G2 INTELLIGENCE

Diagnostic Testing &Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

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Molecular Diagnostics Market Growing at 15% Per Year

The molecular diagnostics market is growing at about 15 percent a year and is expected to reach $7 billion in 2011, estimates G2 Intelligence. This compares to a growth rate of about 5 percent to 6 percent for the lab industry as a whole, according to Stephanie Murg, managing director of G2 Intelligence, who gave an overview of the MDx market during G2's annual molecular diagnostics conference, held in Boston April 13-15.

Although molecular diagnostics tests are rapidly becoming the standard of care in diagnosing many illness and conditions, they still are offered by only a fraction of clinical laboratories, Murg noted. In part, this is because of numerous challenges facing the MDx market, including reimbursement issues, lack of standardization across platforms, quality-control concerns, high expectations for accuracy, the inability to fully interpret test data, clinical utility, increasing cost-management pressures, lack of personnel and expertise, the need for technologies that make MDx easier to automate and less expensive, smaller markets, and more complex targets.

More established health care players, such as GE Healthcare and Novartis, are now entering the MDx market through acquisitions and they, too, face challenges of oversight, pricing, and value. For more on challenges and opportunities in the molecular diagnostics market, see the special focus section starting on p. 8.

Gen-Probe on the Auction Block; Possible Buyers Include J&J, GE, Abbott Labs

Molecular diagnostic testing company Gen-Probe (San Diego) reportedly is searching for a buyer. According to Bloomberg, Gen-Probe has hired investment bank Morgan Stanley to facilitate the sale of the company, which generated profits of more than $100 million last year. While Gen-Probe will not comment on the possible acquisition, analysts say they are not surprised.

Gen-Probe has strong market dominance in sexually transmitted disease screening, with roughly 50 percent of the global market, and in donated-blood testing, for which the company estimates it processes nearly 60 percent of the worldwide market. The company also boasts a strong balance sheet with 2010 profits of $107 million on revenue of $543 million and a robust pipeline,

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▲ **Gen-Probe on the Auction Block,** *from page 1*

including two molecular diagnostics, the Progensa prostate cancer test and Aptima human papillomavirus test, which are awaiting U.S. Food and Drug Administration approval.

In the diagnostics industry, where consolidation of smaller players and expansion of molecular diagnostics offerings drive acquisitions, transactions have been completed at three to six times annual sales in recent years. Gen-Probe might go for a premium, which could put a sale of Gen-Probe in the $5 billion range, or over $100 per share, analysts have speculated. Bloomberg cited Novartis AG, Thermo Fisher Scientific Inc., Danaher Corp., Abbott Laboratories, Johnson & Johnson, and Life Technologies Co. as possible bidders.

Gen-Probe's first-quarter 2011 net income was $23.3 million on record revenue of $143 million. The company reaffirmed annual revenue projections for 2011 of $570 million to $595 million. With growing cash on hand, Gen-Probe has spent millions on strategic expansions and acquisitions in the past two years, including the $53 million acquisition of transplant test company GTI Diagnostics (Waukesha, Wis.) this past December, a $60 million acquisition of Milwaukee-based Prodesse, a privately held company specializing in molecular testing for influenza and other infectious diseases in October 2009, and a $50 million strategic investment in Pacific Biosciences (Menlo Park, Calif.), a private sequencing company, in June 2010.

DNA Blood Test Detects Early Organ Rejection

Researchers have developed a sequencing-based method for detecting early signs of organ rejection. In a proof-of-concept study published online ahead of print in the *Proceedings of the National Academy of Sciences*, researchers from Stanford University and Howard Hughes Medical Institute demonstrated that elevated levels of donor DNA circulating in the blood of the transplant recipient can be used as a sign of organ rejection in heart transplant patients. The test could change the standard for routine monitoring and treatment of organ rejection and is expected to be applicable to all solid organ transplants.

Using high throughput shotgun sequencing, the authors measured the signature of dying cells from the transplanted organ circulating in the recipient's blood. Before rejection events the genetic signature increases substantially, as confirmed by endomyocardial biopsy, the authors reported. The endomyocardial biopsy, the gold standard for diagnosis of rejection, is an expensive and invasive procedure that carries the risk of serious complications and patient discomfort. Analyzing samples from 48 patients, the authors found a mean value less than 1 percent as being "normal." During organ rejection mean DNA values increase to 3 percent to 4 percent of the total cell-free DNA.

"The implication is severalfold," explains Hannah Valantine, M.D., senior associate dean and professor of medicine at Stanford University School of Medicine. "First, it could help avoid heart biopsies. Once we see early damage we can intervene, and I believe intervention can include lowering immunosuppressants to much lower levels than we use now. I'm thinking if we start to see donor DNA we can tweak immunosuppressants, change the dose slightly, and avoid the higher levels of medication we use."

Valantine told *DTTR* they are already moving forward on additional studies including an assessment of test performance that will be quickly followed by a randomized

control trial. She believes it is conceivable that within two years the test could be used for routine monitoring of transplant rejection and that the test will be "widely applicable" to other solid organ transplants.

