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RainDance Taps Cambridge Consultants to Help Build Microfluidic, Microdroplet Assay Tech

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This article has been updated from a previous version to clarify the relationship between RainDance and Cambridge Consultants and between RainDance and ESPCI and to correct Cunningham's title.

Emerging New England biotech RainDance Technologies has developed a chip that combines microfluidics and microdroplet technology for performing a variety of cellular and biochemical assays, and has tapped UK-based Cambridge Consultants to help develop accompanying instrumentation, *CBA News* learned this week.

With Cambridge's engineering acumen and approximately $170,000 in National Institutes of Health funding in its pocket, RainDance hopes to launch the combined system in January 2008. But first, the company faces the tall order of distinguishing its product from those offered by established microfluidic tool vendors Caliper and Fluidigm.

RainDance was founded in 2004, and its core technology, the NanoReactor Chip, is an amalgamation of expertise from three academic institutions, Bob Cunningham, vice president of business development for RainDance, told *CBA News* this week.

According to Cunningham, researchers from Harvard University developed the chip's microfluidic component; scientists from the Medical Research Council in Cambridge, UK, were responsible for many of the biological assay components; and researchers from Paris' Ecole Supérieure de Physique et de Chimie Industrielles developed emulsion chemistry used in the core microdroplet technology.

RainDance has licensed patents from Harvard and MRC, and has since developed its own intellectual property portfolio around specific applications and commercial aspects of the technology, Cunningham said.

The NanoReactor Chip can be thought of as a combination microfluidic flow cytometer and well plate, and the term "nanoreactor" is interchangeable with "microdroplet," according to Cunningham.

The technology takes an aqueous sample that one might typically put in a single well of a microtiter plate, and forms miniature droplets from the sample by exposing it to a stream of fluorinated oil. The so-called emulsion droplets are then circulated through the channels of RainDance's microfluidic chip.

"One way to think of this is that every one of our droplets is equivalent to an individual well on a microplate," Cunningham said. "Anything you can put into a well on a plate – a variety of reactants, one or more cells – we can put into a droplet.

"Some people have referred to this droplet phase as digital microfluidics, because you create these individual packets of aqueous sample that are totally surrounded by this oil as it flows through the channels," he added.

The microdroplets can accommodate anything from one or more cells – including yeast, bacteria, *Drosophila*, and mammalian – to beads with cells attached, to small molecules, enzymes, or other biochemical entities. Whatever is inside the microdroplets can be labeled with a biomarker for readout as the droplets flow through the chip's channels.

Around last summer, RainDance contracted Cambridge Consultants to help develop instrumentation that would be compatible with the NanoReactor Chip. In December, Cambridge delivered optical and electronic components that were integrated into the Personal Laboratory System, or PLS, a benchtop, laser-based interrogation system that enables a wide variety of optical assays at processing speeds of up to 10,000 droplets per second.

“These are standard optical technologies,” Cunningham said. “Right now we’re working with readouts such as fluorescence light scattering, fluorescence polarization, and FRET – for the most part, we didn’t want to change peoples’ assays or how they understand their readouts; we just wanted to give them a unique way of packaging their samples and sampling them.”

Will It Be a Rainmaker?

With a variety of other microfluidic chip technologies and accompanying instrumentation on or nearing the market, RainDance hopes that the droplet format will help distinguish its product from competing products. Cunningham said that the NanoReactor most typically gets compared to Caliper’s LabChip and Fluidigm’s MSL technology.

“The difference from other microfluidics techniques from, for example, Caliper or Fluidigm is that those are continuous-flow, single-phase fluidics [platforms],” Cunningham said. “In other words, they have their samples flowing through the channels of their chips in a continuous aqueous phase.

That one main difference, Cunningham said, leads to several additional, related benefits.

“One is that the samples that go into our droplets never have any air interface, so there is never any change in concentration, which happens very rapidly in microfluidics conditions,” Cunningham said. “Our droplets also never have any contact with the channels themselves – they’re always surrounded by this oil interface – so there is no cross-contamination from sample to sample, and there is none of the adherence and clogging that other microfluidics chips are subject to.”

The NanoReactor Chip has a broad list of applications that include cell and enzyme screening, fluorescence-activated cell sorting, antibody engineering, drug formulation, therapeutic enzyme development, RNAi screening, and even the optimization of biofuel production.

But until its technology is proven, RainDance may have to zero in on applications that do not directly compete with companies such as Caliper, which markets LabChip primarily for high-throughput biochemical- and cell-based drug screening; and Fluidigm, which plays primarily in high-throughput protein crystallization, real-time PCR, and genotyping.

“This is not to say that we can’t do screening. All of the microfluidics advantages that people talk about – low sample consumption and rapid processing – we do, but we’ve sort of been driven by the unique things that people have pointed out about the droplet methodology.”

“In the very short term, we’re getting a tremendous amount of interest from people who do any sort of evolutionary biology,” Cunningham said. “For example, we’re working with people who are … evolving enzymes for various industrial applications, particularly with respect to bio-fuel processing. We’re also working with people who are doing evolutionary drug discovery, where they are looking at naturally occurring biomolecules, and evolving and optimizing the materials that they can harvest from a diverse collection of cells.”

In the longer term, RainDance may sniff around the diagnostics space, particularly in the identification of rare cell-surface markers that typically occur below the threshold of current sorting techniques. An application such as this would take advantage of the fact that RainDance can process individual droplets extremely rapidly, and amplify even the weakest of signals from biomarkers using the PLS instrumentation.

“This is not to say that we can’t do screening,” Cunningham said. “All of the microfluidics advantages that people talk about – low sample consumption and rapid processing – we do, but we’ve sort of been driven by the unique things that people have pointed out about the droplet methodology that we want to take advantage of.”

RainDance, which has already secured an undisclosed amount of money from private investors, plans to close a round of financing by the end of this quarter to help it launch the product in January 2008, Cunningham said. In addition, in 2006 the company began a two-year grant from the National Human Genome Research Institute, the first year of which was worth $169,750. The company has also applied for additional NIH funding.

The company plans to preview its product at the upcoming Association for Laboratory Automation conference in Palm Springs, Calif., after which it hopes to land beta-testers in pharma, biotech, and academia. Although it hasn't placed units yet, the company has demonstrated the product to potential customers at its Guilford, Conn., research labs, Cunningham said.

And despite the wide array of potential applications for its technology, RainDance for the moment intends to foster a single-track business model of instrument and consumable sales.

"There may be certain applications for which we will try to provide a service for customers, because we do have the ability to individually label each droplet with [specific] dyes," Cunningham said. "So, for example, we could create a labeled library of 200 of the most common kinases the drug companies want to screen their compounds against … and be able to pull out that little aliquot when someone's compounds come in, and screen it for them.

"Again, it's not our primary business objective, but something we can see ourselves doing," he added.