Diagnostic Testing and Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

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CONTENTS

WASHINGTON G-2 REPORTS

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★ SPECIAL SUPPLEMENT

Biomarkers Making Personalized Medicine a Reality

Molecular biomarkers—defined as specific molecular alterations of a cell on the DNA, RNA, metabolite, or protein level—are not only facilitating the progress of the much-buzzed about concept of personalized medicine but also forging new links among diagnostic and pharmaceutical companies, academe, and laboratory medicine. Biomarker-based tests can enable presymptomatic disease diagnosis, help distinguish between different phases or forms of a disease, indicate an individual's likely response to therapy, track disease progression, and monitor treatment. Despite the promise of biomarkers, their development for clinical applications remains challenging. Biomarker validation requires analysis of complex genomic information and the commitments of a variety of stakeholders, from the R&D phase to marketing and reimbursement. *Continued on p. 7*

Beginning with this issue, DTTR *is expanding its coverage of several critical areas of diagnostic testing with in-depth coverage every other month of such areas as pharmacogenomics, trends in molecular testing, and infectious disease testing. See p. 7 for our special supplement focusing on some of the most exciting biomarker-related developments and discoveries, from the promise of microRNA to new alliances among in vitro diagnostics companies, pharmaceutical companies, and academic medical centers.*

Inverness to Spend $532 Million on Health Management Businesses

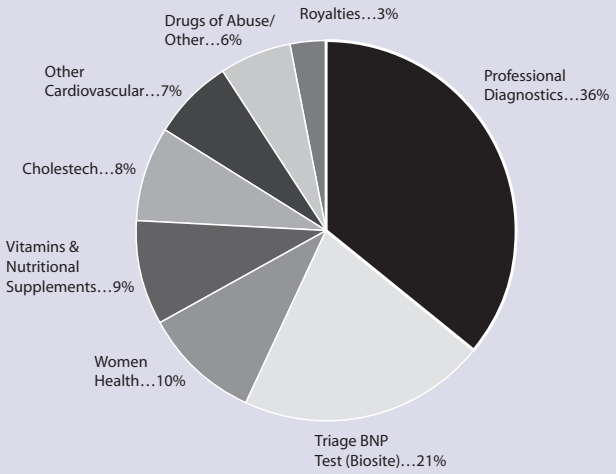
Inverness Medical Innovations (Waltham, MA) is trying to stay several steps ahead of the rapidly growing and ever-evolving point-of-care and cardiology testing markets by buying up health services businesses that focus on cardiac disease management, self-testing, and at-home monitoring services. Having spent 2007 acquiring such IVD companies as Biosite, Bio-Stat, HemoSense, and Cholestech, Inverness rounded out the year by entering into agreements to acquire two disease management companies. In late November, the company announced it would acquire ParadigmHealth (Upper Saddle River, NJ) for $230 million in cash. That deal was signed only weeks after Inverness announced that it would spend $302 million in cash and stock to buy Alere Medical (Reno, NV).

Founded in 1991, ParadigmHealth provides and integrates care and disease management services for acutely ill and "clinically complex" patients, including neonatal intensive care and oncology patients. The company earned 2007 revenues of approximately $60 million. Inverness CEO Ron Zwanziger calls the acquisition "a significant step in our strategy to become a leader in disease and health management services." *Continued on p. 2*

▲ **Inverness,** *from page 1*

Like ParadigmHealth, eleven-year-old Alere helps patients with chronic illnesses manage their conditions through a combination of at-home monitoring, patient education, and nurse-patient relationships. Alere specializes in home health management for congestive heart failure, which plays to Inverness's strength in the cardiology market (it now owns Biosite, Hemosense, and Cholestech) and its strong R&D pipeline of cardiology products. Alere's 2007 revenues are expected to exceed $77 million.

Breaking Down Revenue at Inverness*



*As of March 31, 2007, after Biosite and Cholestech mergers
Source: Inverness Medical Innovations

Inverness plans to integrate these two companies with Quality Assured Services (QAS), the Florida-based provider of home testing and health services that it purchased in June for $25 million in cash and stock. The QAS acquisition gave Inverness an established in-home patient service and distribution network, as well as a leadership position in the prescription self-testing market, especially in coagulation monitoring.

With approximately 5,000 employees, Inverness had pro forma revenues of $955 million for the fiscal year ended Sept. 30, 2007. This includes recent significant acquisitions and also reflects the impact of the company's consumer market joint venture with Procter & Gamble.

New SACGHS Report Cites Gaps in Genetic Testing Oversight

In a new draft report on genetic testing oversight, a top HHS advisory panel recommends that federal policy to help assure quality and safety include beefed-up CLIA regulations, especially proficiency testing and a go-slower approach by the FDA in regulating lab-developed tests.

The HHS Secretary's Advisory Committee on Genetics, Health & Society (SACGHS) released the draft for public comment. The panel was charged by HHS Secretary Michael Leavitt to examine trends in genetic testing technologies and clinical practice, gaps in oversight that could lead to harm for patients, and the scientific information and regulatory structures needed to ensure that tests are properly developed and used.

While the report's "overarching recommendation" emphasizes new federal/private-sector collaborations, the Committee also advises Leavitt that CMS

and the FDA need to work closer together on oversight issues and that HHS needs to improve coordination with other involved federal agencies, such as the Federal Trade Commission and research units at CDC and the National Institutes of Health.

In a statement to SACGHS, the College of American Pathologists (CAP) said any changes in federal oversight of genetic testing should be made within the CLIA program, which CAP says provides the necessary safeguards for quality and access. The College also took issue with the report's assertion that genetic testing is different from other lab work and with its definition of genetic testing, which CAP says is too broad.

