

BioMarker Strategies LLC

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Written By Jim Kling (Contributor)
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Summary: Targeted cancer drugs are all the rage--and with good reason--but it remains challenging to accurately predict which patients will respond to them. BioMarker Strategies LLC has developed SnapPath, an ex vivo biomarker system that disperses solid tumor tissue in media. It then exposes live cells to growth factors and other stimuli to induce them to produce phosphoproteins and other ex vivo biomarkers to reveal the functional circuitry of the patient's tumor cells.

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BioMarker Strategies LLC

Ex vivo biomarkers for solid tumors

Johns Hopkins Science + Technology Park

855 North Wolfe Street

Suite 603

Baltimore, MD 21205

Phone: (410) 522-1008

Web Site: www.biomarkerstrategies.com

Contact: Scott Allocco, President

Industry Segment: Ex vivo Biomarkers

Business: Tissue-based cancer diagnostics

Founded: May 2006

Founders: Scott Allocco; Kathleen Murphy, PhD (Johns Hopkins); Douglas P. Clark, MD (Johns Hopkins)

Employees: 8

Financing to Date: \$4.2 million

Investors: Individual investors; Abell Foundation (Baltimore)

Board of Directors: Scott Allocco; Douglas P. Clark; Kären Olson, CEO; Christy Wyskiel (formerly Maverick Capital)

Scientific Advisory Board: Scott Diamond, PhD (University of Pennsylvania); Kathleen Murphy; Douglas P. Clark

Targeted cancer drugs are all the rage--and with good reason--but it remains challenging to accurately predict which patients will respond to them. Human epidermal growth factor receptor 2 (HER2) overexpression is a classic example. It is targeted by **Genentech Inc.**'s trastuzumab (*Herceptin*) and is overexpressed in about 20% of all breast cancers, but only about half of these patients respond to *Herceptin* therapy, and sometimes only partially.

Why should this be? Receptors like HER2 exist in a much larger network of signal transduction ligands and receptors. Immunohistochemistry analyses of HER2 show only a small part of the bigger picture. Current methods of tissue preservation, little changed since they were first developed in the Civil War, kill the cells immediately after a biopsy and make it difficult to analyze for much else than DNA and RNA. Not only does this process eliminate the ability to interrogate an otherwise living cell, but the process destroys proteins and forces a reliance on static biomarkers that reveal little about the actual functioning of the signal transduction network.

It's a key concern as there are more than 600 new targeted cancer drugs being developed but few have companion biomarkers, according to Scott Allocco, who is president of **BioMarker Strategies LLC**. "We see a growing number of targeted cancer therapeutics that are about to get approved, and yet there are only a handful of biomarkers available to direct patient therapy. Nevertheless, the FDA and EMEA are starting to significantly increase biomarker requirements on drug labels, and it's only a matter of time before they transition from having recommended biomarkers to requiring them," says Allocco.

Allocco viewed the problem from his vantage point as the vice president of government affairs at the insurance company Coventry Health Care, where he managed prescription drug benefits for state Medicaid agencies. He saw the key role that targeted cancer drugs were likely to play in cancer therapy. They would be very expensive and would rely on molecular diagnostics to determine which patients should receive them, and insurance companies would depend on them to make reimbursement decisions. At the same time, Douglas P. Clark, the director of cytopathology at **Johns Hopkins University School of Medicine's** Department of Molecular Microbiology and Immunology, was frustrated by the antiquated pathology infrastructure. "He was concerned that traditional tumor processing methods were compromising the biological integrity and value of the tumor samples, which were being used by the entire drug industry to develop drugs and diagnostics," says Allocco.

So the two teamed up with Kathleen Murphy, then the director of the Hopkins Molecular Diagnostics Laboratory, to co-found BioMarker Strategies in 2006, and Allocco became the company's first full-time employee in early 2007. By the end of the first year he had raised more than \$1 million from high net worth individuals and signed a lease to become one of the first commercial companies in the Johns Hopkins Science + Technology Park.

Starting in 2007, BioMarker Strategies set about developing a technology that could take solid tumor samples from minimally invasive fine-needle aspiration biopsies and maintain them in a live state for ex vivo stimulation, then fix them for off-platform analysis. The result is the company's *SnapPath* ex vivo biomarker system, which disperses solid tumor tissue in media, and then exposes live cells to growth factors and other stimuli to induce them to produce phosphoproteins and other ex vivo biomarkers to reveal the functional circuitry of the patient's tumor cells.

