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Biocept Looking to Redefine CTC Dx Market, Plans Product Launch

In the midst of a $5 million financing round, microfluidics company Biocept is looking to launch its first diagnostic test, as it embarks on “redefining what a circulating tumor cell is.”

Thirteen years after its founding, and following changes in its technology focus and other adaptations, the company plans to soon launch its first diagnostic test, directed at breast cancer, Biocept President and CEO Stephen Coutts told *GenomeWeb Daily News*.

As part of the financing round announced three weeks ago, San Diego?based Biocept raised $2.3 million in a tranche to fund a clinical trial for the test, as well as to further develop other tests in its pipeline.

When launched, the breast cancer test, called OncoCEE?BR, would represent a milestone for the company, which has not had a commercial product since being founded in 1997 as a microarray business by Soon Kap Hahn and Bo Reiss, who died of renal cancer in 2005.

After about seven years after its founding and as it struggled against competition in the sector, Biocept turned its attention to the microfluidics space

“I think [the company] lost the battle to Affymetrix and the like,” said Coutts, who joined Biocept in October 2008.

In its new iteration, the company initially focused on pre?natal ailments, but by the time Coutts came in as CEO, it switched to the cancer market.

“Now we’re focusing on isolating circulating tumor cells from blood and disseminated tumor cells from bone marrow and potentially finding aspirates from lymph nodes, though we haven’t developed that yet,” Coutts said.

The company’s core platform, called Cell Enrichment and Extraction, is “essentially a rare cell capture technology,” he said, and is based on *in situ*hybridization technology developed on the company’s proprietary microfluidics platform.

According to Biocept’s website, a mathematical model is used to develop flow rates and place posts in a microfluidic device in order to maximize the capture of cells in the microelectromechanical channel. Specified antibodies are then used to selectively attach to target cells, which create an enriched cell sample.

After capture, those cells can be used for molecular diagnosis either as intact cells or after lysis.Veridex, a company owned by Johnson & Johnson, already markets a circulating tumor cell test called the CellSearch system, considered the leading platform for detecting and identifying such cells from blood. According to Coutts, the Veridex system provides prognostic information by counting tumor cells captured from a sample: the more cells captured, the more aggressive the cancer is.

But in a focus group held by Biocept when Coutts first joined the firm, oncologists voiced a need for a predictive CTC test that would provide guidance on the best course of treatment for a patient.

Such tests exist for tissue, but “no one’s been doing them on circulating tumor cells,” Coutts said. “So that’s where we see our niche today.”

The OncoCEE?BR assay, targeted for an October launch, would have such predictive capabilities, Coutts said, because it will test for estrogen receptor and HER2 receptor upregulation. Based on the results, a physician can then decide whether a patient would need to be put on tamoxifen or Herceptin (trastuzumab) therapy.

In addition, Biocept’s CEE technology could solve a pervasive weakness in blood?based CTC tests. Even with automated instruments, circulating tumor cells are captured in only about half of patients, “so half the samples are uninformative,” Coutts said.

Two reasons account for this, he said — the failure of existing platforms to capture them, and the failure to identify them.

The CellSearch platform is a single?antibody approach that uses magnetic ferrofluid to attach an antibody against an adhesion

protein expressed by epithelial cells. When these cells slough off, however, they transform from epithelial cells to mesenchymal cells, which have no need for adhesion molecules and down?regulate them, Coutts said.

And once the adhesion molecules drop below a certain level — about 2,000 copies per cell, according to Coutts — they escape capture by immunoassay?based capture methods, such as Veridex's CellSearch.

Biocept's CEE technology, in contrast, uses 10 antibodies against a range of antigens for both epithelial and mesenchymal cells.

"It's difficult to do [that] if you have to attach each [antibody] to a ferrofluid, but we have our soluble, and we use a secondary antibody with a biotin hook on it, and we have tethers stripped out on the silicone polymer of the channel, so it's easy for us to use a cocktail of antibodies," Coutts said.

Biocept is also attempting to make improvements in identifying CTCs by moving away from anti?cytokeratin methods. The identification of CTCs in blood samples has depended on the

presence of cytokeratin. In the epithelial?to?mesenchymal transition, cells tend to lose their cytokeratin, though, "so they can't always be identified by anti?cytokeratin," Coutts said.

Biocept has sidestepped this barrier by attaching fluors to the biotin in the 10 antibodies used in the CEE technology "so we have a way of lighting up cells that have lost their cytokeratin," he said.

In addition, they are developing a method for analyzing chromosomes. The upregulation of a certain number of specific chromosomes — for breast cancer, chromosomes 6, 8, 11, and 17 — is correlated with CTCs, Biocept has found.

The sum total of what the company is doing then, Coutts said, is "redefining what a circulating tumor cell is."

Biocept is currently validating preliminary findings in its CLIA?certified laboratory. It has validated the six FISH probes, licensed from Abbott and used in the OncoCEE?BC test to show that they localize to the centromeres of the correct chromosomes, "and that the gene probes for HER2 and for estrogen receptors localize on the right chromosome."

With that done, Biocept is comparing blood and tissue samples from the same patient to see if their FISH analysis done on blood samples correlates to analysis of the tissue sample done by an outside lab.

Biocept will be commercializing the OncoCEE?BC test as a laboratory?developed test. It is doing this alone, but the company is also developing a non?small cell lung cancer test, planned for a Q1 2011 launch, which it will introduce possibly with a commercialization partner, Coutts said. The company plans to launch a colorectal cancer test simultaneously with the NSCLC diagnostic, he added.