

Univ. of Toronto Spinout Rolls Out New Biomarker System with Eye on Bead Array Market

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NEW YORK (GenomeWeb News) – Scientists from the University of Toronto have launched a new instrument combining flow cytometry and atomic mass spectrometry that they say can quantify biomarkers in parallel in numbers not achievable with other technologies.

While the researchers have initially focused on developing the technology as an improvement on current flow cytometry instruments, they also are working on adapting the technology for a multiplexed bead array instrument, Scott Tanner, the president and CEO of DVS Sciences, a company created to commercialize the technology, told *GenomeWeb Daily News* this week.

The first iteration of the platform, called CyTOF, which its inventors dubbed a mass cytometer, has been available since November but was officially launched at the International Society for the Advancement of Cytometry last week. Armed with new funding from the Ontario Institute for Cancer Research announced in late April, the researchers are now building out the technology's capabilities.

"Basically, what it does is ...take flow cytometry into the next dimension into the multiparameter stage and it does it without requiring that the user do a lot of compensation, do a lot of math and correction," said Tanner, who is also a professor of chemistry at the University of Toronto.

He and his colleagues also developed and commercialized Maxpar, reagents for use on CyTOF. They can also be used with conventional ICP-MS analysis for solution analysis, such as multi-parametric ELISAs or Western blot format.

The CyTOF mass cytometer is DVS' lead technology. In essence, it is a hybrid instrument comprising elements of a flow cytometer and an atomic mass spectrometer, specifically an inductively coupled plasma mass spec.

Like a flow cytometer, CyTOF is for the multiparametric analysis of cells, but instead of using fluorescence tags or lasers, it uses a stable isotope of an element, preferably a lanthanide stable isotope. The stable isotope is placed on an antibody, a cell is probed, and then flowed one at a time into the mass spectrometer.

The MS vaporizes, atomizes, and ionizes the cell. The ions are extracted from the resulting state-of-the-matter plasma and analyzed by mass spectrometry at about 1,000 cells per second.

According to Tanner, the advantage of the CyTOF over conventional flow cytometers is that the mass spec allows "exquisite resolution" between the mass channels without overlap, "which means there's no

need for compensation like there is in fluorescence. Therefore we can do as many measurements as there are stable isotopes and for which there is a non-cross-reactive antibody panel."

Tanner said that with the CyTOF, DVS can typically do a 35-parameter experiment because there are 35 lanthanide stable isotopes that they use as tags, making it the first instrument that allows flow cytometry to be done in more than 20 parameters.

The atomic mass spectrometer does complete ionization so results are quantitative, he added.

"The signal we get at the detector is exactly proportional to the number of atoms that went in the front end, which are exactly proportional to the number of antibodies that were present, which is proportional to the number of antigens in the cell," Tanner said. "So what we do is provide the ability to measure many antigens simultaneously and quantitatively."

The CyTOF lists at \$600,000. The technology is amenable to any affinity assay as long as there is an affinity product that recognizes the target, "so it could be a hybridization gene array ... or it could be an antibody assay or an aptamer or a lectin or hapten," Tanner said. Presently, CyTOF is for use with protein and RNA biomarkers and is suited for targeted biomarker work rather than discovery research, he added.

Meanwhile, DVS is continuing to work on increasing the capabilities of the existing CyTOF platform, including increasing the automation on the front end and increasing the dynamic range of the detection by between four and six orders of magnitude

While the use of electrospray mass specs are becoming common in biology, atomic mass specs are still a rarity and are used more for chemical analysis research. The idea to use the atomic mass specs to quantify and analyze cellular components stems from Tanner's work while he was at MDS Sciex, where he worked before moving to the University of Toronto. At MDS Sciex, his team helped develop ICP-MS instruments.

Bead Array Challenger

DVS researchers, though, are also working on adapting the technology for a multiplexed bead array instrument for "gene array equivalency," Tanner said. If the instrument makes it to market, it would provide a new competitor for entrenched technologies offered by Luminex and Illumina.

Last year, Tanner and his colleagues received a three-year, \$469,031 grant from the NIH for the project. And last month, OICR, a non-profit institute funded by Ontario's Ministry of Research and Innovation, also announced it had made a second tranche investment into DVS, for C\$200,000 (\$191,329). While it said that the funding is generally for the development of molecular diagnostics for cancer screening and treatment, Tanner this week confirmed that OICR's interest is in the multiplexed bead array instrument.

However, that platform is a "few years" from being ready for commercialization, he said.

Tanner, Vladimir Baranov, Dmitry Bandura, and Olga Ornatsky founded DVS in 2004 to exploit their technology. Like Tanner, the other three also have positions at the University of Toronto. DVS currently has 10 employees. Four researchers at Tanner's lab at the school also do work for the company.

The firm's first outside funding of C\$500,000 came from OICR in 2008. In total, DVS has received C\$16.8 million in funding through investments and grants. OICR remains the only outside investor in the company, though Tanner said that discussions have been held with potential investors, including venture capitalists and other companies.

"We have an aggressive growth plan and it will require investment in one form or another, whether it's in venture capital or from a corporate partner," he said.