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CLN Clinical Laboratory News

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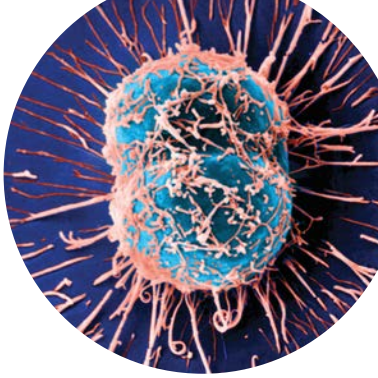

CERVICAL CYTOLOGY AUTOMATION

Study finds automation comparable to traditional cytology

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LABORATORY INFORMATICS

SMALL STEPS, BIG WINS

Molecular-Minded Colorectal Cancer Care

Procalcitonin in Practice

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Features

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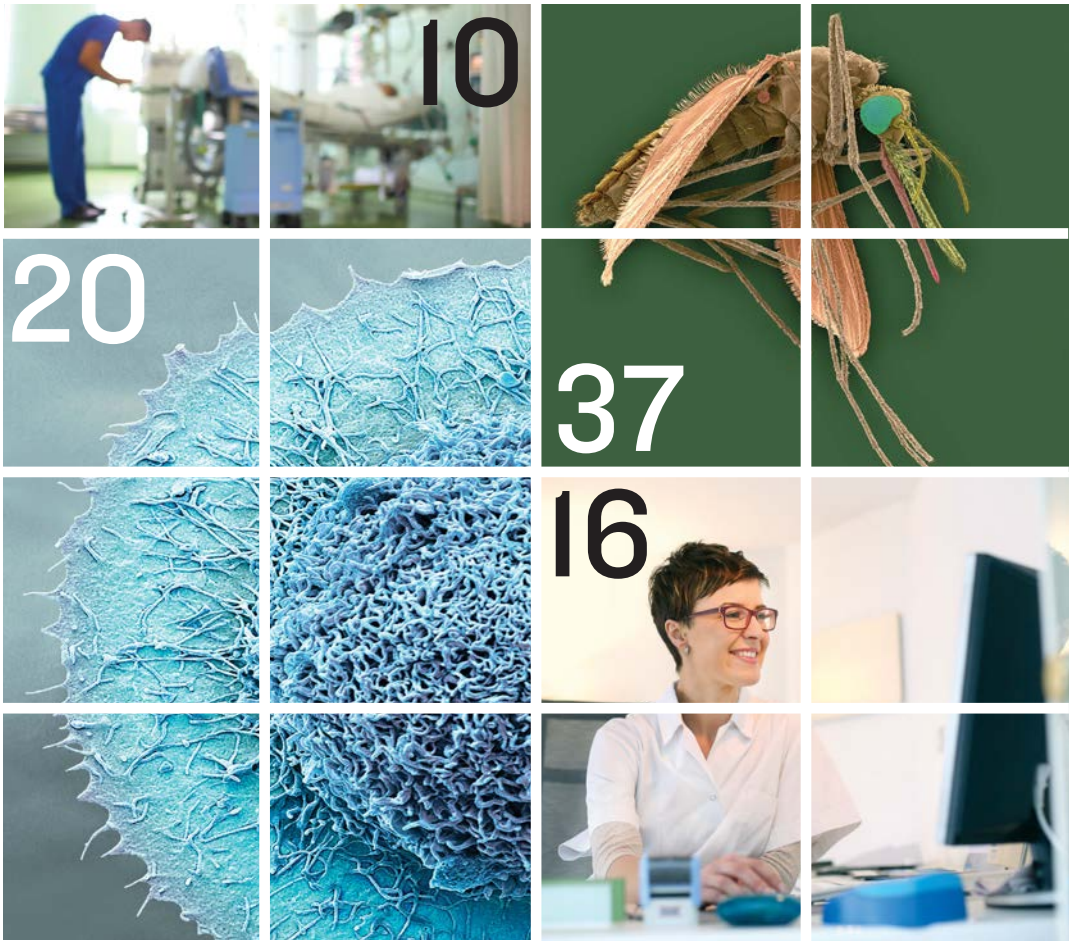
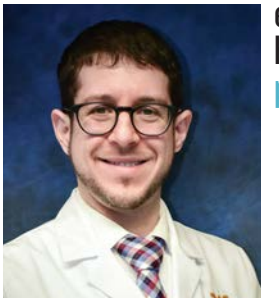


Departments



Recent research has revealed that cold-induced storage lesions alter the metabolic and functional profile of PLTs such that they effectively curtail hemorrhage.
p40

Federal Insider

Labs Rebuked After Charging for Specimen Validity Testing

After an Office of the Inspector General (OIG) report in February found some $66 million in over-billing, the Centers for Medicare and Medicaid Services (CMS) is cracking down on laboratories that code specimen validity testing as a separate service when they perform urine drug tests. A Medicare Learning Network bulletin released in March emphasizes that "providers performing validity testing on urine specimens utilized for drug testing shall not separately bill the validity testing."

Validity testing includes assays for urinary pH, nitrates, oxidants, creatinine, specific gravity, and other indicators of specimen adulteration. Labs are only allowed to bill for screening and quantitative testing. Billing code descriptions for both types of tests contain the phrase, "includes sample validation when performed, per date of service."

CMS is paying closer attention to the billing issue after OIG chastised the agency for failing to prevent the problem with "inadequate" systems. The agency put a fix in place in April 2016 that never worked properly, according to OIG.

Importantly, some of the same assays used to detect an adulterated specimen are also used to diagnose unrelated conditions, such as urinary pH and specific gravity for managing kidney stones and urinary tract infections. In such cases, these tests may be covered by Medicare.

OIG wants CMS to strengthen its billing editing system that detects and prevents specimen validity tests billed by the same provider for the same beneficiary on the same date of service as a urine drug test. However, based on the OIG report, the number of improper claims has shrunk considerably, from $37,054,887 in improper payments in 2014 to $4,335,028 in 2016.

CMS TOUTS VALUE-BASED PAYMENT PLAN FOR HOSPITALS

With a new secretary at the helm of the Department of Health and Human Services (HHS), the administration is laying out how it sees the shift from volume to value-based payment in the 2019 Inpatient Prospective Payment system draft rule for hospitals.

The draft rule floats three main policy changes related to how the Centers for Medicare and Medicaid Services (CMS) will pay hospitals. The first would require hospitals to post their standard list of prices on the internet in a machine-readable format. Currently, hospitals only are required to make them available in "some form."

Second, CMS is taking a fresh look at its electronic health record incentives. The rule would take new steps to ensure health record systems can exchange data and allow patients to access and control their own records.

Finally, CMS wants to eliminate duplicative, burdensome, or out-of-date quality measures through a new initiative called Meaningful Measures that assesses quality based on factors such as reducing healthcare-associated infections.

The American Hospital Association (AHA) praised the idea of less paperwork, noting that an AHA analysis found that providers spend nearly $39 billion annually on administrative work for regulatory compliance. AHA estimates that hospitals could see a payment increase of 1.75% next year based on the draft rule.

In a speech to the Federation of American Hospitals in March, HHS Secretary Alex M. Azar II emphasized that he wants the agency to use market forces to increase efficiency. "Real competition—in the economic sense—has never really been fully tried in our bizarre third-party payer system," he said. But he noted that, contrary to what some might expect from the administration, implementing a plan based on market competition "will require some degree of federal intervention—perhaps even an uncomfortable degree."

Azar also plugged the HHS meaningful measures initiative as a way to simplify paperwork and give more power to providers and consumers. "Value is not accurately determined by arbitrary authorities or central planners," he commented.

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Bench Matters

Point-of-Care Testing Compliance

How Partnering With Nursing Leadership and Sharing Data Upped Performance on a Crucial Parameter

Adil I. Khan, MSc, PhD

One of the hardest aspects of point-of-care testing (POCT) is trying to make the diverse users of POCT devices follow written procedures and perform testing exactly as stated by manufacturers. The simplicity of POCT devices, often involving disposable kits with no maintenance or troubleshooting, tempts users to take shortcuts. The downside of this approach is that when procedures are not followed to the letter, mistakes happen. POCT devices are designed so they can be used by anyone with at least a high school diploma, hence users range from students to physicians.

Here at Temple University Hospital (TUH) and TUH Episcopal Campus, we have worked over time to successfully implement a system for ensuring and documenting compliance with labeling requirements for these POCT devices, starting with glucose meter strips and controls.

Self-monitoring of glucose using glucose meters has been shown to reduce mortality and morbidity associated with the complications of diabetes and therefore is strongly advocated by the American Diabetes Association. Tight glycemic control of hospitalized patients also has been shown to speed patients' recovery and reduce their length of stay. Consequently, TUH, like many other organizations, follows tight glycemic protocols.

The science of glucose meters resides in their strips. These vital components house the reagents and host the reactions that spur redox reactions and generate current, which glucose meters measure and display as a quantitative value. This means that discarding a strip is like throwing away an entire laboratory instrument. Clearly, strip integrity, though easily overlooked, is an essential aspect of POCT-based glucose measurement.

Because of strips' vital importance, regulatory bodies assess for compliance with manufacturers' stringent strip storage recommendations. In particular, once glucose meter strips and controls have been opened, their expiration dates need to be documented, since the strips start deteriorating and can give unreliable results if used past their new expiration dates.

