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Pastel BioScience Combining Protein Capture Agents with NGS to Tackle the Proteome

By Adam Bonislawski

UK-based biotech firm Pastel BioScience is building an array-based proteomics platform with the aim of accessing the entire human proteome.

While still in the early development stage, the company believes that its InVenio platform, which combines protein capture molecules with detection similar to commonly used next-generation sequencing platforms, could eventually allow researchers to study complete proteomes, Stephen Osborne, Pastel's founder and CEO told ProteoMonitor.

The technology is based on proprietary capture molecules derived from a novel human protein scaffold that, according to the company, can be expressed efficiently in Escherichia coli as recombinant proteins. Pastel, Osborne said, has created large libraries of these molecules with randomized binding sites, from which it can select suitable individual capture molecules.

Unlike most capture molecule-based proteomic platforms – Osborne cited Somalogic's Somamer technology as an example – Pastel is not developing capture molecules for each individual protein. Rather, Osborne said, each of the company's capture molecules recognize multiple proteins.

In this, he noted, the technology is somewhat similar to, though substantially different from, work being undertaken by Lund University researcher Carl Borrebaeck, who has developed antibodies that target not individual proteins, but rather short amino-acid sequences, or motifs, that are present in several hundred different proteins (PM 8/12/2011).

By combining these antibodies — which Borrebaeck and his colleagues have dubbed context-independent motif specific, or CIMS, antibodies — with mass spectrometry, researchers can perform proteomic analyses in a semi-untargeted fashion, achieving the enhanced sensitivity of targeted approaches with the breadth of a shotgun-style discovery workflow.

Instead of using mass spec for readout of the capture proteins, Pastel plans to use detection based on next-generation sequencing, Osborne said, noting that the company has been working with "a basic next-generation sequencing platform" similar to that used by Solexa, the NGS pioneer that was purchased by Illumina.

He said that using that system, the company has demonstrated the ability of the InVenio platform to detect proteins at the single-molecule level. This current NGS set-up is fluorescence-based but, Osborne said, the company also is also adapting its technology to work with field-effect transistor-based systems like Life Technologies' Ion Torrent.

Life Tech has in the past expressed interest in developing the Ion Torrent technology for protein detection (PM 7/13/2012). However, with Thermo Fisher Scientific's purchase of Life Tech pending, it's unclear if and how these plans might move forward (PM 4/19/2013).

With its Orbitrap line of instruments, Thermo Fisher already owns one of the most widely used mass spec platforms in proteomics research. FET-based technologies like the Ion Torrent, however, could offer certain advantages compared to mass spectrometry – for instance, more compact size, lower costs, and high sensitivity. In addition to Life Tech, several academic facilities are researching FET-based systems as tools for proteomics, including the University of Copenhagen's Nano-Science Center and the University of California, Santa Barbara's Nanoelectronics Research Lab.

Osborne said that he would ultimately like to partner with an NGS firm to put the InVenio system on their platform. He has spoken to several such firms about this possibility, though Life Tech or Thermo Fisher are not among them, he added.

Pastel is one among several companies or researchers that is exploring NGS as a readout for protein assays (PM 10/7/2011). For instance, in 2010, Belgian biomarker firm Pronota completed a proof-of-concept study for a protein biomarker diagnostic platform using NGS. In 2011, the lab of Ulf Landegren – the founder, a board member, and a shareholder of Olink Biosciences – published on a technique using NGS to quantitate proteins detected via that company's proximity ligation assay technology.

As Landegren told ProteoMonitor at the time, the technique – while offering the possibility of high-precision and easier multiplexing – suffered from poor reproducibility.

NGS-based approaches could also run into problems measuring samples with high dynamic range. In order to achieve good coefficients of variation, researchers will need to measure a

substantial number – 1,000 copies, for instance – of target analytes. In a sample with a large dynamic range, measuring 1,000 copies of low-abundance proteins will therefore require sequencing billions of copies of DNA linked to higher-abundance proteins.

One potential way around this is to decrease the number of probes to high-abundance analytes so that all proteins will report at roughly the same level. Their actual levels can then be calculated on the back end by accounting for the relative number of probes to each protein used.

Pastel has been working with UK-based diagnostics firm QuantumDX to develop the InVenio technology and seek further funding. QuantumDx board member and Executive Advisor Paul Fitzpatrick told ProteoMonitor that the two companies' relationship is ongoing.

Osborne added that Pastel is now looking for additional sources of investment, with the aim of continuing to build its library of capture agents.

"At the moment we only have a limited number of these capture molecules," he said. "The next step is to develop further the number of these molecules and then start building up panels so that we have enough of them to detect, for instance, panels for inflammatory proteins, for cardiac proteins, for cancer markers."

The company has filed for patents on its capture agent technology and awaits a ruling on their applications, he added.

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This story has been updated to clarify that QuantumDx has not yet invested in Pastel Bioscience.

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Adam Bonislawski is the editor of GenomeWeb's *ProteoMonitor*. He covers proteomics and life science mass spectrometry. E-mail Adam Bonislawski and follow his GenomeWeb Twitter account at @ProteoMonitor.

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Trust Sanger Institute came up with a computational method for prioritizing potential disease culprits — including those in non-protein-coding parts of the genome. By formalizing their functional variant and mutation predictions into a computational tool known as FunSeq, the investigators demonstrated that they could identify around 100 non-coding driver mutations using information from 90 tumor genomes.

applications. The firm intends to use the funds to expand commercial operations in the translational research market, scale its laboratory capabilities, and launch clinical applications for non-invasive genomic profiling and monitoring of cancer. Its flagship OnTarget platform performs genomic analysis of cell-free DNA in plasma to detect and quantify mutations in tumor-derived circulating nucleic acids.

the goal of advancing research, training new investigators, and ramping up genomics capabilities and infrastructure across the continent. The new research projects being funded by the H3Africa program, which has thus far dispersed around $74 million in funding, will pursue studies into neurological disorders, respiratory diseases, fevers of unknown origin, tuberculosis, and African sleeping sickness.

This webinar was recorded Oct. 3.

GenomeWeb and Asuragen invite you to view a webinar discussing the use of next-generation sequencing to illuminate druggable targets in oncology while addressing the limitations in DNA quality and yield from formalin-fixed specimens.

Register here to view the playback or download the recording.