The draft 192-page report is posted at www4.od.nih.gov/oba/sacghs.htm. The deadline to submit comments is December 21.

Beckman Coulter to Expand IVD, Flow Cytometry Business

In vitro diagnostics giant Beckman Coulter (Fullerton, CA) is looking to acquisitions to add novel diagnostic technology and instrumentation to its $2.5 billion business. The company recently announced that it will acquire the remaining 80.1% of NexGen Diagnostics (Southfield, MI) for approximately $36 million. Beckman has also signed an agreement to purchase the research flow cytometry instrumentation business of cancer diagnostics company Dako (Glostrup, Denmark) for an undisclosed amount. Both deals are expected to close by the end of 2007.

The NexGen deal would give Beckman access to proprietary technologies that can simplify, automate, and expedite high-sensitivity testing, including immunoassay-based and nucleic acid-based diagnostics. NexGen was created as a spin-off of Lumigen, a company acquired by Beckman last year for $136 million.

The acquisition of Dako's Colorado-based research flow cytometry business would bolster Beckman's instrument portfolio in this area, gaining the gold standard cell sorter, Dako's MoFlo XDP high-performance instrument. The business has approximately 200 employees in sales, marketing, research, manufacturing, and administration. Flow cytometry is used to analyze cells in blood and other fluids for both research applications and the diagnosis of diseases such as leukemia, lymphoma, and HIV.

Gene-Based Assay Useful for Diagnosing Tuberculosis

A new T-cell-based assay is a useful adjunct test for diagnosing extrapulmonary tuberculosis (E-TB), according to a study published in the November 12 issue of the *Archives of Internal Medicine*. The test, an enzyme-linked immunospot (ELISPOT) assay known as T-SPOT.*TB* and manufactured by Oxford Immunotech (Abingdon, England), detects CD4+ T-cells that are produced in response to TB bacteria.

In the study, a team of researchers from Korea's Seoul National University evaluated the performance of T-SPOT.*TB* relative to the tuberculin skin test (TST) in

hospital patients with suspected E-TB. Approximately half of the patients enrolled also had immunosuppressive conditions, which can confound TST results. Of the 72 patients, 32 (44%) were independently classified as having E-TB, including 22 with confirmed tuberculosis and 10 with probable tuberculosis, and 35 (49%) were classified as not having tuberculosis. The remaining five (7%) had possible tuberculosis and were excluded from the final analysis.

The worldwide market for TB diagnostics totaled $900 million in 2006, with the diagnosis of latent TB infection in industrialized countries accounting for approximately $240 million.

Chronic caseating granulomas, acid-fast bacilli stain, M tuberculosis polymerase chain reaction (PCR), and cultures for M tuberculosis were positive in 22 (69%), 5 (16%), 15 (47%), and 18 (56%), respectively, of the 32 patients that were classified as having E-TB. The sensitivity and specificity of the TST were 47% and 86%, respectively. By comparison, the sensitivity and specificity of the ELISPOT assay were 94% and 88%, respectively.

Licensed across Europe in 2004, T-SPOT.*TB* is a *Mycobacterium tuberculosis*-specific region of difference 1 gene-based assay. It was developed by Oxford Immunotech to diagnose both latent TB infection and TB disease in humans. The test can be particularly useful in cases where the TST gives poor or indeterminate results, such as in immunocompromised populations or in those who have had the Bacille Calmette Guerin (BCG) anti-TB vaccination.

Founded in 2002 as a spin-off of Oxford University, Oxford Immunotech calls itself an "international T cell measurement company." The company's CEO is Peter Wrighton-Smith, Ph.D., who co-founded the company after having spent five years at PowderJect Pharmaceuticals, which is now part of Chiron Corporation.

In October of last year, Oxford Immunotech closed on its third round of financing, raising $40 million from a group led by Clarus Ventures and Wellington Partners. The company plans to use the funding to prepare for the launch of T-SPOT.*TB* in the United States. The test is already marketed directly and via distributors in Europe, Canada, and 40 other countries worldwide.

Quest Readies India Lab for Esoteric Testing

Quest Diagnostics (Madison, NJ) will soon open a laboratory in the New Delhi region of India. Set for completion by mid-2008, the facility will mainly perform esoteric testing, as well as clinical trials testing for pharmaceutical companies. According to president and CEO Surya N. Mohapatra, Quest is eager to launch operations in developing—rather than developed—countries. "The pharmaceutical companies are going to India and they need a lab…and then there is our diagnostic business," he said at a recent investment conference.

Company spokesperson Barb X. Short called Quest's India venture a growth opportunity to serve the Indian market rather than a way to outsource laboratory testing that would otherwise be performed in the United States. She also pointed to a growing demand for some of Quest's higher-value esoteric or highly specialized testing, including cancer diagnostics and infectious disease testing.

Automated Test Results Systems Boost Patient Satisfaction

Communication of diagnostic test results is integral to successful clinical outcomes, and that communication goes beyond the laboratory relaying results to clinicians. Failure to communicate test results and follow-up plans to patients is becoming an increasingly significant threat to patient safety (and a malpractice concern).

A number of recent studies have linked poor results communication with treatment delays and missed follow-up opportunities, and a 2005 Applied Strategies for Improving Patient Safety study noted that patient inquiry concerning test results is often "the final safety net for locating lost results." A new study, published in the November 12, 2007 issue of the *Archives of Internal Medicine*, suggests that the use of an automated test results management system can improve patient satisfaction with both communication of test results ordered by their primary care provider and communication of information regarding their condition and treatment plans.