The Nova Biomedical glucose meter strips we use here at TUH have 180-day expiration dates, and their controls expire after 90 days. Imagine the challenge of ensuring that some 2,000 nurses comply with the strip container labeling requirement. It takes just 2-3 days

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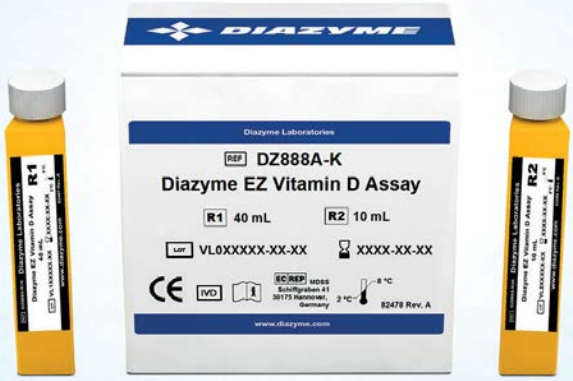

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F1 **Analysis of Glucose Meter Strip Labeling Compliance**

55	6 West									
56	%									
57	93	QC						Strip		
58		Low			High			Date opened	Exp. Date	Initial
59		Date opened	Exp. Date	Initial	Date opened	Exp. Date	Initial			
60	Meter 1	1	1	0	1	1	0	1	1	1
61	Meter 2	1	1	1	1	1	1	1	1	1
62	Meter 3	1	1	1	1	1	1	1	1	1

The 6 West unit had a 93% compliance rate with appropriately labeling the date a glucose meter strip box was opened, its date of expiration, and the nurse initialing these notations.

1, compliant; 0, noncompliant.

to run through a container of strips, or even less on a busy nursing unit. Documenting when a container has been opened understandably is not in the forefront of a nurse's mind, concerned as he or she is with patient care duties and knowing that the container will be finished in a few days anyway. It is an easy task to forgo. However, if we were to have an inspection in the time an unlabeled strip container was in use, we would be at risk for a citation, jeopardizing POCT at the facility. Furthermore, sloppiness in this seemingly incidental aspect of care could give the inspectors the impression of similar carelessness in other areas. Hence it is an important window into quality assurance for the entire hospital.

When I arrived at TUH 10 years ago, our compliance with glucose strip labeling was poor. POC coordinators (POCC) would verbally remind nurse managers or nurses that they needed to improve in this regard, but this was more of a ritual and follow-up was not actively pursued. We employed several approaches to improve compliance. First, we measured noncompliance data so that we could track our progress. We grouped the data by floors according to nurse director and emailed our analysis to them so that each nurse director could see how his or her floor was doing in comparison to peers (See Figure 1). Delivering this information to the nurse directors was vital, since nurse managers report to the directors—not POCCs or anyone in laboratory administration.

To ensure noncompliance was being followed up on, I met regularly with nurse directors. In addition, we circulated to the nurse directors an inspection checklist that included questions that came up in prior inspections (See Box, left). This approach, anchored in our regular interactions and feedback with the nursing leadership, changed compliance over a 10-year period from an average of 37% to 98%. We since have successfully employed this model for other POCT, and in all cases close teamwork with the nursing leadership made the difference. Their success is our success and vice versa.

Inspection Preparation Checklist

Inspectors will ask nurses about point-of-care tests performed on each floor. Nurses will need to:

1. Perform each test according to procedure.
2. Know the name of the instrument they use for testing.
3. Have read and know:
   - Storage conditions
   - Specimen requirements
   - Temperature (operation and storage)
   - How to interpret results
   - How long strips and controls are valid after opening
   - Timing requirements for results

Questions From Our Last Inspection

- What should happen following a critical high (or critical low) glucose result?
- How do nurses know when a glucose meter quality control has been performed?
- Walk the inspector through the steps in performing a whole blood glucose test with a glucose meter.
- How does a nurse identify a patient?
- How are glucose results charted and critical results followed up on?
- Do patient charts have reference ranges?
- Is a manual available or a knowledgeable person accessible to help troubleshoot the instrument/procedure?
- What do you use to clean glucose meters?

Adil I. Khan, MSc, PhD, is director of point-of-care testing at Temple University Hospital (TUH) and TUH Episcopal Campus, director of clinical chemistry at TUH, TUH Episcopal Campus, and TUH Northeastern Campus, and assistant professor of pathology at the Temple University Lewis Katz School of Medicine in Philadelphia.
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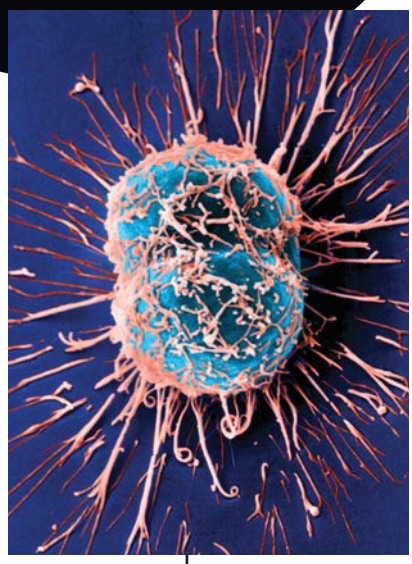


Automated Cervical Cancer Screening Equals Performance of Cytology Triage

A novel automated cervical cancer triage and screening strategy, incorporating a cytologic risk score algorithm and computer-interpreted cytology, performed comparably to traditional cytology triage and could bring high-quality cervical screening to underserved regions (J Natl Cancer Inst 2018;110:djy044). The findings "strongly support the feasibility of totally automated cervical screening without cytology," according to the authors.

The novel approach identified 91.7% of high-risk human papillomavirus (HPV)-positive cases for immediate colposcopy, while discerning 38.4% of all HPV-positive cases recommended for retesting in 1 year. In contrast, a conventional strategy combining HPV typing and nonautomated cytology triage identified 89.1% of high-risk HPV-positive cases for immediate colposcopy and 37.4% for future retesting.

The novel method involves a slide scanner that captures images and features of slides, such as presence of different cell types, nuclear size, and nuclear contour. The algorithm generates a severity score and identifies the most innocuous slides in a batch to reduce and/or guide treatment decisions.

The study involved two parts, including developing and validating the risk score algorithm, and validating an association between higher risk scores and HPV-positive, abnormal cytology cotest results.

The investigators developed and validated the computer algorithm using residual cervical specimens and liquid-based cytology slides from the Kaiser Permanente Northern California (KPNC) cervical cancer screening program. They used 1,839 stored HPV test specimens and liquid-based cytology results from a subset of women who had had baseline or follow-up HPV-positive results.

To further validate the risk score algorithm, the researchers used a set of 243,807 slides from KPNC obtained during routine cervical screening in 2016 and 2017.

While the novel method performed comparably to the conventional strategy, the researchers noted that both methods are imperfect, with "not high" specificity, and with both identifying precancer cases the other missed.

The authors suggested that automated cervical screening and triage might be of particular interest in middle-resource settings because it would enable implementation of "high-quality cervical prevention programs" in areas that lack skilled cytology professionals. At the same time, labs in high-resource settings might want to adopt such a system as an alternative to conventional cytology practice.

WIDE VARIATION IN LYNCH SYNDROME TESTING PRACTICES

An international survey of institutions that specialize in research and clinical care involving Lynch syndrome found wide variations in management and testing practices (Clin Gastroenterol Hepatol 2018; doi:10.1016/j.cgh.2018.04.025).

The authors speculate that this could be due to rapid changes in testing technologies, differences in resources, and "lack of definitive data for many clinical questions."

"In just a few decades, there has been a surge of advances in the knowledge and tools used for diagnosis and management of Lynch syndrome patients and families, and breakthroughs in the understanding and management of genetic cancer predisposition syndromes are accumulating quickly," the authors noted.

The researchers conducted the survey of 128 members of the International Mismatch Repair Consortium, of which 49% from 21 countries responded, to assess potential targets for research and public policy efforts.

Steve Gschmeissner/Science Photo Library

In terms of case-finding practices, 56% of respondents participate in automatic reflex testing of tumors, with 100% reporting testing of colorectal, 50% endometrial, and 13% ovarian cancers, respectively.

Nearly all (98%) respondents said they use immunohistochemistry when testing tumors, and three-quarters (78%) also perform microsatellite instability testing. Reported testing practices to distinguish sporadic mutations from Lynch syndrome cases included *BRAF* mutation (75%) and MLH1 promoter methylation (56%). Only about one-quarter (27%) said they use the new approach of testing for biallelic somatic mutations. Sites that do not perform the latter noted its relatively high cost in comparison to limited benefits.

Consistent with other studies, this survey found that less than 50% of at-risk family members had genetic testing.