EMRs Identify Phenotypes for Genetic Research; VA Launches Genomics-EMR Research Database

Real-world clinical data captured in electronic medical records (EMRs) can be used to identify disease phenotypes with sufficient statistical power for use in genomewide association studies (GWAS), according to a new study published by collaborators from the Electronic Medical Records and Genomics (eMERGE) Network.

In an article published in the April 20 issue of *Science Translational Medicine*, the authors concluded that with improvements in EMR utilization, standardization, and the capture of familial and environmental data, EMRs will play a pivotal role in scaling phenotyping efforts to match the rapid proliferation of genomics data.

Using EMRs from five different study sites—Group Health (Seattle), Marshfield Clinic Research Foundation (Marshfield, Wis.), Mayo Clinic (Rochester, Minn.), Northwestern University (Chicago), and Vanderbilt University (Nashville, Tenn.)—participating institutes selected a disease phenotype and developed algorithms to identify cases from EMR data. These algorithms included methods for structured capture of diagnosis, laboratory tests, and medication data, supplemented with text-mining tools. The five disease phenotypes included dementia, cataracts, peripheral arterial disease, type 2 diabetes, and cardiac conduction defects. The combined repositories included nearly 130,000 patients.

Four of five study sites achieved positive predictive values of nearly 100 percent using EMR data alone to identify their primary disease phenotype with one outlier, Group Health, which correctly identified 73 percent of dementia cases. Across sites researchers identified the five disease phenotypes with negative predictive values of 98 percent to 100 percent.

Despite variations in completeness of data capture across sites, all sites met or exceeded current meaningful use standards. "Significant informatics efforts" were required to tailor algorithms to each institution's EMR, which represented both "home-grown" and commercial systems. Race and ethnicity data were completed between 69 percent and 94 percent of the time. Family history and exposure history (including smoking) were also documented less frequently across all five systems and were often captured in clinicians' notes without consistent nomenclature. Natural language processing tools (NLP) enabled identification of 129 percent more cases of quantitative trait duration, a measure of cardiac conduction, than with structured data and string matching alone. eMERGE identified use of NLP extraction as a "critical tool" to improve data quality for phenotyping.

VA Launches Genomics Database

In early May the Veterans Affairs (VA) research program announced the national launch of the Million Veteran Program (MVP), which aims to establish one of the largest databases consolidating genetic, military exposure, lifestyle, and health information in an attempt to advance genomic research and personalized medicine.

"We have a research establishment that is embedded in an integrated health care system with a state-of-the-art electronic health record [and] fully equipped genomic laboratories," said Joel Kupersmith, M.D., VA's chief research and development officer in a statement. "The merger of these distinct attributes . . . makes VA uniquely able to conduct this ground breaking genomic research."

Participation involves filling out health and health-related behavioral surveys, providing a blood sample, and granting access to medical records. Changes in health status can be characterized longitudinally through electronic data sources within and beyond the VA health care system to further enhance the value of the collected and stored genetic samples. The information will be stored in a secure VA central research database. The database was piloted in Boston and West Haven, Conn., VA medical centers and is expanding to achieve the goal of national participation over the next five to seven years, including sites in Buffalo, N.Y., Cleveland, Durham, N.C., Gainesville, Fla., New York City (Manhattan), Palo Alto, Calif., and Seattle.

"MVP, when fully complete, will be 'the' site for studies that require large datasets for statistical significance, including replication sets to further support and verify the analyses," says Ronald Przygodzki, M.D., acting director of the VA's biomedical laboratory research and development. "This prospective, longitudinal cohort will not undergo any specific genotyping but will be used as a resource for researchers who, under appropriate study oversight committee review, will be granted access to a limited dataset of information and access to blood sample constituents." G2

Patients Unrealistic, Want Lab Results Quickly, Says ASCP Survey

Consumers expect results faster than laboratories can deliver them, according to the first-ever consumer survey by the American Society for Clinical Pathology (ASCP). The survey discovered that 40 percent of consumers expect routine laboratory results, such a cholesterol test, within one day.

"Over the past 20 years there have been numerous technological developments that allow point-of-care testing . . . and while this is a great service to the patient and their physician it may also lead the patient to think that all tests should be available so readily and, unfortunately, that just isn't possible," says David Glenn, CEO, Pathology Services (North Platte, Neb.) and chair of ASCP's communications committee.

For tests involving a serious condition, such as a cancer biopsy, the survey found that 63 percent of patients expect results within a day. ASCP noted these turnaround times are often not feasible given complex processing and analysis, increasing test volumes, priority test processing, and increasing laboratory staffing shortages.

"The consensus is one of surprise, as most of us thought that the patient would not expect most results within a week or so as that is usually the time required for the follow-up visit with the physician," Glenn tells *DTTR*. "However, from the standpoint of when I'm a patient, I understand the curiosity and desire for wanting immediate results—we do live in an immediate gratification culture."

The consumer telephone survey was conducted by Opinion Research Corp. (Princeton, N.J.) in March and involved more than 1,000 randomly selected adults. G2

G2 INTELLIGENCE
Inside the Diagnostics Industry

IRIS Evolving: Diversifying From Urinalysis to Personalized Medicine

Cesar Garcia

Medical diagnostic company IRIS International (Chatsworth, Calif.) was added to the G2 Diagnostic Stock Index this year. *DTTR* recently spoke with IRIS CEO Cesar Garcia to learn about the company's evolution from a traditional in vitro diagnostics company with a core business in urinalysis to a diversified company poised to enter the personalized medicine market.