Test Result Communication and Patient Satisfaction

In the 2007 *Archives of Internal Medicine* study, researchers from Harvard Medical School and New York-Presbyterian Hospital evaluated the impact on patient satisfaction of Results Manager (RM), an automated test result notification system that was imbedded in a browser-based electronic health record (EHR) already in use. They conducted a prospective, cluster-randomized controlled trial of 570 patient encounters in 26 outpatient primary care practices and conducted follow-up patient satisfaction surveys. Patients eligible for the study were those who had a chemistry, hematology, pathology, radiology, or microbiology test ordered by their primary care physician during the test period.

According to the study, the RM provides tracking of all test results associated with an ordering physician and additional tools, such as letter and documentation templates. A continuously updated summary page provides concise information for each patient, including the reference visit date, patient name and medical record number, the test result type, and whether the test result was abnormal or critical. Many of the RM's features were among those that clinicians ranked most desirable in a previous study of test result management system usage.

Half of the clinical encounters studied used the RM, which included patient notification functions. After adjusting for such variables as age, socioeconomic

Fast Facts on Electronic Results and Records Management

- A 2006 Commonwealth Fund survey found that 22% of primary care physicians had remote access to EHRs, 12% had the capability to share records with clinicians outside their practice, and only 10% had the ability to provide their patients access to EHRs.
- Approximately 48% of primary care physicians routinely use electronic technology to access patients' test results, 22% use it to order tests, and 20% use it to prescribe medication.
- In a Washington G-2 Reports survey of 170 laboratory directors, 27% pointed to Web connectivity systems for ordering and results reporting as the key advantage that the two big commercial laboratories have over their local lab competitors.

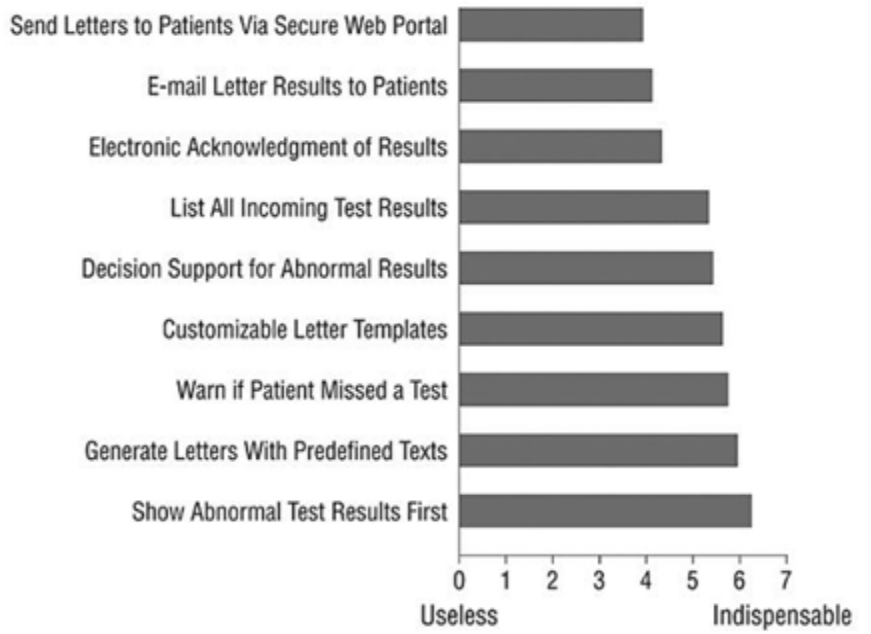
status, and insurance type, the use of the RM was found to significantly increase patient satisfaction with test results communication, and patients in the experimental group were more satisfied with information given to them for medical treatments and conditions regarding their results.

In discussing the limitations of the study, the researchers note that the generalizability of the findings is limited by the tool's development in a custom-built EHR, but add that commercial EHR vendors are quick to adopt new functionalities. They also note the need for further study on the impact of test result communication tools for non-English-speaking patients, as this study was limited to English-speaking patients within the practices studied.

Patient Preferences and Barriers to Efficient Communication

Finally, how do patients prefer to learn of test results, and for which tests? A number of studies have investigated patient preferences for laboratory test results notification. A 2000 *American Journal of Managed Care* study found that the majority (94%) of the 49 patients surveyed preferred to receive notification of normal test results as well as abnormal results. Most preferred to be notified by mail (59%), phone (16%), or during an office visit (12%). Other studies have found that patient preferences vary based on the type of test results, reporting that patients prefer to be notified by telephone for breast biopsy results, and wish to receive timely, detailed, written notification of normal Pap smear results.

Desirability of Features in an Electronic Results Management System



Source: Poon, E. G. et al. *Archives of Internal Medicine* 2004;164:2223-2228.

However, a number of barriers impede efficient communication of test results to patients. These include the inconsistency of results reporting practices among physicians, the varying expectations of patients about test result communication, and the failure of most physicians to discuss their preferences for result communication with patients. Anxiety about data security has also made many physicians reticent to adopt electronic methods to notify patients of test results.