OPTIMAL SCREENING STRATEGY COULD REDUCE PROGRESSION TO MULTIPLE MYELOMA BY 19%

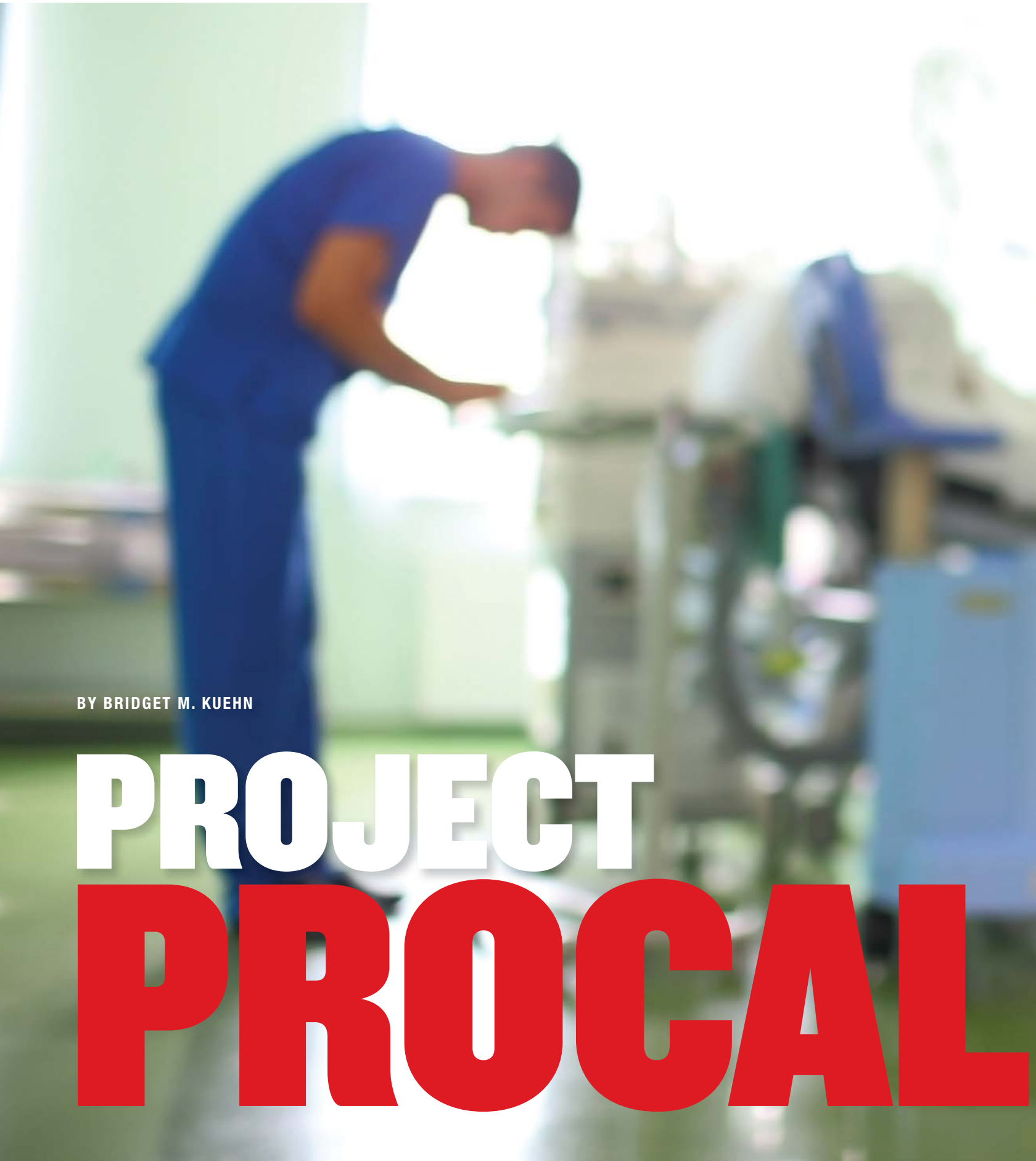
A computational model of progression from monoclonal gammopathy of undetermined significance (MGUS) to multiple myeloma (MM) suggests that starting screening for MGUS at age 55 and conducting follow-up screening every 6 years would reduce the prevalence of MM by 19% (Clin Cancer Inform 2018; doi.org/10.1200/CCI.17.00131). Starting MGUS screening at age 65 and performing follow-up screening every 2 years would reduce prevalence by the same percentage.

The authors were interested in exploring optimal screening scenarios because of recent research findings suggesting that interventions like taking the antidiabetic agent metformin, and aspirin and losing weight, might slow or reduce progression of MGUS to MM. However, it is unclear how best to screen at-risk populations and how to assess the effect of these interventions at the population level.

The investigators developed a Markov chain model to depict the population dynamics of healthy individuals transitioning to undetected MGUS, detected MGUS, MM, and finally, death.

Their computation model considered life tables and epidemiologic data on MGUS and MM, which depend on genetic background, sex, and age, and correlate with ethnicity. The researchers fashioned screening scenarios based on a person's age when first screened, the spacing between follow-up screens, and risk reduction after a positive screen.

In model simulations, they considered scenarios ranging from baseline low-risk MGUS incidence to elevated risk for certain groups, such as high-risk African-Americans, whose lifetime risk of MGUS is about twice that of individuals with low baseline risk.



BY BRIDGET M. KUEHN

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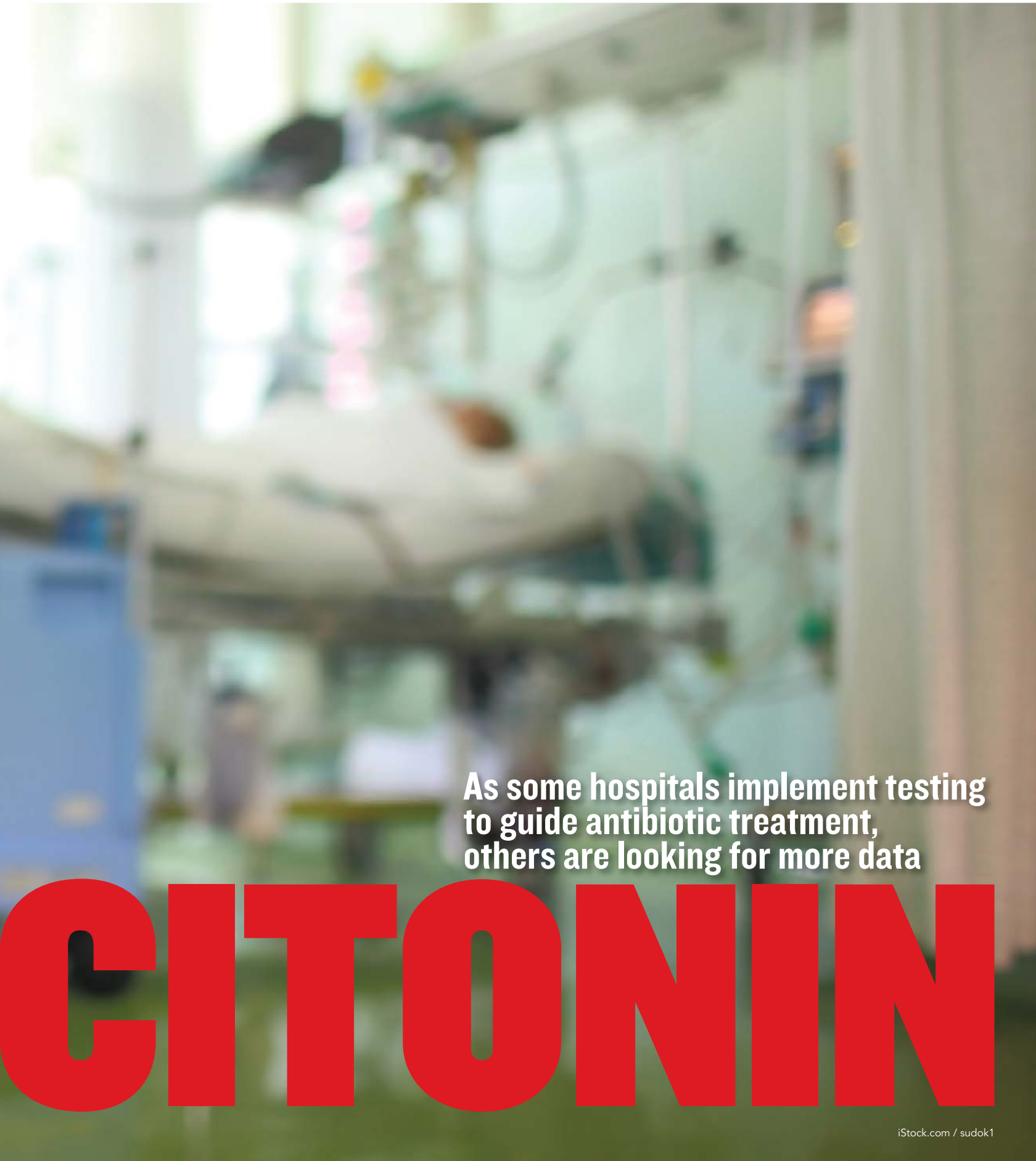

As some hospitals implement testing to guide antibiotic treatment, others are looking for more data

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A desire for better antimicrobial stewardship led Los Angeles County + University of Southern California (LAC+USC) Medical Center to implement testing for procalcitonin (PCT), a protein released in response to bacterial infections, to guide the treatment of sepsis and respiratory infections.

This PCT testing strategy has become common in Europe. However, it hasn't been as widely embraced in the United States. A growing number of PCT tests have made it more accessible and affordable for U.S. labs, but debate continues about the value of the test in improving clinical care.

"There are definitely some pros and cons to use of procalcitonin and the jury is still out on whether

it has helped curb use of antibiotics at our institution," said Allison Chambliss, PhD, director of clinical chemistry and point-of-care testing at LAC+USC. "But I believe that the positive impact has been that it has allowed providers to give second thought about antibiotic use."

Discordant Data

If LAC+USC has yet to see clear-cut benefits from implementing PCT testing, it is not alone. While some studies have found PCT results helpful in moderating antibiotic therapy, others have drawn less definitive conclusions. On the plus side, a PCT level below 0.25 µg/L may suggest that a patient with a respiratory infection doesn't need antibiotics. Monitoring PCT levels over time also may help clinicians determine when it is safe to stop antibiotics. A recent meta-analysis of PCT testing in respiratory infections found it associated with lower 30-day mortality, an average 2.4-day reduction in antibiotic exposure, and a 25% reduction in antibiotic associated adverse events (JAMA 2018;319:925-6).

"There used to be a lot of discussion about safety because, when you don't use antibiotics or you shorten antibiotic duration, physicians are worried about the outcome of their patients," said review co-author Philipp Schuetz, MD, MPH, chief physician of endocrinology, diabetes, clinical nutrition, and internal medicine at Universität Basel and the Kantonsspital Aarau in Switzerland. "But this analysis shows that this is a very safe way to use antibiotics with improvement of clinical outcome."

A multicenter prospective U.S.-based study by Schuetz and colleagues of 858 patients with sepsis found that an 80% decrease in PCT levels between baseline and day 4 of treatment predicted patient survival (Crit Care Med 2017;45:781–9). A review Schuetz coauthored also found a 1.49-day reduction in the duration of antibiotics (Crit Care Med 2018;46:691–8). PCT testing for sepsis helps individualize therapy, he said, but cautioned that it is not 100% accurate and should be used in conjunction with other tools.