The company's guidance for fiscal year 2011 includes consolidated revenue estimates of $117 million to $123 million, an increase of 10 percent to 15 percent over 2010. Garcia elaborates on the strategic progress IRIS made during the first quarter, including obtaining U.S. Food and Drug Administration (FDA) 510(k) market clearance for its iChem VELOCITY automated urine chemistry analyzers and signing a joint development agreement for the 3GEMS hematology platform with Fujirebio Inc. (Japan) worth up to $6 million. He also discusses plans to expand the offerings of Arista Molecular Laboratory, which IRIS acquired in the summer of 2010, beginning with the company's NADiA ProsVue prognostic prostate cancer test, which is awaiting FDA approval.

IRIS at a glance

2011 Projected Revenue: $117 million to $123 million, up 10 percent to 15 percent from $107.7 million in 2010

2011 Projected R&D Expense: Approximately 14 percent of revenue

2011 First-Quarter Results: IRIS Diagnostics Division consumables and service revenue increased 16 percent to $27 million, comprising 62 percent of consolidated revenue

With the acquisition of Arista and the creation of Iris Molecular, IRIS expanded from its core business of urinalysis and sample processing. How do you envision this will reshape IRIS and its business model in the coming years?

We are evolving from a traditional in vitro diagnostics company to a hybrid company doing traditional in vitro diagnostics and personalized medicine. . . . To capture that vision we changed the official financial reporting segmentation. We have three segments: diagnostics, sample processing, and the personalized medicine division.

What is happening is the limit of traditional diagnostics was reached a long time ago. . . . My parents died from cancer 35 years ago and at that point in time [physicians] provided a therapy to all patients and said only 10 percent of patients benefit from these therapies. Today, the focus is in diagnosing the predisposition of the patient for genetic alterations and then providing therapies that are effective for that patient specifically.

You are awaiting clearance for NADiA ProsVue prostate cancer test which will presumably be offered through your CLIA-certified laboratory. When do you expect it to be commercially available?

The NADiA ProsVue has been with the FDA on and off for about three years now. We believe we are getting into the final stages of the process. The next step is [the agency] requested additional information regarding sample stability and we are

providing that information this quarter. We already scheduled a conference call with the FDA to discuss the results and hopefully, the expectation is that we will get clearance in the second half of this year and shortly thereafter we will begin commercialization.

What else is in IRIS's molecular diagnostics pipeline and what other expansions of Arista's test menu are planned?

We are looking to the basis of NADiA technology. When we combine immunoassay with real time PCR we can identify residual amounts of proteins from many, many diseases. What we are doing next is actually combining NADiA with a technology we have that we call the bubble separation technology and we are using those microbubbles to separate circulating cancer cells, specifically circulating epithelial cells. So the next assay will use the microbubble to capture those circulating epithelial cells and then phenotype those cells to know what cancer [patients] have or what expressions they have. That is the next application and the whole idea is that it would be another product to feed into the Arista molecular laboratory. The quality of research of the assay should be finished at the end of this year and then we will move into the development phase in 2012. We haven't decided if we are going to submit this to the FDA or sell it as a lab-developed test, so depending on that route it could be on the market as early as 2013 or later depending on our decision to go to the FDA or not.

"I call it a razor-razor blade business for diagnostics companies. As they grow and become mature the consumable revenue becomes the majority of the revenue and we have been between 55 and 60 percent of revenue coming from consumables and service."

–Cesar Garcia, IRIS CEO

In your recently released first-quarter results, IRIS Diagnostics Division consumables and service revenue was up significantly (16 percent) and accounted for the majority of revenue (62 percent). Do you expect this trend to continue?

Basically that is why I call it a razor-razor blade business for diagnostics companies. As they grow and become mature the consumable revenue becomes the majority of the revenue, and we have had between 55 and 60 percent of revenue coming from consumables and service. So, that is a trend we would like to continue. We'd like to increase that and with the recent release of the VELOCITY that will also accelerate generation of consumables. In the international market we have been selling only the i200 and now with clearance of the VELOCITY it will be available globally. With 510 clearance we can sell not only in the U.S. but we can sell it in China, Mexico, Thailand, Korea.

Last quarter you also announced expansion in another business line—a joint development agreement for the 3GEMS hematology platform. Where are you currently in the development of this platform and what is the timeline for commercialization?

The way we have been successful [in urinalysis] is by having a flow microscope that can take images of the particles, characterize them, and quantify them. We are taking essentially the same technology and employing it in hematology.

Hematology is very similar to that of urinalysis. On average about 30 percent of samples go to microscopic review. . . . With the 3GEMS hematology application the objective is that we are going to automate the whole process and eliminate the slides, reducing the review rates from 30 percent to less than 10 percent and do it in a simple machine, in a compact format, at a lower price, and [with] high throughput. That would be the first entry in the field of hematology. We believe that would be a significant differentiation to allow us to enter that market and compete with the bigger companies that will not have that capability. . . . Now we are proving that we can do the expanded differential integrating into one machine so we can have one prototype, an engineered prototype that will have all of the functionality built together into one system by the end of this year and launched into the market in 2014.