The Next Big Thing: miRNA Biomarker Tests

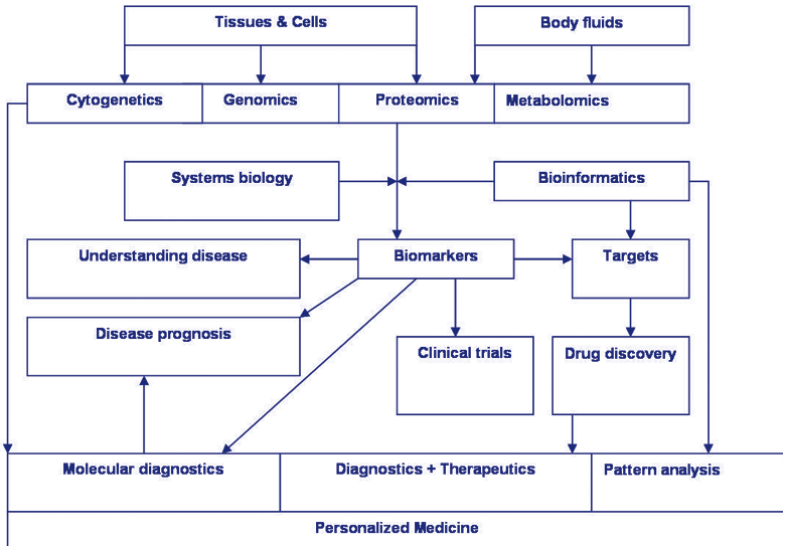
For the past few years, "personalized medicine" has been the buzzword of the in vitro diagnostics industry. As that trend becomes a reality, it is clear that the popular term encompasses a broad, developing area of clinical practice that promises to enable more specific diagnosis, provide insight into prognosis, help predict treatment response, and aid in disease monitoring. Although it remains to be seen how—or whether—the IVD, pharmaceutical, laboratory, and academic worlds will come together around this new paradigm of testing and treatment, one particular area of personalized medicine is already cementing cross-sector collaborations: microRNA (miRNA)-based diagnostics and therapeutics.

A fairly recent discovery (the first published description of miRNA appeared in 1993), miRNAs are naturally occurring small RNAs that could potentially be used to selectively regulate protein activity, including the abnormal protein activity that causes many diseases. It has also been demonstrated that miRNAs are expressed at different levels in certain diseased versus normal tissues, suggesting a novel diagnostic strategy for many diseases.

"MicroRNAs perform their regulatory function on key cellular processes further upstream than other currently used biomarkers," explains Riccardo Dalla-Favera, M.D., professor of pathology and director of the Institute for Cancer Genetics and the Herbert Irving Comprehensive Cancer Center at Columbia University Medical Center. "This is most likely the reason why they are proving to be such good biomarkers."

Exiqon (Vedbaek, Denmark), the newly public biotechnology company known for its proprietary Locked Nucleic Acids (LNA) technology for miRNA analysis, has announced that it will enter the molecular diagnostics market with a focus on miRNA biomarker-based pharmacogenomic tests for cancer patients. The catalyst for the move into diagnostics is the company's November 2007 agreement to acquire Oncotech (Tustin, CA) in an all-stock deal valued at approximately $45 million. The deal is expected to close this month.

Personalized Medicine and Biomarker Development



Source: Jain PharmaBiotech

A specialized cancer testing laboratory and molecular diagnostics company, Oncotech develops and markets diagnostic tests to optimize the treatment selection for cancer patients. The company's Extreme Drug Resistance (EDR) solid tumor assay is the leading cell-based product to identify drug resistance for cancer patients and has an 80% market share in the United States. The company currently provides molecular oncology testing services to over 7,000 physicians and approximately 1,200 hospitals. In addition to its clinical laboratory division, Oncotech offers integrated drug development services to help pharmaceutical companies conduct smaller, faster, and more cost-effective clinical trials.

What's So Special About Biomarkers?

- ❑ Specifically and sensitively reflect a disease state
- ❑ Could be used for diagnosis
- ❑ Potential to predict drug response
- ❑ Could be used to monitor disease progression and therapy
- ❑ Can be used as drug target in drug development
- ❑ Can serve as surrogate endpoint in clinical trials
- ❑ Might serve to integrate diagnostics and therapeutics

Exiqon has great ambitions for integrating the Oncotech business and says that it will work to leverage the company's expertise in oncology and treatment selection as well as its tumor bank and CLIA-certified California laboratory. Within a year of the transaction's close, Exiqon plans to launch its first molecular diagnostic test based on miRNA biomarkers. The company also reports that Oncotech will serve as the vehicle to market future molecular diagnostic products developed by the combined company.

Meanwhile, seven-year-old Rosetta Genomics (Rehovot, Israel), a leader in miRNA research and development, announced in December that it will collaborate with Columbia University Medical Center (New York, NY) to develop miRNA-based tests for the diagnosis, early detection, and prognosis of three types of non-Hodgkin lymphoma (NHL): diffuse large cell lymphoma, transformed follicular lymphoma, and chronic lymphocytic leukemia. In addition to screening for potential miRNA biomarkers, the collaboration will seek to identify miRNA drug targets for NHL.

"Forty percent of diffuse large cell lymphoma patients respond well to current therapies and have prolonged survival, whereas the remainder succumb to the disease, and we do not know why," says Dalia Cohen, global head of R&D at Rosetta Genomics. "We believe our technology will help answer this question, as well as speed up and simplify the diagnostic process."

Celera and Ipsen to Develop Biomarker Tests for Growth Failure

Celera (Alameda, CA), the diagnostics business of Applera Corporation, will collaborate with specialty pharmaceutical company Ipsen (Paris, France) to develop biomarker and pharmacogenomic tests for growth failure patients. Ipsen hopes to use the resulting tests as companion diagnostics that will help clinicians to optimize use of the company's hormone replacement medicines for the treatment of short stature.

The collaboration will initially focus on the discovery and characterization of genetic markers relating to growth failure. If that phase is successful, Celera will go on to develop diagnostic predictors for use in Ipsen's clinical trials and as potential commercial companion diagnostics for Ipsen short stature therapies. Financial terms of the deal were not disclosed, but Ipsen will pay Celera an upfront fee for the initial phase of the multi-year project with future payments determined by the success of the initial phase.

