



Diagnostic Testing and Technology Report

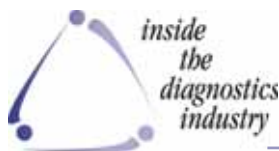
Competitive Intelligence & Analysis for an Expanding Global Market

What's Next For Correlogic?

The past 12 months have been tumultuous for Correlogic Systems (Bethesda, MD), which has developed a novel software system for analyzing blood protein patterns to detect cancer. In March, the company and its distribution partners, Quest Diagnostics and LabCorp, were notified by the FDA that their first product, an ovarian cancer test named OvaCheck, may need a premarket approval before it can be marketed for clinical use.

And now it's become public that two researchers from the National Cancer Institute (NCI) and the FDA have had consulting arrangements with a competitor, Biospect (South San Francisco), even though they were already working under a cooperative research and development agreement (CRADA) with Correlogic. Even more interesting is news that Richard Klausner, M.D., former national director of NCI, helped found Biospect shortly after resigning from NCI in September 2001 and now sits on the company's board of directors.

Peter Levine, president of Correlogic, tells DTTR that he first learned of Biospect and its ties to NCI officials in July 2003 from a colleague in the lab business. Levine says the news literally made him sick. But with a congressional investigative panel now looking into the situation, he says Correlogic has refocused its attention on bringing OvaCheck to the market.



Protein-Pattern Technology Takes Center Stage in NIH Controversy

Correlogic's protein-pattern technology must be awfully good. How else can you explain why five current and former high-ranking officials from the National Cancer Institute (NCI), a unit of the National Institutes of Health, and the FDA (see table on page 6) would risk their careers and reputations to help get a competing firm working on similar technology off the ground?

The Timeline of Events

The idea behind Correlogic and its protein-pattern technology for identifying cancer began in the late 1990s. That's when Peter Levine, a former

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government trial lawyer who had specialized in the evaluation of data patterns and the presentation of computer-generated evidence in litigation, and Ben Hitt, Ph.D., a biochemist who had served as senior principal software engineer for Raytheon Systems, crossed paths and began talking about starting a company that would capitalize on advances in pattern-recognition technology, which solves problems by searching for patterns in huge volumes of data.

In June 1999, the pair had lunch with Emanuel Petricoin, Ph.D., who was then co-director of the Clinical Proteomics Program, a new joint venture of the NCI and FDA. At this meeting, the notion of detecting cancer by looking at protein patterns rather than single biomarkers was discussed.

In May 2000, Hitt and Levine formed Correlogic and signed a research agreement with the Clinical Proteomics Program. Within 12 months, researchers at the FDA, NCI, and Correlogic had developed a system for detecting protein patterns associated with ovarian cancer. Hitt was credited as the inventor of the core algorithms that power Proteome Quest, the software that is used to create computational “models” of disease states, while the concept and process for identifying blood protein patterns associated with specific diseases was invented by Hitt, Levine, and scientists at the FDA and NCI, including Petricoin.



Emanuel Petricoin, PhD

On Feb. 16, 2002, a paper published by *The Lancet* showed that in an analysis of 116 blinded blood samples—50 from patients with cancer and 66 with non-malignant disease—Correlogic’s method was able to correctly identify all 50 cases of ovarian cancer, including all 18 Stage I cases. The single flaw in the performance was predicting ovarian cancer in three of 66 control cases. Overall, the test had a predictive value of 94% (50 of 53) vs. 35% for CA-125, the current standard for testing for ovarian cancer. The data produced in the study was a joint effort of Correlogic and the FDA/NCI Clinical Proteomics Program. Correlogic’s partners were Petricoin and Lance Liotta, M.D., Ph.D., a researcher for the NCI.



Lance Liotta, MD, PhD

After publication of the results, Petricoin stated in an FDA press release, “We’re particularly excited about the potential of this technique to diagnose additional types of diseases. It may also be able to provide an early warning of impending toxicity.”

In light of the encouraging results, in April 2002, the research agreement between Correlogic, the FDA, and the NCI was converted into a cooperative research and development agreement (CRADA), and Petricoin and Liotta were named as co-principal investigators. One of the goals of this CRADA was to develop a strategy for commercialization of protein pattern recognition tests, first for ovarian cancer.