We look to Fujirebio as a partner for Japan. In the terms of the agreement we give them the option, but not the obligation, that if they want to expand into other Asian-Pacific countries they have first right of refusal with, of course, an incremental contribution in the development costs. The Fujirebio partnership is a win-win for both because it is difficult for American companies to go and sell direct in Japan. … It will be the same basic unit shipping to all countries but we will incorporate [Japanese requirements] from the first release. They are contributing monetarily, developing marketing information, helping us in development reviews, and we can get into the Japanese market faster that way.

The hematology opportunity is huge, about $2.5 billion in sales a year. There are about 30,000 midrange and high-end machines and they get replaced every five to seven years. So, on average there are about 5,000 new hematology machines sold every year. If we manage to only get 10 percent, 500 machines a year, that by itself would be a bigger business than the core urinalysis is today.

If you were to look into your crystal ball how do you see IRIS five years from now?

I think the company five years from will have next-generation products in urinalysis and hematology. Five years out hematology will be ramping up. There would be significant revenue. In personalized medicine we will have three or four applications where a laboratory chain would be the primary supplier of those services. At that point in time we would be open to licensing to others either for development, for drug discovery, for research, or simply for people that can target regions that it would simply not be practical for us to cover.

As Molecular Diagnostics Market Consolidates, Regulatory and Reimbursement Challenges Still Loom Large

The rapidly growing market for molecular diagnostic testing was the focus of a conference held April 13-15 in Boston by G2 Intelligence, and among the key themes to emerge was the intricate relationship between regulation and reimbursement of tests in this area. As the molecular diagnostics market continues to consolidate, even as new players emerge, a new crop of larger, established stakeholders are grappling with issues of regulatory oversight, pricing, and value, explained Patrick Terry, a principal at life sciences consulting firm Scientia Advisors (Cambridge, Mass.), in a conference presentation that discussed some of the marketplace dynamics that shape regulation and reimbursement for molecular diagnostic tests.

> ***"Regulatory agencies are doing a lot of hand-wringing over how do they deal with this onslaught of potential products with a toolkit that was written in 1972, finalized in 1974, and institutionalized under law in 1976. That's basically the toolkit the agency has been given. Ultimately, we're going to be trying to stuff round pegs into square holes."***
>
> ***–Patrick Terry***

"These organizations are committed to certain business models, certain routes to market, certain regulatory and pricing strategies, and ultimately will start setting some firm precedent of what the pathway is for product development, regulatory clearance, and reimbursement strategies," said Terry of the diverse companies that have invested billions in molecular diagnostics in the last several months.

The growing list of influential players includes GE (Fairfield, Conn.), which in December acquired cancer testing laboratory Clarient for $587 million through its GE Healthcare unit, and pharmaceutical giant Novartis (Basel, Switzerland), which recently snapped up Genoptix for $470 million. On May 17, Quest Diagnostics (Madison, N.J.) announced that it had completed its acquisition of Celera, including the Berkeley HeartLab subsidiary, in a deal valued at $671 million.

Terry, a co-founder of Genomic Health, predicts continued consolidation in the molecular diagnostics market and foresees the relationship between diagnostics and pharmaceuticals becoming increasingly significant. He pointed to the growing influence of novel drugs that are administered and now frequently developed alongside a diagnostic test. "In the next three years there will be multiple targeted therapeutics launched," he said. "Their entire value will be derived from being premium products as directed by a diagnostic assay of some sort."

The maturing pipeline for companion diagnostics and companion therapeutics is likely to reverberate throughout the marketplace. "When you have molecular end points that are tied to a therapeutic benefit indication, then that necessitates a label inclusion, a cosubmission or separate submission through the regulatory bodies that would permit that therapeutic on the market," he said. "So ultimately pharmacogenetics and genomic testing will be pulled by a force of gravity into a regulatory schema." While not true for all advanced diagnostics, this development is already eliciting responses from the public policy community as well as from regulatory bodies as they consider how to standardize their handling of these products.

However, even as biomarker-based products are increasingly being developed in a paradigm traditionally reserved for pharmaceuticals, regulatory challenges loom large. "Regulatory agencies are doing a lot of hand-wringing over how do they deal with this onslaught of potential products with a toolkit that was written in 1972, finalized in 1974, and institutionalized under law in 1976," said Terry. "That's basically the toolkit the agency has been given. Ultimately, we're going to be trying to stuff round pegs into square holes."

Still a small fraction of clinical laboratory revenue and overall health care spending, the molecular diagnostics market is poised to grow by between 14 percent and 22 percent within the next five years, and payers are taking notice. Terry believes immediate developments in the payer marketplace will be shaped by manufacturers of molecular diagnostic analyzers and test kits rather than clinical laboratories. "The real drivers here are the platform and kit companies that are morphing some of their business models with acquisitions of CLIA laboratories, embracing translational laboratory medicine in their product development paradigm, kind of endorsing the CLIA route to market as just an incremental step to a further regulatory process with the agency," he said.

