BUILDING A MOLECULAR DIAGNOSTICS STARTUP FROM THE GROUND UP

Capio Biosciences has developed a new LIQUID BIOPSY TECHNOLOGY for cancer detection and management. Now it needs to develop the laboratory, and the company, to support it.

In an age of molecularly targeted medicines and immunotherapies, oncologists rely heavily on insights that can only be obtained with an invasive biopsy. But tumours also shed small numbers of cells into the bloodstream. Many experts anticipate a future in which 'liquid biopsies' make it possible to probe these circulating tumour cells (CTCs) to obtain the same diagnostic and prognostic information by simpler and safer means.

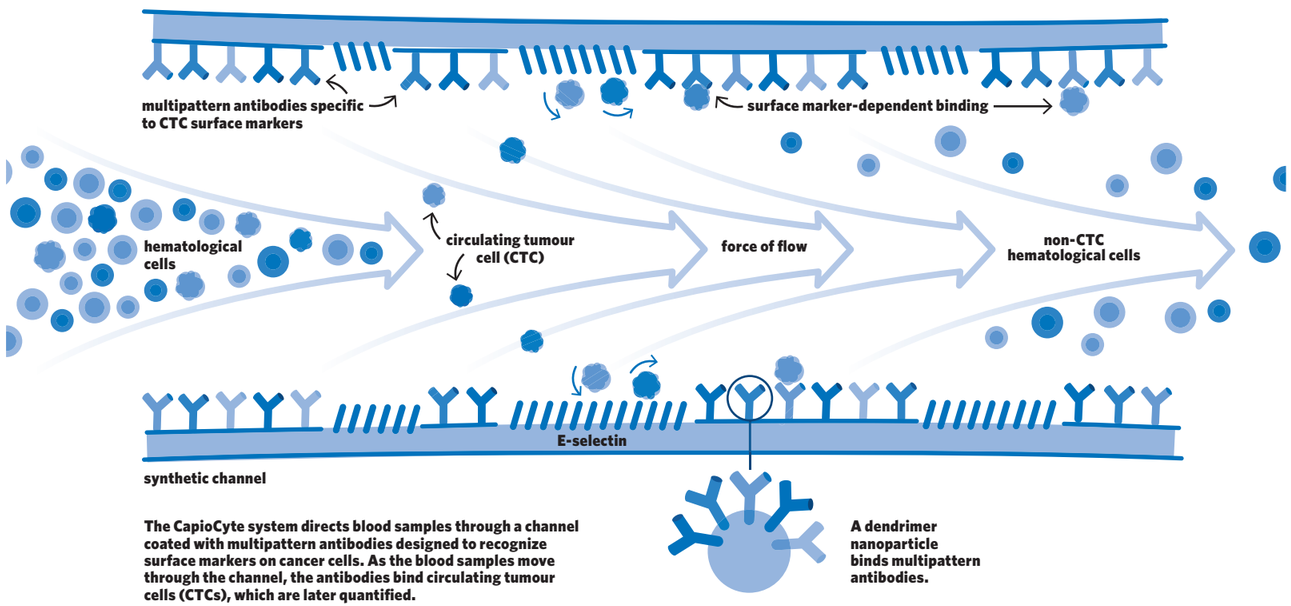
Capio Biosciences, a startup based in Madison, Wisconsin, is now developing a device to enable the detection and analysis of these exceedingly rare cancer cells with unprecedented sensitivity. The CapioCyte system directs blood samples through a synthetic channel, exploiting the tendency of CTCs to adhere and roll along the surface of blood vessels. As the cells interact with the surface of the channel, they are captured by a layer of nanoparticles engineered to display tumour protein-specific antibodies. The trapped CTCs can then be quantified microscopically and further analyzed.

Co-founders, Seungpyo Hong of the University of Wisconsin at Madison, and Andrew Wang at the University of North Carolina at Chapel Hill, are now testing CapioCyte in several clinical studies, and Hong recently discussed his experiences in attempting to translate a successful benchtop proof-of-concept into a robust commercial diagnostic system.

What led to the decision to commercialize your technology?

Andy and I were both postdocs at MIT under the mentorship of Robert Langer. Although we were working on different projects at the time, we started discussing the possibility of developing technologies to improve CTC capture. He's a clinician and I'm a technician and engineer, so we made a good team. Once we became faculty members, we began research on this idea. It took us almost six years to get solid proof-of-concept data; we did an initial clinical study with blood samples from Andy's patients. Once we had that data, we decided to start the company. That was in 2013.