It’s at this juncture that the relationship between Correlogic, the FDA, and the NCI started to go sour. Sometime between May and August 2002, NCI decided to unilat-

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Greenwood's subcommittee on consulting deals was prompted by a report in the *LA Times* that documented hundreds of payments, totaling millions of dollars, by drug and biotech companies to NIH scientists.

erally sponsor clinical trials on the ovarian cancer test instead of executing a clinical research CRADA with Correlogic.

On June 18, 2002, Biospect was incorporated with a mission statement—"developing technology for identifying and assaying protein biomarker patterns"—that was virtually identical to Correlogic's. Richard Klausner, M.D., is listed as a founder, a board member, and a paid consultant to Biospect. Klausner had resigned from his position as national director for the NCI on Sept. 30, 2001.

In addition, Carol Dahl, Ph.D., former director at NCI's Office of Technology and Industrial Relations, has served as vice president for strategic partnerships at Biospect. And Svetlana Shtrom, Ph.D., former technology development specialist at NCI, currently serves as director for business development at Biospect. While at NCI, Shtrom was responsible for negotiating the CRADA with Correlogic.

Finally, there's Petricoin and Liotta, who each entered into consulting contracts with Biospect in late 2002. Liotta was paid \$49,375 by Biospect between December 2002 and May 2004 for consulting services, according to records from the NIH. Payments to Petricoin have not yet been made public. Petricoin and Liotta were not available for interviews with DTTR.

The circumstances of Correlogic, Biospect, which recently renamed itself Predicant Bio-

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NCI and FDA Employees and Their Ties to Biospect		
Name	Role at NCI or FDA	Role at Biospect
Richard Klausner, M.D.	Served as director of NCI from Aug. 1, 1995 through Sept. 30, 2001	Helped found Biospect in early 2002 and is also on board of directors
Carol Dahl, Ph.D.	Former director, Office of Technology and Industrial Relations, at NCI	Served as vice president for strategic partnerships
Lance Liotta, M.D., Ph.D.	Currently chief of the Laboratory of Pathology at NCI	Worked as a paid consultant from December 2002 through May 2004
Emanuel Petricoin, Ph.D.	Currently lead microbiologist at FDA's Center for Biologics Evaluation and Research	Worked as a paid consultant from October 2002 through May 2004
Svetlana Shtrom, Ph.D.	Technology development specialist at NCI (negotiated CRADA agreement with Correlogic)	Serves as director for business development
Source: DTTR from NIH and Biospect Websites		

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Top NIH researchers can earn as much as \$300,000 in government salaries and tens of thousands more from outside consulting jobs.

sciences, and their relationships with NCI and FDA employees have now fallen under the microscope of U.S. Rep. James Greenwood (R-PA), chairman of the Energy & Commerce oversight and investigations subcommittee. Greenwood held a special hearing on May 18 to look into possible conflicts of interest between the consulting arrangements Petricoin and Liotta had with Biospect.

During the hearing, both researchers noted that their consulting agreements with Biospect had been cleared by their bosses at the NCI and FDA, although they were kept secret from Correlogic. Liotta said he saw no conflict of interest because Correlogic is developing software for protein-pattern analysis, while Biospect is developing diagnostic equipment.

Even after Correlogic found out about the consulting agreements and complained to officials at the NIH in mid-2003, the arrangements were allowed to stay intact. It was only in the days before the Greenwood hearing that Petricoin and Liotta ceased their relationships with Biospect. (Klausner was asked to testify at the May 18 hearing, but refused).

“It was obvious to others in the broad diagnostic, biotech industry that Biospect was a competitor of ours. Anyone who did even just a casual read of Biospect’s [press releases] could see that,” says Correlogic’s Levine. Executives at Biospect did not return phone calls from DTTR seeking comment.

“What company will want to enter into a CRADA with NIH if this is the way conflict-of-interest issues are managed? This isn’t transparency. This is an outrage,” said Greenwood in his opening remarks for the May 18 hearing.

“As a result of these secret deals, progress appears to have slowed on a public-private partnership that could lead to prompt commercialization of lifesaving, ovarian cancer diagnostic tests,” Joe Barton (R-TX), chairman of the House Energy and Commerce Committee, said. “Public trust has been damaged.”