Whether positioned as laboratory suppliers or service providers, organizations must now focus on evidence—linking diagnostic tests to clinical outcomes—if they want to thrive in a maturing market. "This industry has not necessarily built an acumen and a capacity to develop and deliver rigorous evidence, controlled trials, evidence demonstration, and publications," explained Terry. "It really is about a much different legacy and paradigm, but this is being foisted on the industry. Maturation [of the market] will demand higher levels of evidence, more robust evidence, and to understand current best practices. How that's done is important."

At a time when molecular diagnostic test utilization is coming under greater scrutiny, bolstering the evidence behind diagnostic tests is also at the core of a shift to value-based reimbursement. According to Terry, test development must now begin with the goal of addressing an unmet clinical need, ideally one that is compelling to patients. The product is then designed around that need and the value perception for that patient-customer.

"For example, Genomic Health did nothing new, basically," said Terry. "We just took the diagnostic paradigm and said, 'OK, let's weight this more on a continuum of a therapeutics perspective, let's look at these different attributes, and let's go with pharma's strategy rather than the traditional diagnostics strategy.'" With this approach, the company was able to drive a value-based pricing decision around the OncoType DX breast cancer test. Launched in January 2004, the test currently retails for approximately $4,000.

The ability of the molecular diagnostics market to implement value-based pricing is threatened by the evolving reimbursement system. All eyes are now on the coding changes slated to be enacted next year that would see reimbursement for some high-profile molecular diagnostic tests reduced by as much as a half. Still, Terry advocates a holistic approach that considers direct, indirect, and "soft" issues. "I call this the constellation of value. You should think about your products and your product development in that mindset," he said. "Think about what the

perceived value is and get away from this idea of time, motion, cost of goods, these value units that are just an anchor to innovation, an anchor on a return on investment, and an anchor on creating a sustainable enterprise for innovation and novel products."

Novel Genomic Test May Predict Chemotherapy Response and Survival for Invasive Breast Cancer Patients

A new genomic test that combines a patient's estrogen receptor (ER) status, endocrine therapy response, and chemotherapy resistance and sensitivity can help to predict chemotherapy response and survival benefit in women with invasive breast cancer, according to findings published in the May 11 issue of the *Journal of the American Medical Association*. If validated in future studies, the test could guide therapy for approximately 80 percent of women who have been newly diagnosed with invasive breast cancer and who are candidates for chemotherapy.

"The test helps us understand both resistance and response to chemotherapy more specifically, how sensitivity to endocrine therapy would impact a predictor, and how to focus on specific subtypes of breast cancer—in this case HER2-negative disease stratified by estrogen receptor status—because we've learned that they are so intrinsically different," said W. Fraser Symmans, M.D., a professor at the University of Texas M. D. Anderson Cancer Center and an author of the study.

The study began by enrolling 310 women who had been newly diagnosed with invasive breast cancer. All were HER2-negative and received the same chemotherapy regimen followed by endocrine therapy if they were hormone receptor-positive. The researchers used findings from microarray-based tests of these women to develop different predictive signatures for drug resistance and response.

Using the genetic signatures along with other genomic predictors of chemotherapy response, the researchers predicted breast cancer treatment in another group of 198 breast cancer patients with similar diagnosis and treatment. They later evaluated distant relapse-free survival (DRFS) and absolute risk reduction (ARR) in these women.

The algorithm-based test was found to have a positive predictive value of 56 percent. In the 28 percent whom the test predicted to be treatment-sensitive, the three-year DRFS was 92 percent, ARR was 18 percent, and they had a fivefold reduction of risk of distant relapse. When analyzed by ER status, treatment sensitivity was predicted in 30 percent of the ER-positive women and in 26 percent of those who were ER-negative. At three-year follow-up, DRFS and ARR were 97 percent and 11 percent, respectively, in the ER-positive cohort, compared to 83 percent and 26 percent, respectively, in the ER-negative cohort.

Future studies will determine if this novel genomic test will one day be used to assist physicians in selecting therapy for invasive breast cancer. The results could identify those patients best suited to standard chemotherapy, or those at greater risk for recurrence, or those who could most benefit from participation in a clinical trial.

Researchers Developing Test for Pancreatic Cancer

Researchers at the Mayo Clinic (Rochester, Minn.) are developing a DNA-based screening tool for pancreatic cancer, one of the deadliest forms of the disease. Preliminary results of this work were presented at the 2011 Digestive Disease Week conference, held May 7-10 in Chicago.

Using stool samples, the researchers looked for methylation (a type of modification strongly associated with cancers and precancers) of the DNA of 127 patients, 60 of whom had been diagnosed with pancreatic cancer and 67 who were not diagnosed with cancer. The goal was to reliably detect methylated genes in the stool samples of those in the study group who had already been diagnosed with pancreatic cancer.

"We found that a marker was reliably detected in both tissue samples and in the stools of pancreatic cancer patients and that it compared favorably with another kind of marker—the mutation of a gene called KRAS," said John Kisiel, M.D., the Mayo Clinic gastroenterologist who presented the study's findings. "When we looked at those two markers together, the combined accuracy of both markers was significantly better than with either marker alone." The methylated marker (BMP3) and the mutated KRAS genes were detected in 70 percent of those in the study who had pancreatic cancer, and the researchers were able to detect the markers regardless of the stage of cancer or the location of the cancer within the pancreas.