Celera has experience in biomarker discovery for a range of conditions. In 2007, researchers from the company developed a genetic risk score (GRS) that can predict risk for coronary heart disease based on five gene variants. After adjusting for traditional risk factors, individuals with a high-risk GRS had a 57% increased risk of incident coronary heart disease, which is similar to the magnitude of disease risk associated with smoking, hypertension, hypercholesterolemia, or obesity.

Veripath Builds From Breast Cancer Biomarkers

Veripath OncoDiagnostics, part of the pathology department at the University of Texas Southwestern Medical Center (Dallas, Texas), has always been ahead of its time. The reference laboratory's leadership saw the clinical promise of biomarkers early in their development and recognized that the future of cancer testing would be personalized. Today, the Southwestern Medical Center laboratory, spread out over several University of Texas campuses as well as two university hospitals, offers flow cytometry, molecular diagnostics, and cytogenetics. Veripath, now over a decade old, focuses primarily on onco-molecular testing of solid tissue samples.

"We had a vision that at some point the cancer-associated testing was going to go separate ways and become more individualized."

"The evolution of the laboratory came about because in the early 1990s people were beginning to test biomarkers for breast cancer, the routine estrogen/progesterone type of testing," says Raheela Ashfaq, M.D., director of Veripath and a professor of pathology at the University of Texas Southwestern Medical Center. "At that time, there wasn't a great deal of standardization. These cancer markers were being done using old technology, but new methodologies were coming in and a lot of the testing was going to a reference laboratory. We had a vision that at some point the cancer-associated testing was going to go separate ways and become more individualized."

However, Ashfaq knew that individualized testing would require greater standardization. "We wanted to have a laboratory that focused on cancer diagnostics," she says. "The focus of this lab would be prognostication and predictive markers for tumors and all of the targeted therapies. We wanted to have a platform in our medical center where, as new technology evolved and as new biomarkers evolved, we would be able to bring those markers for our cancer patients into this lab and provide a springboard for that kind of testing."

The University of Texas has a deserved reputation for excellence in basic science research, with four Nobel Laureates on campus. According to Ashfaq, "We wanted this really as a platform for translating some of the basic science data into more clinically applicable tests that we could bring to our patients."

The Veripath OncoDiagnostics part of the reference laboratory performs between 8,000 and 10,000 tests annually. The most common tests are associated with breast cancer testing: ER/PR, HER2, and p53. The laboratory also works with other cancer types, such as colon cancer, and with DNA-mismatched genes. "I am anatomic pathology trained, and my major interest has been tumor and tissue pathology. Most of the lymphomas and leukemias are handled by flow cytometry. We really wanted to focus on tests that could be performed on tissues and also with commonly available techniques like immunohistochemistry."

Veripath does not perform human papilloma virus (HPV) testing. "For me, that is more a risk-association marker rather than cancer-associated," says Ashfaq. "We are really dealing with patients who have been diagnosed with cancer and then we're testing the

biomarkers. This is best for the doctor to use to determine management strategies, risk of recurrence, and so forth. That's the type of analysis we do in our lab." HPV testing is handled by other areas of Southwestern's laboratory.

Like many who work with biomarkers and molecular testing, Ashfaq thinks that reimbursement is a major concern. "These are expensive technologies, and sometimes the reimbursement lacks and is not at the level of the testing because the kits are specialized," she says. "The reagents are expensive, and the overall costs for some of these tests are very high. As a result, the lab space faces increasing pressure."

New Genetic Biomarker Linked to Aggressive Prostate Cancer

A single nucleotide polymorphism (SNP) in the DAB2IP gene is associated with the risk of aggressive prostate cancer, according to results from two genome-wide association studies published in the December 11 online edition of the *Journal of the National Cancer Institute*. The biomarker finding, which could prove useful in both screening and treatment for prostate cancer, was a joint discovery by research teams from the Translational Genomics Research Institute (TGen), Wake Forest University School of Medicine, the Karolinska Institute, and Johns Hopkins Medical Institutions.

The researchers screened DNA samples from 498 Swedish men with advanced prostate cancer and 494 age-matched controls. From the whole-genome screening, the team focused on 60,275 SNPs that were previously evaluated by a National Cancer Institute study. From that group of 60,275 SNPs, they identified seven SNPs that appeared to be linked to disease aggressiveness.

Subsequent screenings of both African and European Americans included 1,242 men with advanced prostate cancer and 917 controls. These studies found that one particular SNP located on chromosome 9q33 was statistically associated with the risk of aggressive prostate cancer after adjusting for multiple testing. The SNP was found to map to the DAB2IP gene, which is thought to be involved in tumor suppression, suggesting that this protective mechanism goes awry in men with the variant form.

"Because there is no way to tell whether a person has or will have the aggressive version versus the mild version of prostate cancer, both forms are treated the same—with radiotherapy or surgery to remove the prostate gland," notes John Carpten, Ph.D., director of TGen's division of integrated cancer genomics and senior author of the paper. "The identification of this genetic variant could lead to better risk assessment for aggressive disease, providing doctors with more information on how to best treat men who may be diagnosed with prostate cancer."

In an accompanying editorial, Jer-Tsong Hsieh, Ph.D., and colleagues note that criteria for defining aggressive prostate cancer should have been consistent among different study groups, considering that there is no consensus for defining "aggressive" forms of the disease. They also note that the combined screening data suggests that the SNP is also associated with a moderately increased risk of nonaggressive prostate cancer and the strength of the SNP's association with cancer may differ based upon ethnic groups.

Jianfeng Xu, M.D., Dr.PH, a senior author of the paper and a professor of epidemiology and cancer biology at Wake Forest University School of Medicine notes that the team's finding could lead to a blood test to gauge prostate disease type so that physicians could make better informed treatment decisions.

