genome sequencing to create an individualized fingerprint for a given patient's tumor. The New York-based startup has raised a $12 million series A round to back the development of its technology, which came out of Cornell and the New York Genome Center.

This approach is expected to be used shortly after surgery, and frequently thereafter, to monitor for that specific circulating tumor DNA signature for both recurrence and drug resistance. It can offer a much higher sensitivity than that achieved with existing genomic panels. This could make it useful across all solid tumor types, regardless of how little ctDNA is shed into the bloodstream due to the tumor location.

Broad not deep

Proof-of-concept data for C2i's approach was recently published in *Nature Medicine*. This financing is expected to advance it across the board including pilot and pivotal trials in various oncology indications.

The startup is already working with a global research network to further validate its efforts, particularly via retrospective analyses of existing tumor samples. It is also starting to reach out to biopharmaceutical companies to partner for use of its technology in drug development clinical trials. C2i aims to have an FDA approval in hand for its first couple of indications within the next two years.

"Instead of going into an isolated sight very deeply, we thought that statistically it's the equivalent of looking for a mutation at maybe tens of thousands of sites at a much shallower depth and aggregating the signal across these many mutations back," Dan Landau, core faculty member at the NYGC and assistant professor of Medicine at Weill Cornell Medicine as well as C2i's scientific co-founder and a member of its scientific advisory board, explained to *BioWorld*.

"This was the Eureka moment where we realized that by thinking differently about the problem, we can really transform the problem here and overcome this limiting relationship between how many genomic equivalents you have in your plasma sample and your sensitivity," he continued. "Obviously, that required a bunch of different innovations in terms of how do we identify mutations in confidence – how do we build the right algorithms to aggregate the signal across the entire genome? But this expression allowed us to build tools that can wrap that up. What we realized is that this comes with a whole set of additional clinical practical advantages."

The whole genome sequencing of circulating tumor DNA (ctDNA) is based on a very small amount of plasma and conducted at the point-of-care or a local hospital. The data is uploaded into C2i's cloud-based system; the liquid biopsy analysis platform then detects and quantifies the thousands of mutations to create a kind of individualized tumor fingerprint.

Upon subsequent use, that novel genome-wide tumor signature, paired with machine learning and mathematical inference models, enables highly sensitive quantification of the amount of tumor DNA in the patient's blood that defines cancer recurrence and/or treatment failure months or even years earlier than current methods.

Validation plans

"It's a paradigm shift in technology," said C2i co-founder, CEO and CSO Asaf Zviran. "We are looking now at the problem from a pattern recognition approach. Instead of trying to detect and follow up a specific mutation. One of actual clinical problems with monitoring the specific mutation is that you actually receive the dynamic of that specific mutation, which is not necessarily the tumor dynamic. "

"One of the underlying principles that we developed together is working on the tumor in a holistic manner," he added. "So, most of the patients that we are looking at their biopsies, they have a very wide signature including thousands of mutations, many amplifications and deletions, so basically tens of thousands of features across the genome. Most of them are unique to that specific tumor; we call it a tumor fingerprint."

A proof-of-concept study on its whole genome pattern recognition technique was recently published in *Nature Medicine*. C2i is already working with a network of major research institutions on retrospective analyses of existing cancer samples. It aims to proceed with a series of pilot and pivotal studies in specific cancer indications, with lung and colon cancer applications expected to come first.

The clinical program will focus on demonstrating the predictive value of the whole genome pattern recognition as compared to other monitoring methods such as imaging. The idea is to demonstrate that, as the cost of whole genome sequencing has dropped to $100, this liquid biopsy approach can be used in conjunction to improve recurrence and treatment monitoring.

The test is expected to be useful within a few weeks after tumor removal surgery – and then subsequently employed as frequently as every month or two to detect any problems, with that data then being used to update the treatment paradigm.

Catching up to hematology

“In blood tumors, you see that methods that measure tumor burden are currently being used clinically in diseases like ALL and myeloma, where you have good markers that can guide therapy,” said Landau. “This is the ambition: to be able to switch between therapies to provide adequate therapy based on real time monitoring of disease. Not to wait for a patient to have disease that's rampant and affecting multiple organs.”

“The vision is through these tools that provide higher sensitivity to be able to replicate this type of success,” he continued. “To be able to guide conditions along with the clinical course of the patient as to what is the level of disease that the patient has, how is disease responding to an intervention, and whether they need to modify intervention.”

Landau noted that this could open up the potential for surrogate markers, which are becoming more commonly used in hematological cancer trials, into solid tumors as well thereby potentially drastically reducing study times and facilitating provisional approval ahead of long-term survival data.

The recent financing to support C2i’s development efforts was led by Casdin Capital with participation from new investors including NFX Capital, The Mark Foundation for Cancer Research and other, undisclosed investors.

“Genomic tools are bringing enormous benefit to the cancer patient treatment through more powerful and precise care and therapeutic development,” said Eli Casdin, managing partner of Casdin Capital. “The C2i approach breaks through sensitivity limitations of current approaches by exploiting the team’s unique capabilities at the intersection of genomic and data sciences. The series A financing catalyzes progress towards making an impact by supporting clinical development partnerships and collaborations with the biopharma industry.”