These findings may lead to more early detection of pancreatic cancer, which could significantly increase the survival rate for those who have the disease. This particular screening tool could be particularly effective because it relies on stool samples, which can be collected by patients at home and sent to their doctor.

Study Identifies New Genetic Links to Immunodeficiency Disease

The newly published findings of a genomewide association study may lead to the first predictive diagnostic test for common variable immunodeficiency disease (CVID), a serious immunodeficiency disease in children. If the disorder can be diagnosed early, affected children may receive lifesaving treatments before the disease can progress. The study was published online April 15 in the *Journal of Allergy and Clinical Immunology* and appears in the June issue of the journal.

In this study, researchers analyzed the gene expression patterns of 363 patients with CVID, compared to 3,031 healthy controls. They detected a strong association with genes in the major histocompatibility complex region, an area known to play an important role in immune-related conditions, and previously linked to CVID. The researchers also found single-nucleotide polymorphisms in an area that codes for a family of proteins involved in immune responses. More than a dozen novel genes with direct or potential relevance to the immune system were also found to vary in copy number with CVID.

The findings of the genomewide association study were then used to develop a predictive algorithm. When the researchers tested that algorithm on cohorts of CVID cases and controls, they were able to distinguish CVID from healthy controls with 99 percent accuracy.

Biomarkers Absent in Updated Alzheimer's Clinical Diagnostic Guidelines

The use of biomarkers as diagnostic criteria for Alzheimer's dementia and mild cognitive impairment due to Alzheimer's will be limited to a research agenda only and are not intended for clinical application at this time, according to the first new guidelines for diagnosing Alzheimer's disease issued in 27 years.

***The new Alzheimer's disease diagnostic guidelines were published online in* Alzheimer's & Dementia: The Journal of the Alzheimer's Association.**

The guidelines were developed by a workgroup led by the Alzheimer's Association and the National Institute on Aging. According to the guidelines, the new definition of the disease must reflect not just the observable disease but also preclinical Alzheimer's disease, a presymptomatic period in which detrimental changes are progressing in the brain measurable only by changes in biomarkers. Both fluid and imaging measures are being tested as possible biomarkers for Alzheimer's. But, the authors cautioned, additional research is needed to validate the application of biomarkers before they can be used in a clinical setting.

"The challenge for Alzheimer's now is that there is currently no single, generally accepted way to identify the disease in the earliest stage—before symptoms are evident," said the authors in a statement. "It is hoped that the research agenda outlined in the new preclinical Alzheimer's article will correct this deficit."

Effectiveness of Universal MRSA Surveillance Unclear

In an attempt to limit the spread of antibiotic-resistant superbugs some hospitals and state legislatures are turning to mandatory screening of all patients in intensive care units (ICUs) for methicillin-resistant staphylococcus aeureus (MRSA). Two studies published in the April 14 edition of the *New England Journal of Medicine* reported conflicting results on the effectiveness of these active surveillance measures on the incidence of MRSA and vancomycin-resistant enterococcus (VRE) infections.

A group of investigators led by researchers at the Mayo Clinic evaluated the effects of surveillance and the expanded use of barrier precautions in more than 9,100 admissions to adult ICUs in 18 hospitals over a six-month intervention period. Results of the surveillance cultures were only reported to the intervention ICUs. The intervention was not effective in reducing the transmission of MRSA or VRE, as there was not a significant difference between the intervention and control ICUs in the mean incidence of colonization or infection events per 1,000 patient days. Researchers found that when patients were assigned to barrier precautions the contact precautions (clean gloves, gowns, and hand hygiene) were employed less frequently than required, possibly impacting the efficacy of active surveillance.

A study by Veterans Affairs (VA) researchers assessed the effect of implementing a systemwide quality improvement initiative known as the "MRSA bundle" that began in 2007 and included universal nasal surveillance, contact precautions, and an internal cultural shift, which made infection control the responsibility of all personnel with patient contact. The VA researchers found that over nearly three years and close to 2 million admissions the rates of health care-associated MRSA infections declined significantly, decreasing by 62 percent in ICUs and falling 45 percent in non-ICU admissions.

Patrick Murray, Ph.D., chief of microbiology service in the National Institutes of Health's Clinical Center, whose laboratory oversaw the Mayo testing, tells *DTTR* there were some differences between the studies. In the Mayo study all nasal swabs were sent to the NIH's Clinical Microbiology Laboratory for culture testing, creating a five-day wait that delayed implementation of the added infection-control measures, whereas the VA used local clinical microbiology laboratories.

So how does one interpret these divergent results and what does the future of MRSA testing hold? Murray predicts that more and more reliable molecular tests will be introduced and hospital infection coordinators, hospital administrators, and laboratories will have to evaluate if the test can be easily integrated into other testing, if it is affordable for that institution, and if there is a measurable clinical value and for what subset of the patient population.