Previous researchers have used manual techniques to evoke these ex vivo biomarkers from cancer patient samples, but the method can't be easily applied in a clinical setting unless it is automated, which is what *SnapPath* is designed to do, says Allocco.

It remains to be demonstrated that ex vivo stimulation of a patient's live tumor cells is a good model for in vivo tumors. Researchers at BioMarker Strategies are investigating that question, and Allocco is optimistic. "First, we're not culturing cells [which can cause changes in cells that could skew an assay], and it is impossible to evoke new biomarkers from dead cells. Our proof-of-concept experiments and a recent scientific review of ex vivo biomarkers show that this is a viable approach," he says.

Company researchers have developed an alpha unit and are using it to work with mouse xenograft and human tissue samples. The company is in discussions with researchers at Johns Hopkins Medicine and **University of Texas' MD Anderson Cancer Center** to incorporate *SnapPath* into future drug clinical trials, and BioMarker Strategies is using its sponsored research agreement at Johns Hopkins to compare *SnapPath* automated processing with the current tumor-processing method.

In 2008, Allocco recruited Kären Olson, who was a board member at the time, to become CEO. None of the co-founders had run a private company, whereas Olson had been CEO of Adhesives Research, where she helped develop a medical products division that produced a medicated dissolvable thin strip for drug delivery and other FDA-regulated products.

In September 2009, the company won a Fast-Track SBIR Phase I/II combination contract from the **National Institutes of Health's National Cancer Institute**, which will bring in up to \$2.3 million if the company completes its Phase I milestones this spring. Those funds will be used to develop the *SnapPath* platform. Under the contract, the company will develop several beta units by early 2011 that can be placed in academic medical centers and tested in clinical trials. Separately, company researchers are developing ex vivo biomarker tests that will be used with it.

After a transitional research-use-only period, they plan to commercialize the *SnapPath* technology for clinical applications with companion ex vivo diagnostics.

To date, the company has raised about \$4.2 million from angel investors and the non-profit **Abell Foundation**.

Allocco plans to implement at least one companion diagnostic development program, funded primarily by a pharmaceutical company partner. It will likely also develop some test indications independently, including its first ex vivo biomarker test for metastatic breast cancer. Initially, the company will focus on metastatic cancer because most clinical trials using targeted therapeutics are investigating advanced disease. Overall, there are about 650,000 patients in the US with solid-tumor-based metastatic cancer, Allocco says.

"We're in discussions with several oncologists about the prospects of utilizing the technology in a variety of different contexts, potentially in conjunction with drug-based clinical trials. Obviously, predictive biomarker-based tests to guide patient therapy and the ability to stratify your patient population in a clinical trial are of great interest to the pharma manufacturers," says Allocco.

When it comes to its tumor tissue acquisition and processing protocols, Allocco sees an existing technology as a model for *SnapPath*. Researchers at **Nodality Inc.** have focused on ex vivo analysis of leukemia and lymphoma, which are fluidic, single-cell cancers that can be analyzed using flow cytometry. For routine clinical characterization of lymphoma by flow cytometry following a fine-needle biopsy, samples are delivered to a flow lab along some very strict time lines. If they miss the deadline, the samples are rejected and flow cytometry is not performed. "That model, of taking a live solid-tissue-based tumor and processing it quickly in *SnapPath* is exactly what we are shooting for," says Allocco.

Other competing approaches include chemotherapy drug resistance assays (CDRAs), in which pathologists send excised live tissue samples to companies such as **Exiqon AS** and **Precision Therapeutics Inc.**, which culture and expose them to various chemotherapy drugs and predict to which regimen a patient is most likely to respond. "They're not really biomarker-based tests, though. They're more like live-tumor assays," says Allocco.

Other competitors include companies that are using the current pathology infrastructure of formalin-fixed samples, including **Genomic Health Inc.** Those products have been successful, but they remain limited by the Civil War-era technology that underpins tissue preservation.

In fact, while these methods don't preserve proteins very well, they do preserve DNA. "That probably explains why there are so many nucleic-acid-based diagnostics," says Allocco. Ex vivo biomarkers could shift that paradigm.

—Jim Kling