"If you have a sick patient, a sepsis patient in the emergency department, you should start your whole sepsis bundle and then use procalcitonin more as a monitoring marker for the patient," Schuetz said.

Not all studies have found a clinical benefit. A meta-analysis of PCT testing found an average 1.28 day reduction in antibiotic therapy in patients with sepsis but no reduction in mortality, mechanical ventilation, clinical severity, or reinfection (Cochrane Database Syst Rev 2017; doi: 0.1002/14651858.CD010959.pub2).

Benefits Tied to Usage

Suboptimal use of PCT tests in the real world may also limit its benefits. A recent retrospective cohort study that included 20,750 U.S. sepsis patients found that about 1 in 5 had a PCT measurement (Clin Infect Dis 2017;64:1509-15). Of those, only 1 in 3 had the serial measurements of PCT recommended by the Infectious Diseases Society of America as part of antibiotic stewardship programs. This analysis didn't find a reduction in antibiotic use, the incidence of *Clostridium difficile* infections, or in hospital mortality.

The study's senior author, Allan Walkey, MD, MSc, an associate professor of medicine at Boston University School of Medicine, cautioned that the data were from 2012 when hospitals may not have been using some of the rapid tests now available. If physicians have to wait a day or two for a result it may "eliminate the potential benefit." A recent survey he led of Massachusetts' hospitals found few currently offer rapid tests (Ann Am Thorac Soc 2017;14:1489–91).

Walkey suggested that better implementation of PCT testing may help. For example, he suggested having algorithms for PCT use and setting up a system in which a first PCT test order automatically triggers a follow-up test. "If you are deciding to use it in your hospitals, there are ways to implement it that mirror what was done in the trials," he said.

Cost: A Stumbling Block?

The relatively high cost of PCT testing also has held back some labs from offering it. "There's no denying that procalcitonin is an expensive test, especially when there was only one Food and Drug Administration [FDA]-approved assay," said Joshua Hayden, PhD, assistant director of the central laboratory at Weill Cornell Medicine in New York City. But the availability of more FDA-approved tests has helped.

Siloed budgets also make PCT testing a difficult investment for laboratories, Schuetz said. He explained that labs incur the tests' cost while pharmacies may reap any savings from decreased antibiotic use, so if institutions aren't looking globally at costs and benefits PCT testing can be hard to justify. Hayden agreed. But a recent cost-effectiveness analysis found that PCT testing beginning on day 1 of intensive care unit admission for sepsis reduced hospital stays by 1.2 days and saved patients an average of $2,757 on total hospital costs, though

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lab costs were $81 higher (Chest 2017;151:23-33).

"Procalcitonin is a great example of why we need to change the paradigm of lab testing and lab reimbursement," Hayden said. "We need to start thinking, we do lab testing so that we enjoy the benefits of higher quality, higher value care."

The availability of tests with more rapid turnaround times has also helped. Initially, Hayden's lab was running PCT tests in batches 3 times a day with an average turnaround time of 6 hours. Recently, the lab implemented a new system with a more rapid turnaround. "Now, you can get your result back in time to decide what to do with the next dose of antibiotics," Hayden said.

A Team Approach

"Labs want to make sure that if they're going to invest in procalcitonin testing, they have a comprehensive team that is going to make sure that it is ordered appropriately," Hayden said.

Both LAC+USC and Weill Cornell Medicine provide clinicians with detailed interpretation algorithms and reference intervals and have educated appropriate departments. Pharmacists also discuss PCT testing during daily rounds.

"Now that we've had the test for over a year, we see much more appropriate ordering patterns," said Chambliss. She noted that some hospitals limit PCT test orders to certain departments or clinicians to ensure proper use.

Consulting with the departments that would use the test is a good place to start, Hayden suggested. Chambliss said she and her colleagues aim for a 2-hour turnaround for PCT tests ordered stat. But at some institutions longer turnarounds such as 4 to 6 hours may be sufficient. "If a lab is worried about providing a rapid turnaround, ask your clinical colleagues. It may not be needed as quickly as one might think," she said.

There also are some unanswered questions about the use of PCT. More study of its use in infections other than sepsis and respiratory infections is needed, Schuetz said. In addition, some controversy remains about appropriate PCT test cutoffs. LAC+USC and Weill Cornell Medicine use cutoffs that are common in the field based on the studies to date. But many of those studies used older versions of the test and there isn't much comparative data available about newer tests.

"There are a lot more assays out there than there used to be, and we don't have good data as far as how harmonized these assays are," Chambliss said. For now, she and her colleagues are collecting data and collaborating with laboratorians at other institutions to optimize and assess the use of PCT.

LABS THAT INVEST IN PROCALCITONIN TESTING NEED A TEAM TO MAKE SURE IT'S ORDERED APPROPRIATELY

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Disclosures: Dr. Hayden reports receiving honoraria from BD and research support from Agilent Technologies in the past year, and honoraria from Roche 2 years ago. Dr. Schuetz reports research support from bioMerieux, Thermo Fisher, Roche, and Abbott.

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Analytes: Procalcitonin

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GETTING STARTED WITH Laboratory Infor

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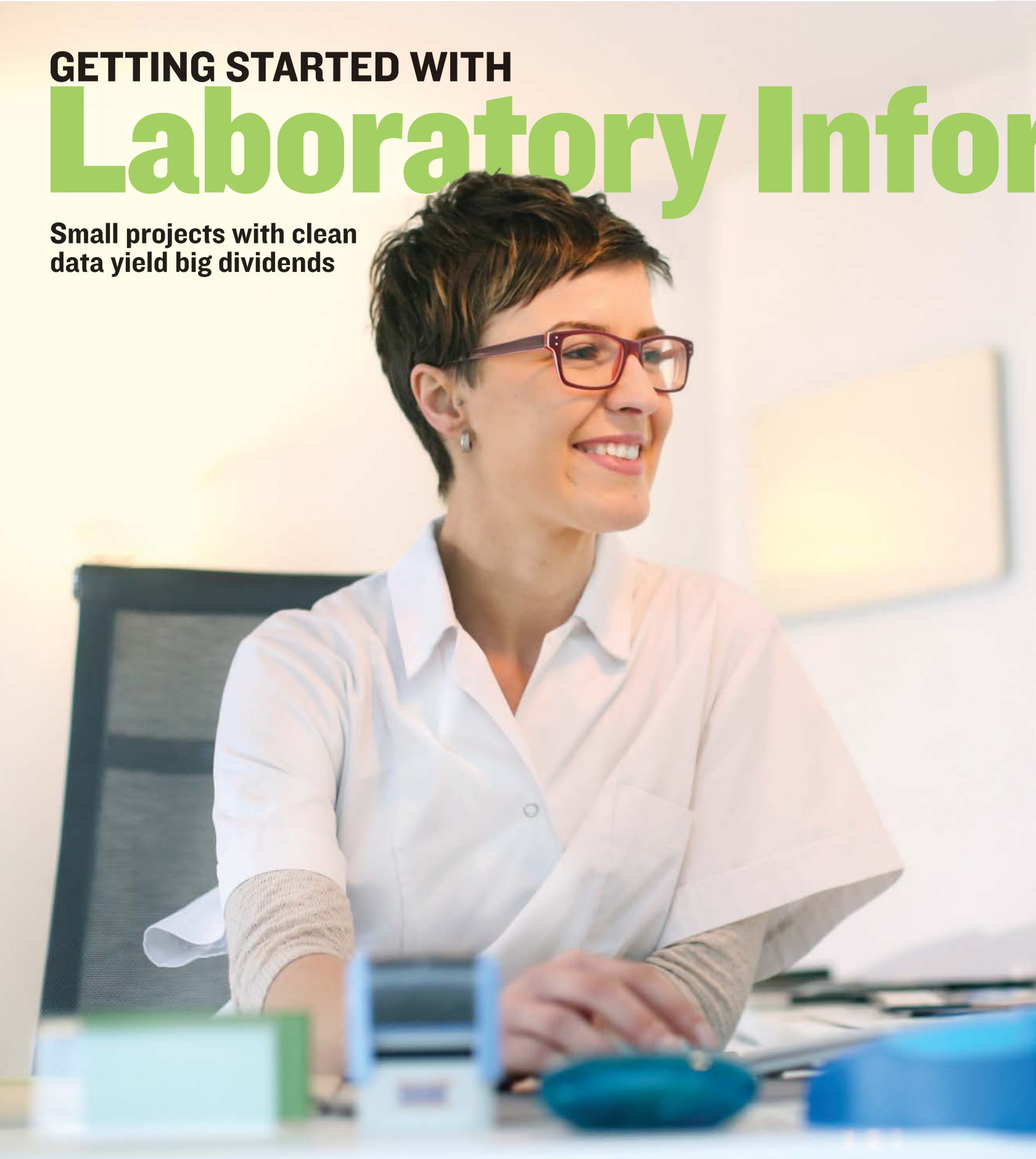