Myriad Stakes Position in Companion Diagnostics With Rules-Based Medicine Acquisition

Myriad Genetics (Salt Lake City) announced in late April that it will acquire Rules-Based Medicine (RBM; Austin, Texas) for $80 million in cash, establishing its position as a major player in the field of companion diagnostics. The acquisition expands Myriad's research portfolio into new disease states, including psychiatric disorders, infectious diseases, and inflammatory diseases, and adds eight new molecular diagnostic product candidates to Myriad's pipeline.

RBM's proprietary multiplex immunoassay technology for novel protein biomarker discovery will complement Myriad's strength in DNA and RNA technologies. RBM has developed over 550 immunoassays, the company says, and its biomarker discovery platform is utilized by pharmaceutical companies to accelerate drug development and improve clinical trials outcomes. RBM has strategic alliances with over 20 major pharmaceutical and biotechnology companies. When coupled with Myriad's position in PARP inhibitors and PI3K inhibitors, the combined entity is positioned well, with a robust pipeline, in the rapidly evolving companion diagnostics market.

"We believe the acquisition of RBM will enhance Myriad's capacity to deliver transformative molecular and companion diagnostic products to patients suffering from major, common diseases," said Peter Meldrum, president and CEO of Myriad Genetics in a statement. "RBM's extensive product pipeline includes tests for anti-psychotic drug safety, hepatitis C drug response, and detection of kidney damage in diabetes patients and will augment Myriad's strong oncology pipeline."

RBM, a privately held company, had 2010 revenues of approximately $25 million, with operations approaching breakeven. Myriad believes the acquisition will be accretive to earnings within two years and expects the transaction to close by the end of May. At the close of fiscal year 2010 Myriad had annual revenue of over $363 million and $494 million cash on hand as of Dec. 31, 2010.

RBM operations will continue from Austin as a wholly owned subsidiary of Myriad called Myriad RBM, but its commercial diagnostic operations will operate under Myriad's molecular diagnostic laboratory in Salt Lake City.

Spectracell's LPP Test Licensed in New York

SpectraCell Laboratories (Houston) has been granted a license to offer its Lipoprotein Particle Profile (LPP) test in New York state. The test, which was awarded a patent in February for its ultracentrifugation method for separating lipoprotein, measures the size, density, and number of particles in each lipoprotein subclass. The test allows physicians to better stratify risk of heart disease, allowing for therapies tailored for the patient's specific lipid profile.

The basic test panel specifically measures four risk factors not measured with routine cholesterol testing including the RLP remnant lipoprotein, which can be converted into arterial plaque; Lp(a), which contributes to clot formation; HDL2b, which indicates how well cholesterol is being cleared from the patient's system; and small, dense LDL that can damage the vascular wall through plaque formation. The comprehensive panel (LPP+) additionally tests for hemocysteine, insulin, apolipoprotein B, and HS-C reactive protein.

The license includes all components of the basic and comprehensive LPP+ panel, except for insulin, which the company is licensing separately, says Heather Vorce, director of marketing for SpectraCell. The list price for the test is $160.

OVA1 Detects Cancer More Accurately Than Recommended CA 125 Test

The OVA1 blood test can more accurately identify women with cancerous ovarian masses prior to planned surgery than the CA 125 blood test currently recommended by the American College of Obstetricians and Gynecologists (ACOG), according to a new study published online ahead of print in *Obstetrics & Gynecology*.

The study shows that replacing CA 125 with the multivariate index assay improves the sensitivity and negative predictive values of ACOG referral guidelines. Accurate assessment of cancer risk prior to surgery can affect referrals, treatment decisions, and outcomes for women with ovarian cancer.

The study evaluated the CA 125 test versus the OVA1 test in 516 women across a diverse group of primary and specialty care centers. OVA1 accurately detected 94 percent of all malignancies across women of all ages, compared to 77 percent with CA 125 alone. OVA1 improved detection in premenopausal women, identifying 91 percent of younger women with ovarian cancer, compared to 58 percent with CA 125. However, the OVA1 test was about two times more likely to create false positives, incorrectly identifying women as high risk for ovarian cancer when they were not.

"The high sensitivity in premenopausal women and early stage cancers is where CA 125 and the [ACOG] guidelines have underperformed," wrote primary author Rachel Ware Miller, M.D., assistant professor of gynecologic oncology at the University of Kentucky's Markey Cancer Center. "Identifying these patients for referral is valuable because many are not receiving appropriate surgical staging and treatment."

The test utilizes five biomarkers—Transthyretin, Apolipoprotein A-1, β2-Microglobulin, Transferrin, and CA 125 II—and proprietary software to determine the likelihood of malignancy in women with ovarian mass for whom surgery is planned. The test, developed by Vermillion (Austin, Texas), is exclusively offered by Quest Diagnostics (Madison, N.J.) in the United States and India. Vermillion funded the study.