The Fallout

Following the May 18 hearing, Lester Crawford, acting commissioner of the FDA issued a press release stating, “In light of recent questions about possible conflicts of

Life After the NCI

Since resigning as director for the NCI on Sept. 30, 2001, Richard Klausner, M.D., has led a busy life. In addition to helping found Biospect in early 2002, Klausner is listed as a co-founder and board member of Infinity Pharmaceuticals (Cambridge, MA), a drug discovery firm. According to Delaware’s Division of Corporations, as well as Infinity’s own Web site, Infinity was incorporated in February 2001. (Note: Rep. Greenwood is investigating Klausner’s relationship with Infinity while he was still NCI director.)



In addition, Klausner is a scientific and strategic advisor to GenPath Pharmaceuticals (Cambridge, MA), which describes itself as “a biotechnology start-up founded to discover and develop breakthrough drugs to fight cancer as well as other disorders with a genetic basis.” GenPath was founded in early 2002.

Finally, Klausner became executive director for global health of the Bill and Melinda Gates Foundation in May 2002.

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Peter Levine

interest involving HHS agencies, I have also directed a comprehensive review of all current outside activity requests from all FDA employees. Once that review has been completed, FDA will issue a final policy on the review and approval of outside activities.”

Elias Zerhouni, M.D., director of the NIH, has ordered all agency employees to report the financial details of any consulting payments received from pharmaceutical or biotech over the last five years or face dismissal. The financial information will be turned over to members of Congress.

The NIH relaxed its rules covering outside income and activities in 1995 in an effort to attract better researchers and improve its science. Now some members of the subcommittee are pushing for a complete ban on any NIH employee accepting outside consulting jobs. Speaking at the May 18 hearing, Rep. Diana DeGette (D-CO) said that unless NIH accepted a “blanket restriction on outside compensation, serious conflicts of interest and the appearance of conflicts of interest will continue.”

Greenwood intends to hold another hearing, focusing on other possible conflicts of interest in June.

What’s Next for Correlogic?

Levine says that Correlogic is trying to move past the current controversy and complete negotiations with the NCI on a clinical research CRADA for the OvaCheck test. Did Petricoin’s and Liotta’s involvement with Biospect slow down progress on bringing OvaCheck to market? “That’s difficult to assess at this point. It’s like the classic onion case. Every time a layer is peeled away, there’s another layer of information,” answers Levine.

Will Correlogic file a lawsuit against Petricoin, Liotta, the NCI, or FDA for possibly sharing trade secrets with a competitor and violating the CRADA agreement? “We have no plans to sue. The last thing we want to do is get tangled up in a lawsuit with this branch of the government. We want to normalize our relationship with the NCI and continue work on OvaCheck,” says Levine.

Levine says that he met with officials from the FDA in March to discuss whether or not a premarket review for OvaCheck would be necessary. He says that Correlogic remains in contact with the FDA, but no conclusions have been reached yet. “I can’t imagine that this issue will hang out too much longer,” he says.


Levine believes that OvaCheck should be allowed to be marketed by its distribution partners, Quest Diagnostics and LabCorp, as a laboratory-developed, or “homebrew,” test.

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The process for performing an OvaCheck test involves Quest or LabCorp obtaining a patient blood specimen at one of their patient service centers. The specimen is then shipped to either Quest's Nichols Institute (San Juan Capistrano, CA) or LabCorp's Center for Molecular Biology and Pathology (Research Triangle Park, NC), explains Levine. He says that Quest or LabCorp then does the prep work on the specimen, including mass spectrometry. This data is then sent electronically to Correlogic via T1 lines. Correlogic then runs this data through its pattern-recognition software programs and sends the results back to Quest or LabCorp, whose professionals review the results and share them with the patient's doctor.

Under an agreement signed in late 2002, Quest and LabCorp are the only two companies licensed by Correlogic to market OvaCheck. Under the terms of the agreement, Correlogic will receive signing, milestone, and per-test royalty or service fees, as well as development fees for additional refinements to the technology. Additional terms have not been disclosed. 

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