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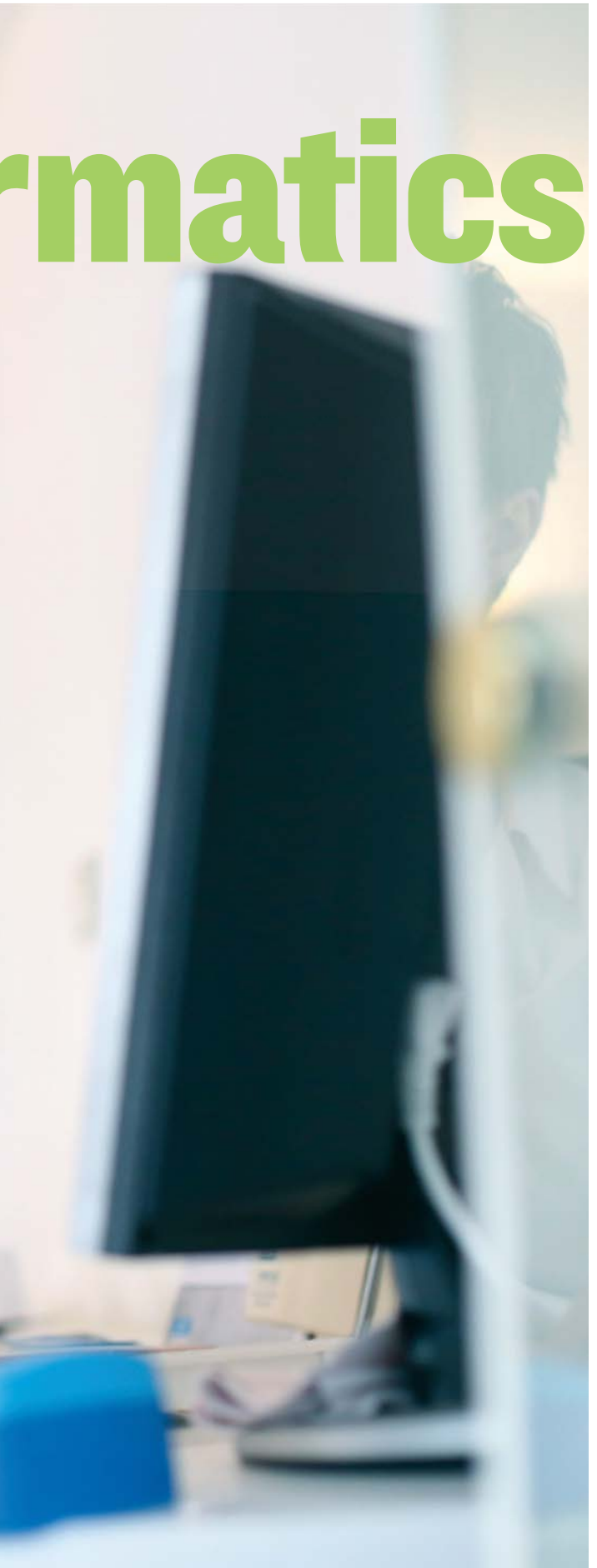

BY JULIE KIRKWOOD

Artificial intelligence, super computers, and predictive analytics may be the wave of the future, but clinical laboratorians shouldn't be intimidated by these buzzwords. Labs don't need IBM Watson and a huge research budget to reap the benefits of informatics for improving laboratory efficiency and quality. Plenty can be accomplished working on desktop computers with free or relatively simple software, said Christopher McCudden, PhD, DABCC, FAACC, FCACB, a clinical biochemist at Ottawa Hospital in Ottawa, Ontario, Canada.

McCudden, who taught himself the statistical programming language R, uses data for big research projects or system improvement initiatives, such as tracking down doctors who seem to be ordering unnecessary or expensive tests. He also uses it for simple tasks, such as figuring out whom to contact about updates to a test: He simply runs a report to find out who orders the test in question most frequently.

Getting to this point took a lot of work, but his laboratory has become a resource within the wider healthcare system for data analysis and information, McCudden emphasized. "We bring information to the table rather than just pushing out a result," he said. There are many ways for laboratorians to get started with informatics. McCudden outlined several in an opinion piece he co-authored last year (J Lab Precis Med 2017; doi: 10.21037/jlpm.2017.09.07).

What Data Can Do

A great place to start with lab informatics is in improving test utilization, according to Julia Drees, PhD, DABCC, scientific director of clinical chemistry at Kaiser Permanente Regional Laboratory, Northern California in Richmond. "That's very simple but very powerful because if you suspect that people are ordering this expensive test wrong, you can say, who's ordering it?" Drees commented.

One of her colleagues analyzed laboratory data to figure out why clinicians were ordering immunofixation electrophoresis multiple times a year. This expensive test is best suited for identifying the clone of the paraprotein upon diagnosis, and the clone rarely changes over the course of disease. But the IFE test at their laboratory also provided levels of IgG, IgA, and IgM.

It turned out that it was this quantitation the providers wanted with their frequent orders. They used it to determine if levels were decreasing with treatment. The lab was able to redirect the majority of repeat orders to the less expensive test that simply quantifies IgG, IgA, and IgM.

Another of Drees' colleagues, a physician, performed an analysis to show his fellow clinicians that they were frequently ordering vitamin D tests on patients older than age 70, while the data showed that those patients were some of the least likely to be insufficient for vitamin D, probably because they were taking multivitamins.

A second valuable use for laboratory data is in identifying populations for reference ranges. Using data compiled from several sources, Drees' laboratory can select a healthy reference population by excluding samples from certain patients whose charts contain any diagnosis codes, prescriptions, or results related to the disease or condition of interest. This gives the staff confidence that the reference range is derived from a truly healthy population, she said.

Another simple but powerful use of laboratory informatics is to monitor and improve turnaround time. Daniel S. Herman, MD, PhD, assistant professor of pathology and laboratory medicine at the Hospital of the University of Pennsylvania in Philadelphia, monitors how quickly the lab returns troponin results for emergency patients. The laboratory has been monitoring this with monthly reports and is now collaborating with data specialists to see if they can produce daily, and ultimately, live dashboards.

"There are various factors that impede our ability to quickly perform our testing and return [results] to clinicians," Herman said. "Building these reports will allow us to identify which ones we could actually improve upon."

His laboratory also used data to improve hemoglobin A1c turnaround time. The staff started by setting a goal to return results by the end of the day for all specimens received by noon and by noon the next working day for the rest. Technologists used the turnaround

time reports to identify problematic testing factors, such as higher volume on Mondays and delays for repeat tests, and suggested operational changes. They are now meeting their goal for more than 97% of test orders, Herman said.

While Herman and Drees both work at larger institutions and have support from data analytics experts, projects on a smaller scale still produce actionable results, according to experts.

"It's important for labs to remember, it's not about technology. It's fundamentally about the problem you're trying to solve. … The technology makes it easier, but it doesn't do it for you."

First Steps

Even before digging into data projects, one of the most foundational informatics tasks a laboratory should undertake is making sure the laboratory information system (LIS) and electronic medical record system are working effectively, noted Brian R. Jackson, MD, MS, associate professor of pathology at the University of Utah and medical director of IT and pre-analytic services at ARUP Laboratories in Salt Lake City. "That's not sexy, but it's what every lab needs to do," said Jackson, who also serves on *CLN*'s Patient Safety Focus editorial board.

This includes actively managing the test menu options so that clinicians can quickly find the appropriate tests. For example, if the hospital infectious diseases team has decided that a certain respiratory virus panel is the appropriate first line test for influenza A in hospitalized patients, a clinician likely will search the menu for "influenza" and may not find the right test if it's listed under "r" for "respiratory."

Jackson also recommends performing chart reviews based on what clinicians see online, not just how results look on paper. In addition, labs should ensure they have a good test directory website and that stakeholders know about it and can find it. Finally, he suggests that labs make it easy for clinicians to contact them by getting into the loop with whichever systems clinicians use to communicate, such as secure text messaging.

"If the lab is not doing that stuff really well, then it's not usually going to be well positioned to go beyond that in terms of interesting informatics," Jackson said.

Beyond the Basics

For laboratorians who are ready to take the next step, the first hurdle is getting access to data, McCudden said. LISs generally are built for inputting data—not taking data out. Access will require help from the information technology team and often support from administrators, who may worry about the security and privacy of the data.

Then there is the question of tools. Basic spreadsheet programs, such as Excel, can be useful for small datasets, McCudden said. However, laboratorians who expect to analyze data regularly using large datasets and who want automated reports should consider third-party software such as Tableau or Microsoft's Power BI, or even learn to program in R (the software is free and there are many free online educational tools).

Though necessary, tools are secondary to the business problem at hand, said Jackson at ARUP. "It's important for labs to remember, it's not about technology," Jackson said. "It's really fundamentally about the problem you're trying to solve. … The technology makes it easier, but it doesn't do it for you."

Often the data are only a starting point, McCudden agreed. "It's not a substitute for talking to people, holding meetings, and implementing change management," he said.

A first look at the data should always include a reality check to make sure it's not garbage, McCudden noted. Is one doctor ordering all the tests for an entire division? Is it taking 6 hours to report a troponin result? Something may be wrong with the data. Check your findings using knowledge of the laboratory. Talk to people in other departments. The last thing the laboratory needs is a glossy report based on bad data. "It's one of the biggest risks," he said. "You can get 10,000 rows of data really easily, but it could be a massive pile of junk if it's not validated."

Armed with good data, there are many business problems laboratories can take on. For example, data on how often a test is performed can be used to determine how often to run quality control, or whether a test should be batched, sent to a reference lab versus performed in-house, or whether a new instrument is warranted. Data on test volume helps with scheduling staff and couriers, too. Turnaround time data can be used to monitor whether a laboratory is meeting clinical goals, to discover bottlenecks, or see if changes have been effective.

The key, Herman emphasized, is to choose a project that is actionable and to talk to your colleagues to make sure the data makes sense. "If you don't understand where the data's coming from, it's really tough to draw the right conclusions from it," he said, "and very easy to make mistakes."