IVD Stocks Up on Rumored Sale, Positive First-Quarter Growth

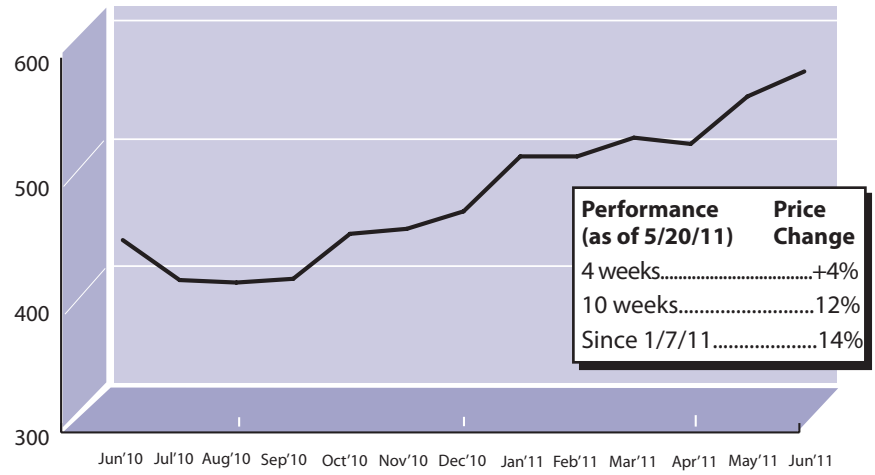
The G2 Diagnostic Stock Index was up 4 percent for the four weeks ending May 20, with 12 stocks up in price, six down, and one unchanged. The G2 Index outperformed both the Nasdaq and the S&P with the Nasdaq declining 1 percent and the S&P unchanged over the same period.

Among the biggest gainers for the period was **Quidel's** (San Diego) stock, which was up 21 percent. In late April the company reported positive first-quarter earnings. The company's total revenues were up 110 percent to $59.6 million, compared to the first quarter of 2010 and were driven by influenza and other respiratory product sales. The $25.6 million in cash flow from operations generated in the first quarter was used to pay down debt. In a statement, CEO Douglas Bryant said that Quidel also completed the clinical trial for its next-generation influenza assay.

Gen-Probe's (San Diego) 17 percent rise in stock price was fueled by a report by Bloomberg that the company hired investment bank Morgan Stanley to shop for buyers for the company. The report caused a one-day 13 percent jump in stock price from $70.16 on April 27 to $79.61 on April 28. The stock has virtually remained above $80 per share since.

Sequenom's (San Diego) first-quarter reports also helped to push its stock higher by 7 percent. The company reported revenue of $13.5 million for the first quarter of 2011, an increase of 27 percent compared to 2010, which helped to bring the company's net losses down by 25 percent to $12.7 million as compared to $16.9 million in the first quarter of 2010. The increase in revenue reflected increases in MassARRAY system sales as well as higher sales in both consumables and the company's diagnostics business. In a statement the company also reported progress on two forthcoming tests. Sequenom completed the pivotal clinical validation study for its SensiGene Trisomy 21 laboratory-developed test. The company also expects publication of its study on a genetic model to estimate the risk of developing age-related macular degeneration (AMD) to coincide with the commercial launch of RetnaGene AMD test in June.

G2 Diagnostic Stock Index



Source: The G2 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	$53.31	3%
Abaxis	30.85	6
Affymetrix	5.93	3
Alere	40.75	5
BectonDickinson	88.90	6
Bio-Rad	124.12	3
Gen-Probe	81.93	17
Illumina	72.86	4
Johnson & Johnson	65.69	3
Luminex	20.33	7
Qiagen	14.71	21
Sequenom	7.77	7
Unchanged		
Beckman Coulter	83.01	0
Down		
Cepheid	31.14	-1%
Immucor	20.40	-3
IRIS	9.04	-1
Meridian	23.17	-6
OraSure	7.68	-10
Qiagen	20.05	-3

G2 Insider

Genetics Education Needed to Capitalize on Advancing Technology. . . In the final report issued by the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS), *Genetics Education and Training*, the group discusses the genetics education and training necessary for point-of-care health professionals, the public health workforce, and consumers to realize the health benefits of emerging genetic knowledge and services.

The group warns that while collaboration across the health care field will be necessary to process, interpret, and apply genetic information, health professionals must have the proper educational tools to appropriately apply the developing information and technological base. The group's six recommendations outline the steps necessary to promote the genetics education and training necessary to ensure that advances in genomics benefit the public's health. SACGHS used research reviews, surveys of health professional organizations, and interviews to develop the following six recommendations:

- Convene a task force of entities involved in health professional training to identify innovative approaches to ensure genetic content in credentialing exams, institutional accreditation, and continuing education.
- Evaluate the composition of the public health workforce to identify those with responsibilities related to genetics and fund the development of programs to meet those training needs.
- Support programs that increase the genetic competencies of the health care workforce in underserved communities and ensure consumer materials are culturally and linguistically appropriate.
- Identify effective communication strategies to translate known genetic knowledge into information consumers can use to make health decisions.
- Create and maintain a Web-based portal to disseminate comprehensive and trustworthy genetic information.
- Improve the use of family health history tools.

Company References

Alzheimer's Association 312-335-8700
American Society for Clinical Pathology 312-541-4999
eMERGE Network 615-343-0121
Gen-Probe 858-410-8000
IRIS 818-709-1244
Myriad Genetics 801-584-3600
Quest 973-520-2700
Quidel 858-552-1100
Scientia Advisors 617-299-3000
Sequenom 858-202-9000
SpectraCell Laboratories 713-621-3101
VA research program 866-441-6075
Vermillion 512-519-0400

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