As with most startups growing out of academic labs, we set up a virtual company first. I was lucky that I got some funding from my university — by then I'd moved to the University of Illinois at Chicago (UIC) — and we got some shared facilities there with a very small amount of cash.



The CapioCyte system directs blood samples through a channel coated with multipattern antibodies designed to recognize surface markers on cancer cells. As the blood samples move through the channel, the antibodies bind circulating tumour cells (CTCs), which are later quantified.

What were some of the early challenges?

We were renting a shared space and a mailbox in the UIC incubator, which was a challenge. I've started two academic labs, first at UIC, and later here at the University of Wisconsin at Madison. In this setting, you have well-established research facilities and equipment, as well as supporting staff and mentoring faculty. Starting a lab outside academia was like starting from scratch.

Seungpyo Hong, co-founder of Capio Biosciences

How did you then grow the company from concept to reality?

Once we had our proof-of-concept results, our first priority was to expand our patient data, so that we could show that our device would work in clinical situations. We started presenting our results at conferences and Andy ended up meeting with an emerging Chinese pharma company [Betta Pharma], which eventually became a strategic partner and a series A investor. With funding, we set up a real lab for the company, and now we are conducting three different clinical studies. We are also trying to develop our first commercial-level prototype.

What have been the challenges in developing a commercially viable device?

In a lab, you tend to work at the small scale. You can better control the dimensions and parameters at the small scale, and you're conserving resources as well. We initially started using a lot of smaller devices, like microfluidic systems with really small channels and flow systems. But, we figured out early that this could be a problem. Viscous solutions, like human blood, can clog channels, which limits throughput. We actually had to change our dimensions from the micrometer level to the millimeter or centimeter level, and we had to increase the size of our flow chamber to fit well with a standard glass slide. At first, we were using these commercial flow-chambers, and then we designed our own. Beyond the development of a commercial-level prototype, we are working with an engineering company to design a launch product.

How did you identify suitable engineering companies?

We mostly found them at conferences. We showed them our process from beginning to end: how to prepare the surface and how to functionalize it, and what kind of system that we're looking for. Not every company is very responsive or professional, so those companies are out of consideration. We have been talking with three companies so far, each of them highly experienced and with a strong expertise in making similar systems to what we are trying to make. It comes down to the cost and what kind of team they can form.

What about in terms of your capture reagents?

So far the volume has been fairly small. We have been purchasing antibodies and reagents from known vendors in the space. We have been buying academic-level quantities, but at some point we're going to need partners who can provide those expensive reagents at a lower cost, at volume. That's something we are negotiating.

Are you encountering any challenges with reproducibility as you scale up?

So far we've been using cell lines to make sure that our system is working on different days and with different batches, with operator-to-operator variations. We've repeated this a number of times, and we've found that as soon as we get fairly well-trained operators, those variations are acceptable. It's still not less than 10% — probably closer to 20% or 30%. But I think that is still acceptable at this stage. At the same time, we are building a more robust internal control system, where instead of using actual cells, we are using well-defined microbeads, where we know the exact surface presentation of whatever we've attached.

We have three locations: one in Madison; we just set up a lab in a facility for CTC analysis at UNC, which is Andy's institution; and we also have an identical system with a joint venture in China. We are not producing the capture surface at a very high throughput. We are actually developing a robotic system so we can produce those surfaces in a consistent fashion and at high volume, and then use those particular surfaces for all three locations. Right now, we are only preparing the surfaces in Madison, and then we ship them over to China and UNC.

Have there been any other unexpected challenges?

Some of the conditions optimized for a small academic lab do not really translate at the commercial level. For example, we had parameters optimized for fluorescence imaging in the lab, which turned out to give potential false-positive and false-negative readings. We are now collaborating with engineering companies to create a commercial-level analytical system without large variations. We have also hired a developer with extensive industry experience. The combination of partnership and hiring necessary talent seems to be our path to overcoming challenges in a fairly short period.

How do you decide what processes to keep in-house and which aspects of the business to outsource?

Our core technology is the surface preparation of the chips, and we don't want to outsource that. But for every other part, building a flow-system or building a fluorescence analyzer, for example, it's better to partner with somebody with more experience. We put different priorities on the core technology versus the technology that is not unique to us. People are important. We are putting together an executive team with a technical background, a business background, a clinical background, and a development background. Those are the four core components supporting the core technology. Everything else can be outsourced. To be successful as a small company with limited funding, finding reliable partners is the key, and we are really developing those relationships right now.

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