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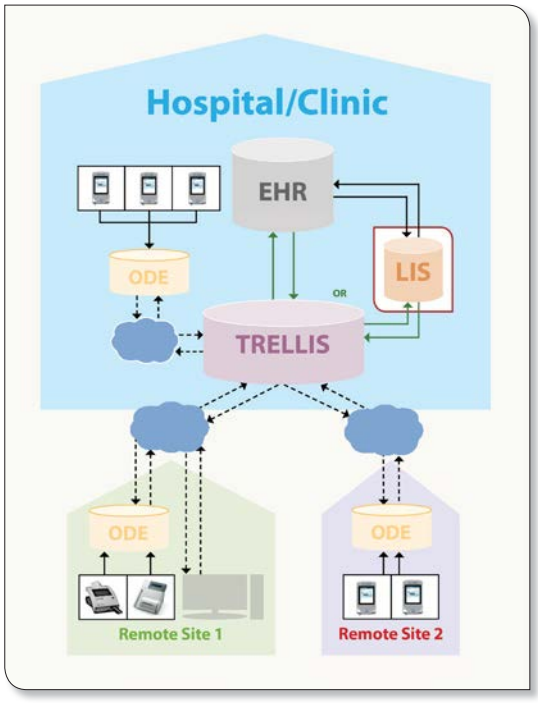

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Colorectal Cancer: TUMOR-TAILORED TREATMENT

BY ZAHRA SHAJANI-YI, PHD, NRCC, AND MARK A. CERVINSKI, PHD, DABCC, FAACC

Historically, treatment for colorectal cancer (CRC) has been guided primarily by cancer stage, morphology, and family history. However, as technological developments over the last decade have reduced the turnaround time and cost of molecular methods, DNA testing of tumor tissue has rapidly become the standard of practice for personalizing treatment, particularly in the case of metastatic disease.

Predictive biomarkers help direct therapy decisions by providing information on differences in treatment response in biomarker-positive patients compared to biomarker-negative patients. Molecular analysis of tumor tissue also provides treatment-independent prognostic information on outcomes such as overall survival (OS) time or progression-free survival time.

In 2017, the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and American Society of Clinical Oncology established evidence-based guidelines for molecular biomarker testing of colorectal tumor tissue as an aid in directing treatment *(3)*. The guideline committee reviewed 123 articles published from January 1, 2008, to February 12, 2015, and established 21 guidelines. Six of these centered on specific tumor tissue biomarkers (*NRAS, KRAS, BRAF, PIK3CA, PTEN)* and mismatch repair (MMR) testing that may determine etiology, stratify patients by prognosis, or measure treatment response. We expand on five of these guideline statements in this article.

A Molecular History of CRC

CRC is a heterogeneous disease resulting from the accumulation of genetic and epigenetic alterations. The etiology of CRC impacts treatment, prognosis, management, and surveillance frequency.

The overall 5-year CRC survival rate is approximately 65%, with the main prognostic factor for survival being cancer stage at diagnosis. The 5-year survival rate is approximately 90% for Stage I and declines to about 70% for Stage II, 58% for Stage III, and less than 15% for Stage IV, with mortality largely attributed to metastasis *(1)*. At the time of diagnosis, 25% of CRC patients present with metastasis and nearly 50% of all patients with CRC will develop metastasis, with the liver being the most common site *(2)*. Early intervention and successful resection of the primary tumor are often curative; however, early stage disease typically does not present with symptoms, highlighting the importance of CRC screening programs.

Colonoscopy remains the gold standard CRC screening method but suffers from low compliance due to the invasive nature of the test. Noninvasive stool-based screening tests such as fecal occult blood tests (FOBT) and fecal immunochemical tests likewise have less than ideal participation rates. The dietary restrictions patients need to adhere to before FOBT also limit its uptake, and this method generally has low overall sensitivity.

The serum-based tumor marker carcinoembryonic antigen (CEA) has low sensitivity and specificity for CRC, particularly in the early stages when resection would have the most impact. Consequently, CEA testing is only recommended for monitoring cancer recurrence, not detecting the disease.

Most CRC tumors are sporadic (70%–80%), and age remains the greatest risk factor. The genes most commonly mutated in CRC include *APC* (in about 80%–82% of cases), *TP53* (48%–59%), *KRAS* (40%–45%), and *PIK3CA* (14%–18%); however, numerous other genes show mutations at significantly lower frequencies *(4)*.

The pattern of mutations and epigenetic alterations of these genes influence how normal colon tissue progresses to CRC. The two most common pathways of tumor development are chromosomal instability (CIN) and microsatellite instability (MSI), responsible for 60%-75% and 10%–20% of CRC cases, respectively.

CIN is the most common pathway of CRC pathogenesis and also the cause of most sporadic CRC *(5)*. The hypothesis is that as adenomatous tissue grows, it also accumulates genetic mutations or epigenetic changes to gene expression. Notably, only a small percentage of adenomatous polyps progress to CRC. Tumors arising in this pathway typically have aneuploidy and multiple somatic mutations. These can include loss of heterozygosity of *APC* and/or *TP53* genes as well as activating mutations in *KRAS* and *NRAS*.

MSI drives the remaining 10%–20% of sporadic CRC and can be detected as alterations in the length of DNA microsatellite sequences that lead to a very high level of mutations. Functional defects in the DNA MMR system cause MSI-related tumors *(5)*.

Biomarkers Used to Determine Etiology

Guideline Statement #2b BRAF p.V600 mutational analysis should be performed in deficient MMR tumors with loss of MLH1 to evaluate for Lynch Syndrome Risk. Presence of BRAF mutation strongly favors a sporadic pathogenesis. The absence of BRAF mutation does not exclude risk of Lynch syndrome. Strength of Recommendation: Recommendation

MSI occurs in a minority of sporadic CRC cases. In about 75% of these cases, MSI arises from epigenetic silencing via CpG methylation of the promoter for the *MLH1* gene, one of the four MMR genes. Sporadic mutations in the other MMR genes (*MSH2*, *MSH6*, and *PMS2*) also occur, albeit more rarely. In addition to a sporadic pathogenesis, MSI arises

T1 Important Terms

Biomarker	A protein or DNA sequence used for diagnostic, predictive, or prognostic monitoring of diseases such as CRC.
Tumor Marker	A quantifiable protein or hormone typically measured in serum, urine, or body fluids to tumor response to therapy, or to surveil for cancer recurrence.
Mutations	Changes in DNA sequence that alter the function of the gene product. Mutations can be deleterious (loss of function), as in the case of tumor suppressors, or activating (gain of function), as in the case of tumor promoter genes.
Epigenetic Alterations	Non-coding alterations to DNA, such as methylation, that change the transcription of DNA sequences. These changes may repress or enhance the expression of gene products such as proteins.

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from germline mutations to one of the four MMR genes or the *EPCAM* gene. These are the causative mutations of Lynch syndrome, the most common hereditary cause of CRC, accounting for between 2% and 4% of all CRC.

For tumors demonstrating a loss of *MLH1*, the current recommendation is to perform *BRAF* p.V600 mutational analysis of the tumor tissue. The *BRAF* p.V600 mutation is rarely associated with the germline mutations found in Lynch syndrome but occurs in approximately 75% of epigenetically silenced *MLH1* in sporadic MSI tumors. As noted in the guideline statement, the presence of the *BRAF* mutation strongly suggests that the etiology of the disease is sporadic, rather than hereditary.

T1 Description of Strength of Recommendations

Strong Recommendation	Supported by convincing or adequate strength of evidence and clear benefit that outweighs harms.
Recommendation	Some limitations in strength of evidence, quality of evidence, or balance of benefits and harms, but the panel concludes that there is sufficient evidence and/or benefit to inform a recommendation.
Expert Consensus Opinion	Serious limitations in strength of evidence, quality of evidence, or balance of benefits and harms, but the panel concludes that there is sufficient evidence and/or benefit to inform a recommendation.
No Recommendation	Insufficient evidence or agreement on the balance of benefit and harms, values, or costs to provide a recommendation.

While the treatment modalities for sporadic and Lynch syndrome tumors may not differ, identifying patients with Lynch syndrome is important, as it is inherited in an autosomal dominant manner and increases the risk of endometrial, ovarian, gastric, and other cancers *(6, 7)*.

Biomarkers for Predicting Treatment Response

Guideline Statement #1: Patients with colorectal carcinoma being considered for anti-EGFR therapy must receive RAS mutational testing. Mutational analysis should include KRAS and NRAS codons 12 and 13 of exon 2, 59 and 61 of exon 3, and 117 and 146 of exon 4 ("expanded" or "extended" RAS). Strength of Recommendation: Recommendation.

Patients with unresectable or partially resectable metastatic CRC may benefit from adding anti-epidermal growth factor receptor (EGFR)-targeted monoclonal antibody therapies (cetuximab and panitumumab) to their standard chemotherapy regimen. Early studies examining the effectiveness of anti-EGFR therapy demonstrated that this approach improved overall response and reduced risk of disease progression when compared to a standard chemotherapy regimen *(2, 8)*.

While impressive, these initial studies examined the effect of anti-EGFR therapy in an unselected population and found that less than 20% of participants benefited *(9)*. Subsequent studies demonstrated that patients with activating mutations in downstream effectors of EGFR such as *KRAS* and *NRAS* had significantly worse response rates *(10-13)*. These activating mutations in *KRAS* and *NRAS* produce effectors that are independent of EGFR's binding to its ligand, rendering the monoclonal antibody therapy ineffective. This applies to a relatively large population of CRC patients as approximately 40% have an activating *KRAS* mutation, and 7% have an activating *NRAS* mutation. Patients with wild-type *KRAS* and *NRAS* have a significantly improved overall response to anti-EGFR therapy with longer progression-free survival and a higher 5-year OS rate.

These studies also found that *KRAS* and *NRAS* mutation status does not influence patient OS for those only receiving supportive care, reinforcing *RAS* mutational status as a predictive rather than prognostic biomarker.

Guideline Statement #4: There is insufficient evidence to recommend BRAF c.1799 p.V600 mutational status as a predictive molecular biomarker for response of anti-EGFR inhibitors. Strength of Recommendation: No recommendation.

The *BRAF* activating mutation *BRAF* c.1799 p.V600 occurs in approximately 8%–12% of patients with stage IV CRC and about 14% of patients with stage II and III disease. This and the *RAS* mutations often are mutually exclusive *(13)*. The low prevalence of *BRAF* mutations clouds their predictive value in patients with stage IV CRC, and testing for whether *BRAF*-mutant tumors are resistant to anti-EGFR antibody remains controversial.

Published studies have yielded varied and conflicting conclusions. Several have reported that patients with this mutation have a poorer response rate to chemotherapy in combination with cetuximab compared to patients with wild-type *BRAF;* however, a modest beneficial impact from adding anti-EGFR agents also has been reported *(13-15)*.