New Point-of-Care Chlamydia Test Promises Simple, Rapid Alternative to Molecular Test

Chlamydia is the most prevalent sexually transmitted bacterial infection worldwide.

Molecular testing for chlamydia, the most prevalent sexually transmitted bacterial infection, is more sensitive and specific than currently available rapid tests. However, nucleic acid amplification tests are relatively expensive, and their turnaround time (one to two weeks) precludes immediate instigation of treatment and notification of partners. A new rapid test for chlamydia developed by researchers at the University of Cambridge (Cambridge, England) can achieve a high level of sensitivity and specificity in women with the use of noninvasive vaginal swab specimens, according to a study published in the December 8 issue of *BMJ*. The test could offer a cost-effective alternative to molecular testing for chlamydia.

The Chlamydia Rapid Test (CRT), which is Conformité Européenne (CE)-licensed, is an immunoassay-based test that detects chlamydial lipopolysaccharide. Results are available within approximately 30 minutes. A team of researchers from the United Kingdom evaluated the test's performance as a potential tool for diagnosis and screening in a study of 1,349 women at three evaluation sites. They compared the CRT's sensitivity, specificity, positive predictive value, and negative predictive value versus those of polymerase chain reaction (PCR) and strand displacement amplification assays (SDA), as well as the correlation between the CRT visual signal and organism load and acceptability to participants of self-collected vaginal swabs as a specimen type for chlamydia testing.

Compared with PCR, the resolved sensitivity, specificity, positive predictive value, and negative predictive value of the CRT were 83.5%, 98.9%, 86.7%, and 98.6%, respectively. Compared with SDA, sensitivity and specificity of the CRT were 81.6% and 98.3%. The organism load of self-collected vaginal swabs was found to correlate well with the CRT's visual signal, and most (95.9%) surveyed participants felt comfortable about collecting their own swabs.

The study's results are encouraging. The CRT's 83.5% sensitivity versus PCR significantly exceeds that of Inverness Medical's Clearview Chlamydia MF test. A recent World Health Organization study found that test to have 32.8% sensitivity versus PCR when used with vaginal swabs.

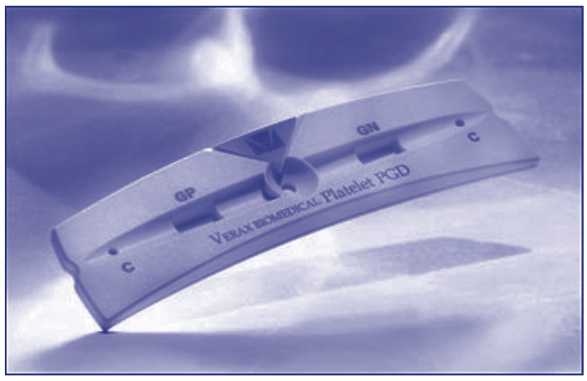
In the *BMJ* paper, the researchers note the need for randomized controlled trials to examine the effectiveness of both opportunistic and proactive chlamydia screening strategies that use both the CRT and nucleic amplification tests in order to determine the most appropriate and cost-effective approaches for the use of these tests in different clinical settings. They also note that chlamydia infections in patients with low organism loads may elude detection with the CRT.

Abbott Launches Rapid Bacteria Test

Abbott (Abbott Park, IL) has launched a single-use, rapid qualitative immunoassay that detects bacteria in human platelets for the United States market. The Verax Platelet Pan Genera Detection (PGD) test is designed to detect bacterial

contamination in platelets before a blood transfusion. Per its 2006 agreement with Verax (Worcester, MA), Abbott has exclusive worldwide rights to distribute the test. The U.S. Food and Drug Administration (FDA) granted Verax 510(k) clearance for the Platelet PGD test system in September of 2007.

The Platelet PGD test is FDA-cleared to detect aerobic and anaerobic Gram-positive and Gram-negative bacteria in leukocyte reduced apheresis platelets (LRAP) as an adjunct quality-control test following testing with a bacterial detection device cleared by the FDA for quality control testing of LRAP. The test is not intended to be used in determining whether leukocyte-reduced platelets may be released for transfusion.



Verax's Platelet PGD test

The test consists of a disposable plastic cartridge that can be stored at room temperature and three dropper bottle sample pretreatment reagents. After pretreating a freshly collected 500uL platelet sample, it is applied to the sample well. Within approximately 20 minutes, a pink-colored bar appears in one of two reading windows on the cartridge if either Gram-positive or Gram-negative bacteria are detected in the sample above the assay's cutoff level. Controls at each end of the cartridge change from yellow to blue violet when the test is ready to be interpreted, allowing visual confirmation that the appropriate sample volume was added to the cartridge and that the test is complete.

The test offers a more rapid turnaround time than culture testing methods, which can take up to three days to produce results. The Verax test, which is designed to target antigens found on all species of bacteria known to be pathogenic to humans, provides results in less than 30 minutes. The test will be priced at under $100, an Abbott representative tells *DTTR*.

Quality Control Leads to New Revenue Stream for Sacred Heart Molecular Lab

The eight-year-old molecular diagnostic laboratory at Sacred Heart Medical Center & Children's Hospital (Spokane, Washington) is realizing the potential of the $4.1 billion market for molecular diagnostic testing. In 2006, the molecular diagnostics lab billed out over $7 million in testing, reporting out close to 24,000 test results. The lab expects to top 28,000 results for 2007. Meanwhile, researchers at the lab have uncovered another unexpected revenue stream—the sale of synthetic molecular controls for confirmation of cystic fibrosis (CF) testing.

Since the laboratory began producing and marketing these controls in 2005, annual revenues have grown from $75,000 to $150,000 in 2006. In 2007, the lab expects to take in close to $200,000 in revenue from the controls, with a net margin of 15% to 20% for the hospital.