Prognostic Markers

Guideline Statement #2a BRAF p.V600 (BRAF c.1799 [p.V600]) mutational status should be performed in colorectal tissue in patients with colorectal carcinoma for prognostic stratification. Strength of Recommendation: Recommendation.

This recommendation is supported by numerous publications that have demonstrated that stage II-IV patients with *BRAF* p.V600 mutations have shorter progression-free survival and OS time *(16)*. While there is currently insufficient evidence to determine whether patients with the *BRAF* p.V600 mutation benefit from anti-EGFR therapy, standard treatment regimens are likely insufficient for this population. There also are encouraging findings from clinical trials exploring the combination of standard anti-EGFR therapy with novel *BRAF* inhibitors.

Guideline Statement #3 Clinicians should order mismatch repair status testing in patients with CRCs for the identification of patients at high risk for Lynch syndrome and/or prognostic stratification. Strength of Recommendation: Recommendation.

In addition to identifying patients at risk for Lynch syndrome, MMR

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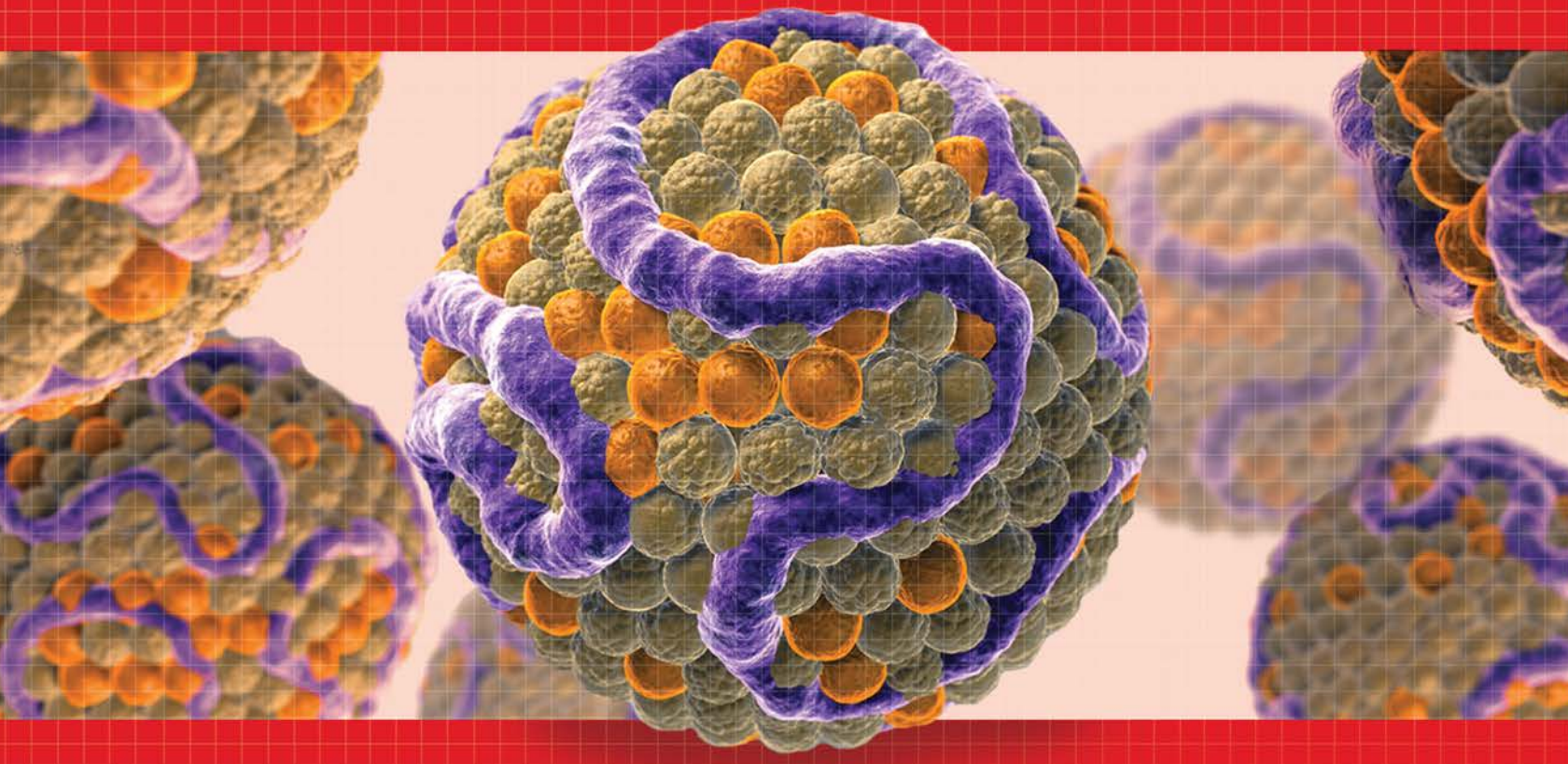
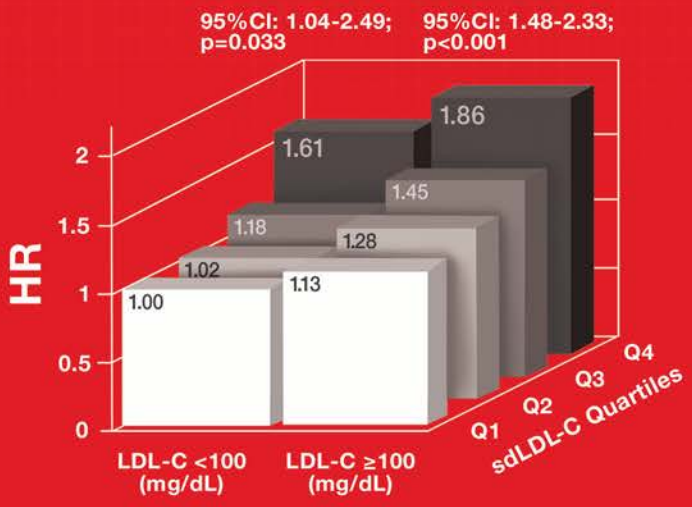


Small dense LDL can help identifying patients at a higher risk for cardiovascular disease and serve for a better management of the risk, especially for whom LDL cholesterol is moderately low.



Adjusted hazard ratios for incident coronary heart disease consisting of myocardial infarction, coronary heart disease death and revascularization by small dense LDL cholesterol (sdLDL-C) quartiles stratified by LDL-C risk categories. Adjusted for age, sex, and race, smoking, body mass index, hypertension, diabetes mellitus, diabetes mellitus medications, and log high-sensitivity C-reactive protein. CI indicates confidence interval (adapted from Hoogeveen et al. Arterioscler Thromb Vasc Biol. 2014;34:1069-1077 with approval).

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testing provides prognostic data for sporadic CRC. Patients with early stage MSI tumors have a better prognosis than those with microsatellite stable tumors. In a meta-analysis summarizing 20 studies that included 9,243 patients, patients with a high level of MSI had a longer OS time. Patients with MSI-positive tumors also had longer overall disease-free survival than patients without MSI-positive tumors *(17)*.

In addition to the prognostic value of MSI status, emerging data indicates that patients with tumors positive for MMR defects may have a better response rate to immune checkpoint inhibitors such as pembrolizumab *(18)*.

Other Potential Biomarkers

Guideline Statement #5 There is insufficient evidence to recommend PIK3CA mutational analysis of colorectal carcinoma tissue for therapy selection outside of a clinical trial. Strength of Recommendation: No recommendation.

Despite screening, some patients with wild-type *RAS* mutations still fail to respond to anti-EGFR monoclonal therapy. Activating mutations in *KRAS* and *NRAS* account for just 40% of anti-EGFR-resistant stage IV CRC patients, suggesting the possibility of other potential negative predictive biomarkers.

Several studies have evaluated *PIK3CA* as a negative predictive marker to anti-EGFR monoclonal antibodies. Approximately 40% of *PIK3CA* mutations co-occur with *RAS* mutations and nearly 50% of *PIKC3A* co-occur with *BRAF* mutations, making it difficult to elucidate the importance of *PIKC3A* as an independent predictive and prognostic marker *(13)*. To understand these effects, more studies are needed with sufficiently large cohorts of patients with wild-type *NRAS*, wild-type *BRAF*, and mutant *PIK3CA*.

Some evidence also suggests that another gene, *TP53*, holds promise as a predictive biomarker to assess treatment response. *TP53* is the most frequent somatic gene mutation in human cancer and is found in approximately half of all adenocarcinomas, making it an exciting potential target for personalized therapy *(4, 21)*.

TP53 has been reported to predict the effect of adjuvant 5-fluorouracil therapy in patients with stage III (N1) CRC *(19)*. In addition, mutant-*TP53* patients with metastatic CRC who received neo-adjuvant chemotherapy had statistically significant poorer outcomes, with decreased 5-year OS rate *(20)*. The role of *TP53* as a prognostic biomarker is still being evaluated: The same study reported no difference in the rate of 5-year OS for mutant-*TP53* and wild-type *TP53* patients who did not receive neo-adjuvant therapy *(20)*.

Unlike *KRAS*, which harbors several high-frequency mutations, numerous discrete *TP53* mutations occur at relatively low frequencies. One study of 456 CRC patients detected more than 130 discrete mutations, with the two most prevalent accounting for just 14% of *TP53*-positive mutations and 7% of all CRCs tested *(21)*. Future studies coupling discrete mutational status with treatment response and overall survival could be immensely valuable for developing exquisitely personalized therapies.

Conclusion

Available treatments for CRC continue to advance, and researchers rapidly are discovering new information about tumorigenesis pathways. These insights are now being translated into new potential treatments in clinical trials targeted to the unique features of each patient's tumor composition, with the goal of improving OS of CRC patients. Continued research will hopefully lead to finely and precisely tailored treatments.