Filling a Need

The Sacred Heart molecular diagnostic lab was forced to design and produce these controls because they were unsatisfied with what was available to them to ensure their CF testing was efficient and of high quality. "We saw the need for a control that would be comprehensive in terms of our CF testing," says Marcy L. Hoffmann, Ph.D., technical director of Sacred Heart's molecular diagnostic laboratory. "But as we put together our own CF test and quality-control program, we saw that what was available in terms of quality control was not meeting the mark. So we set about designing synthetic controls with the sole intent and purpose of putting together control materials for our internal purpose."

While the initial intent of producing these controls was for the Sacred Heart lab, other labs wanted to buy the controls. The research and development of these materials also led to peer-reviewed articles, as well as presentations at several scientific meetings.

The front-end investment in research and development came mostly from money saved from purchasing reagents, explains Todd Christensen, a medical technologist and one of the lead researchers and developers of the control material. "For instance, over a period of a year, this would save us around $60,000 to $70,000 in purchasing reagents," he says. "We put these dollars that were going toward reagents into research and development, and once the controls started to sell, any revenue went back, returning that investment." Given that the revenues were $75,000 in 2005, the initial investment was recouped rather quickly.

A Win-Win Situation

From the standpoint of the hospital, these controls are an important product line because they have improved the quality of the CF testing internally, as well as introduced a comprehensive product into the marketplace that is not available anywhere else, says Gerald Fischer, a Sacred Heart vice president.

"It's kicked up the quality of our testing done in that department on those specific tests," he explains. "This is money we're not spending someplace else, and we have created a very good customer list. People have tried the product and liked it in their operations, and it does generate profitable income."

The success of the CF testing controls product reflects the growth of the Sacred Heart molecular diagnostic lab. Sacred Heart's clinical laboratories are affiliated with Pathology Associates Medical Laboratories (PAML). Both Sacred Heart and PAML are owned by the Spokane-based Providence Health Care, a network of hospitals and agencies in eastern Washington state.

Over 50% of the testing performed in the clinical laboratories at Sacred Heart is esoteric testing for PAML, according to Fischer. "That's really how departments like our molecular diagnostics and cytogenetics have grown," he adds. "Over 90% of the molecular volume is from outside of Sacred Heart medical center—very little has to do with our inpatient testing."

By subcontracting with PAML, Sacred Heart provides a more comprehensive menu of tests and gives PAML a lot more control over the way testing is done

than if it was sent out to another reference lab. "For us, we simply bill PAML on a monthly basis for the testing that is done," says Fischer. "Overall for Providence Health Care, it's an important component of being a comprehensive laboratory."

Rapid Growth and Value-Based Marketing

The Sacred Heart molecular diagnostics lab began with an operating budget of $212,763, although the expenses came in under budget at $143,168. These expenses included salaries for two full-time equivalent (FTE) personnel, reagents, lab supplies, office supplies, and instrument maintenance. The lab has since grown significantly. "In 1999, we billed out $118,175, whereas in 2006, our billables were greater than $7.7 million," says Hoffman. The lab now employs 14 FTEs.

Among the drivers of growth is Sacred Heart's marketing efforts. "Our marketing team has had a couple of successful marketing initiatives with regard to molecular testing," says Hoffman. "Cystic fibrosis is one of those. The PAML marketing team decided to make it a formal marketing initiative, and we then saw dramatic growth with more involvement by making our clients aware that we were marketing this test."

But it can be a challenge to communicate to marketing staff the value of building initiatives around tests. In the case of CF, the value was apparent because the test became the standard of care through national testing guidelines. However, the molecular diagnostics lab now wants to push their menu of genetic tests through marketing initiatives, and they are also currently launching a molecular oncology test menu. According to Hoffman, conveying the value of some of the tests to the marketing staff is largely a matter of education. "We have to get the marketing agenda in alignment with the technical agenda," she adds. "We need to make [the marketing staff] aware that we have an important service to offer and that we've barely even scratched the surface in terms of possibilities."

Advice for Those New to Molecular Diagnostics

For those laboratories new to molecular testing, Hoffman recommends beginning with high-volume tests, such as infectious disease testing for hepatitis C, gonorrhea, and human papilloma virus. "Look for the really high-volume tests that will give you the biggest bang for the buck," she explains. While new tests are constantly entering the market, there are well-established tests with FDA-approved instruments and reagents that are ideal for use in labs with no molecular experience. These tests require little background knowledge and are easy to troubleshoot.

Hoffman also advises not jumping right into genetic testing, which she describes as "a little tricky in that you need more expertise in terms of personnel." For example, even though there are FDA-approved assays for CF testing, the results require highly skilled interpretation. "That test is tricky in that the genetics are not straightforward and in many instances you really need to have access to somebody who is trained in clinical genetics to be able to offer some insight and valuable interpretation of tests results," she says.

IVD Stocks Fall 3%; Nanogen Drops 20%

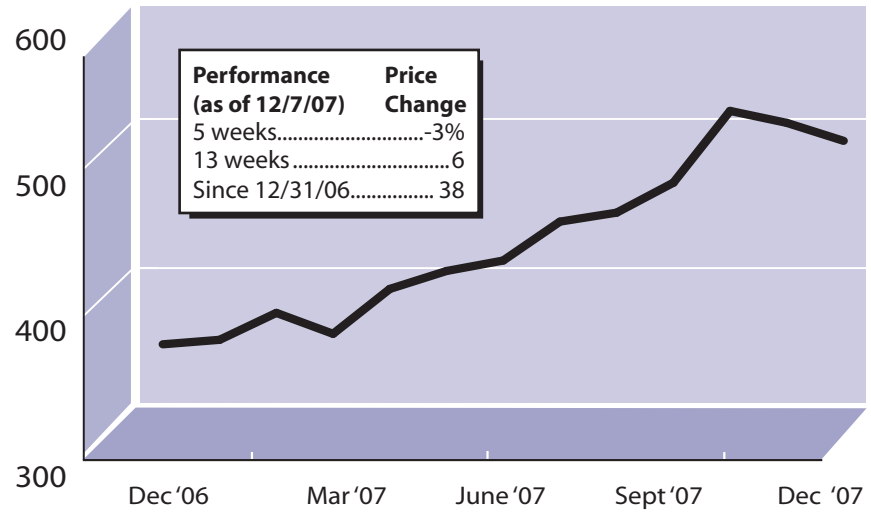
The 19 stocks in the G-2 Diagnostic Stock Index fell an average of 3% in the five weeks ended December 7, with 9 stocks down in price, nine up, and one unchanged. The index has gained 38% in 2007, compared to the Nasdaq, which is up 12% for the year, and the S&P 500, which has gained 6%.

Big changes at **Nanogen** (San Diego, CA) sent the stock plummeting 20% to $0.60 per share for a market capitalization of $38 million. The company recently announced that it will exit the rapidly growing yet highly competitive microarray market. With the goal of achieving profitability after registering a $7.5 million loss in the third quarter of 2007, Nanogen will scrap its microarray business to focus on polymerase chain reaction and point-of-care testing.

"The acquisitions we have made in the past three years have given us a good foothold in both the molecular diagnostics labs and the point-of-care rapid testing market," said Nanogen CEO Howard Birndorf. "We believe the long-term growth prospects for both of these product areas will drive significant future value for the company." According to Nanogen President and Chief Operating Officer David Ludvigson, dropping the microarray business will only minimally impact revenues while reducing operating expenditures by $15 million.

Inverness Medical Innovations (Waltham, MA) fell 9% to $58.65 per share for a market capitalization of $1.67 billion. The company continues its acquisition spree (see p. 1). On December 13, Inverness announced that it had finalized its $36 million acquisition of **Matritech** (Newton, MA), a developer of proteomics-based diagnostic products for the early detection of cancer. Inverness has also agreed to pay Matritech up to $2 million of incremental consideration, in cash and/or stock, based upon the achievement of certain revenue targets over the next year. Inverness and Matritech have worked together since 2006, when they began collaborating on the manufacture and distribution of Matritech's NMP22 BladderChek test.

G-2 Diagnostic Stock Index



Source: The G-2 Diagnostic Stock Index is tabulated weekly by *DTTR* from the average percentage change in the stock price of 19 IVD companies.

UP	PRICE	% CHG
Abbott Labs	$58.22	8%
Abaxis	34.71	18
Beckman Coulter	70.71	1
Bio-Rad	103.77	12
Immucor	32.31	1
Johnson & Johnson	67.68	4
Luminex	16.18	3
Third Wave	9.13	3
Ventana	89.15	4
UNCHANGED		
Becton Dickinson	82.40	0
DOWN		
Affymetrix	21.50	-13
Clinical Data	24.60	-9
Gen-Probe	64.10	-6
Inverness Medical	58.65	-9
Meridian	31.65	-2
Nanogen	0.60	-20
Nanosphere	12.47	-33
OraSure	9.01	-3
Quidel	18.65	-5

G-2 Insider

Roche continues its quest for Ventana . . . On December 6, Roche (Basel, Switzerland) pledged to launch a proxy fight in its campaign to acquire Ventana Medical Systems (Tucson, AZ), which makes systems for automating immunohistochemistry- and in situ hybridization-based analysis of cells and tissues. Roche has publicly pursued Ventana since June of 2007, when it announced its $75 per share hostile bid for the company, a 44% premium to Ventana's closing price on the day before the offer. Roche also tried to woo Ventana privately in the months before the hostile bid, which expires January 17.

Ventana has rebuffed Roche, calling the $75 per share offer "grossly inadequate and not an appropriate starting point for negotiations" and unsuccessfully attempting to head off the takeover bid in court. However, last November, the company allowed Roche to begin due diligence and gain access to nonpublic information. Meanwhile, Ventana has left the door open for a better offer. Other suitors, including Siemens and GE, are believed to also be in the hunt.

Why is Roche so intent on getting its hands on Ventana? One aspect is the company's test kits, including that for HER2, the genetic mutation that is associated with approximately a quarter of all breast cancers. Roche, which sells the breast cancer drug Herceptin (used to treat HER2-positive patients), is eager to bolster its position in companion diagnostics, and Ventana would bring the company not only reagents but also a sizable instrument (or "box") business.

If Ventana continues to reject its $75-per-share offer, Roche will try to replace the company's board with its own candidates at the June shareholder meeting. In addition to installing its own candidates (which include former Oxford GlycoSciences CEO Michael Kranda) in the four seats up for election, Roche plans to call for Ventana shareholders to remove the remaining six directors and replace them with three Roche-backed candidates.

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Abbott 847-937-6100

Beckman Coulter
714-871-4848

Celera 240-453-3000

Dako 45-44-85-95-00

Exiqon 45-45-66-08-88

Inverness 781-647-3900

Nanogen 858-587-1121

Oxford Immunotech
44-1235-442780

Quest Diagnostics
201-393-5000

Roche 41-61-688-1111

Rosetta Genomics
972-8-948-4755

SACGHS 301-496-9838

Sacred Heart Medical Center
509-474-3131

Ventana Medical Systems
520-887-2155

Verax Biomedical
508-755-7029

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