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Future studies coupling discrete mutational status with treatment response and overall survival could be immensely valuable for developing exquisitely personalized therapies.

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Regulatory Roundup

FDA Proposes a New, Streamlined 510(k) Pathway

In the draft guidance "Expansion of the Abbreviated 510(k) Program: Demonstrating Substantial Equivalence through Performance Criteria," the Food and Drug Administration (FDA) proposes new options for demonstrating substantial equivalence for 510(k) submissions through the Abbreviated 510(k) program. Currently, manufacturers seeking 510(k) clearance must prove the safety and efficacy of new devices through comparative testing against predicate devices. However, predicate devices can be old and in certain cases might not closely reflect the modern technology embedded in new devices. If finalized, this guidance would establish a voluntary program for certain well-understood device types that would permit companies to demonstrate that a new device meets FDA-identified performance criteria instead of directly comparing the performance of the new device to a specific predicate device. By allowing a set of objective, transparent, and well-validated performance metrics to serve as the benchmark for evaluating some new devices, FDA aims to offer a more efficient and less burdensome regulatory pathway while maintaining standards for safety and effectiveness.

The agency is seeking comments through July 11 on this draft document at www.regulations.gov.

GUIDANCE FOR NEXT-GENERATION SEQUENCING TESTS FINALIZED BY FDA

The Food and Drug Administration (FDA) has finalized two guidance documents designed to enhance collaboration among researchers and drive the efficient development of novel next-generation sequencing (NGS)-based tests. The first guidance, "Use of Public Human Genetic Variant Databases to Support Clinical Validity for Genetic and Genomic-Based In Vitro Diagnostics," describes a streamlined regulatory approach that allows test developers to rely on clinical evidence from FDA-recognized public databases to support clinical claims for their tests and provide assurance of the accurate clinical evaluation of genomic test results. The second guidance, "Considerations for Design, Development, and Analytical Validation of NGS-Based In Vitro Diagnostics Intended to Aid in the Diagnosis of Suspected Germline Diseases," provides recommendations for designing, developing, and validating NGS-based tests used to diagnose individuals with suspected genetic diseases. The document also clarifies how FDA evaluates premarket submissions to determine an NGS-based test's analytical validity, including how well a test detects the presence or absence of a particular genomic change.

FIRST TEST FOR DRUG-RESISTANT YEAST GETS FDA AUTHORIZATION

Through the de novo premarket review pathway, the Food and Drug Administration (FDA) has authorized the first test to identify the emerging pathogen *Candida auris* (*C. auris*), a yeast that is frequently resistant to multiple antifungal drugs. Specifically, FDA has permitted Bruker Daltonik to expand marketing of the Bruker MALDI Biotyper CA system to include the identification of *C. auris*, adding to the system's already cleared uses for the identification of 424 clinically relevant bacteria and yeast species. The Bruker MALDI Biotyper CA system uses matrix-assisted laser desorption/ionization mass spectrometry in combination with a reference organism database to identify pathogens. FDA evaluated the use of a standard protocol for adding *C. auris* to the system database in conjunction with the performance data from 28 *C. auris* samples and other supporting analytical studies. Findings indicate that the system reliably identifies *C. auris* 100% of the time.

In the future, FDA plans to propose exempting certain mass spectrometry microorganism identification system processes from additional premarket review after a system process receives a first-time FDA marketing authorization.

FDA AUTHORIZES FIRST CONTINUOUS GLUCOSE MONITORING SYSTEM THAT CAN BE INTEGRATED WITH OTHER DEVICES

Dexcom has received Food and Drug Administration authorization through the de novo premarket review pathway to market the Dexcom G6 integrated continuous glucose monitoring system for determining blood glucose levels in children age 2 or older and adults with diabetes. This is the first continuous glucose monitoring system permitted by the agency to be used as part of an integrated system with other compatible medical devices such as insulin pumps. The Dexcom

G6 is a patch device that is applied to the skin of the abdomen and contains a small sensor that continuously measures the amount of glucose in body fluid. The device transmits real-time glucose readings every 5 minutes to a compatible display device and triggers an alarm when a patient's blood sugar levels are too high or low. If the Dexcom G6 is integrated with an automated insulin dosing system, it triggers the release of insulin from the pump in response to a rise in blood sugar.

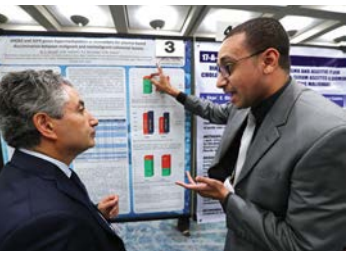
FDA CLEARS CANCER GENETICS' TISSUE OF ORIGIN TEST

Cancer Genetics has received 510(k) clearance from the Food and Drug Administration for its Tissue of Origin (TOO) test following modifications made to test reagents and software. TOO is a microarray-based gene expression test that analyzes a tumor's genomic information to help identify its origin and aid in classifying metastatic, poorly differentiated, or undifferentiated cancers. TOO assesses 2,000 individual genes, covering 15 of the most common tumor types (representing 58 morphologies) and 90% of all solid tumors. These tumors include thyroid, breast, non-small cell lung, pancreas, gastric, colorectal, liver, bladder, kidney, non-Hodgkin's lymphoma, melanoma, ovarian, sarcoma, testicular germ cell, and prostate. Compared to the first version of the test, the current TOO assay uses new labeling reagents and has a higher accuracy rate and shorter workflow with similar precision and reproducibility. TOO is covered by Medicare and provides a pathologist's review and interpretation of a patient's test results and diagnosis.

CURETIS EARNS FDA OK FOR LOWER RESPIRATORY TRACT INFECTIONS TEST

The Food and Drug Administration (FDA) has granted Curetis de novo authorization for the use of the Unyvero system and Lower Respiratory Tract Infection (LRT) application cartridge, which together provide rapid infectious diseases testing with a focus on lower respiratory tract infections. According to Curetis, the Unyvero system identifies the causative pathogen in more than 90% of hospitalized patients with pneumonia and detects genetic antibiotic resistance markers as well. It is also the first automated molecular diagnostic test authorized by FDA for the detection of the atypical microorganism *Legionella pneumoniae*. Using aspirate samples, the test provides results in less than 5 hours. As part of Curetis' FDA application for the Unyvero system and LRT, the company submitted data from a clinical trial that included more than 2,200 patient samples at nine participating U.S. hospitals. Curetis now intends to apply for a label claim extension for the LRT that would include the bronchial lavage sample types, as well as several additional diagnostic targets.

Face Time WITH THE FUTURE





In their day-to-day work, clinical laboratorians often are intensely focused on the present moment: meeting turnaround time goals, calling clinicians with critical values, or troubleshooting instrument problems to make sure patients get the best care possible.

But in a broader sense, laboratory medicine always has been focused on the future. Laboratorians are known for being dissatisfied with the status quo and for continuously searching for ways to improve quality, refine measurements, or discover fresh answers to tough healthcare problems.

This dual citizenship in the present and the future explains why more than 20,000 people from all over the world gather every year at the AACC Annual Scientific Meeting & Clinical Lab Expo. Laboratorians crave new insights and meaningful connections that will nourish their natural curiosity—and professional zeal—to explore the field's latest science and technology.

Importantly, the meeting means a lot more than just a place to process information. In an age when screen time seems ever more pervasive, a face-to-face conference offers authentic connections and an opportunity unlike any other for inspiration, refreshment, and discovery.

Here are a few ways to boost your in-person time with world-renowned experts and like-minded colleagues whom you won't meet anywhere else.

1 Poster Walks

Those who have attended the AACC Annual Scientific Meeting before know that often the best way to meet colleagues and collaborators is during the poster sessions. But with nearly 1,000 posters, no one can see them all. One of the best ways to get a focused experience during the poster sessions is by attending a poster walk. Led by experts from one of AACC's 20 scientific divisions, attendees tour posters by topic areas and participate in engaging discussions of study findings and methods. Check *CLN Daily* on-site for details.

2 Oral Abstract Presentations

Each year, the Annual Meeting Organizing Committee hand-picks a series of outstanding abstracts for special oral presentations. Presenters will also be available at their posters during the poster sessions. There are six topics this year.

Monday, July 30
Global Health
Clinical Applications

Tuesday, July 31
Mass Spectrometry
Molecular Diagnostics and Genomics

Wednesday, August 1
Emerging Biomarkers and Technologies
Hot Topics in Lab Medicine

3 Meet the Experts

With attendance limited to 75 attendees, expect intensive, interactive discussions with plenary speakers Monday-Thursday of the conference. Show up early to these morning sessions and be ready with questions. Plenary speakers include:

Sunday, July 29
Brian Druker, MD: Imatinib as a Paradigm of Targeted Cancer Therapies

Monday, July 30
Kenneth Setchell, PhD: Genetic Defects in Bile Acid Synthesis—Translational Medicine from Mass Spectrometry Discovery to the Bedside

Tuesday, July 31
Denise Galloway, PhD: HPV Associated Cancers and the HPV Vaccine

Wednesday, August 1
James Collins, PhD: Nucleic Acid Detection Using CRISPR-Dx

Thursday, August 2
Timothy Amukele, MD, PhD, and Lee Schroeder, MD, PhD: Essential Diagnostics—Meeting the Needs of a Global Population

4 New for 2018: Explore Topic Tracks

Eight topic tracks provide paths through different areas of laboratory medicine and include both large symposia as well as more intimate brown bag sessions. Talking with fellow attendees after a symposium or during a brown bag session is a great way to gain real-world insights into the content.

- **Endocrinology**
- **Genomics/Genetics**
- **Mass Spectrometry**
- **Pediatric/Maternal-Fetal**
- **Point-of-Care Testing**
- **Precision Medicine and Oncology**
- **Toxicology/Therapeutic Drug Monitoring**
- **Utilization and Lab Management**

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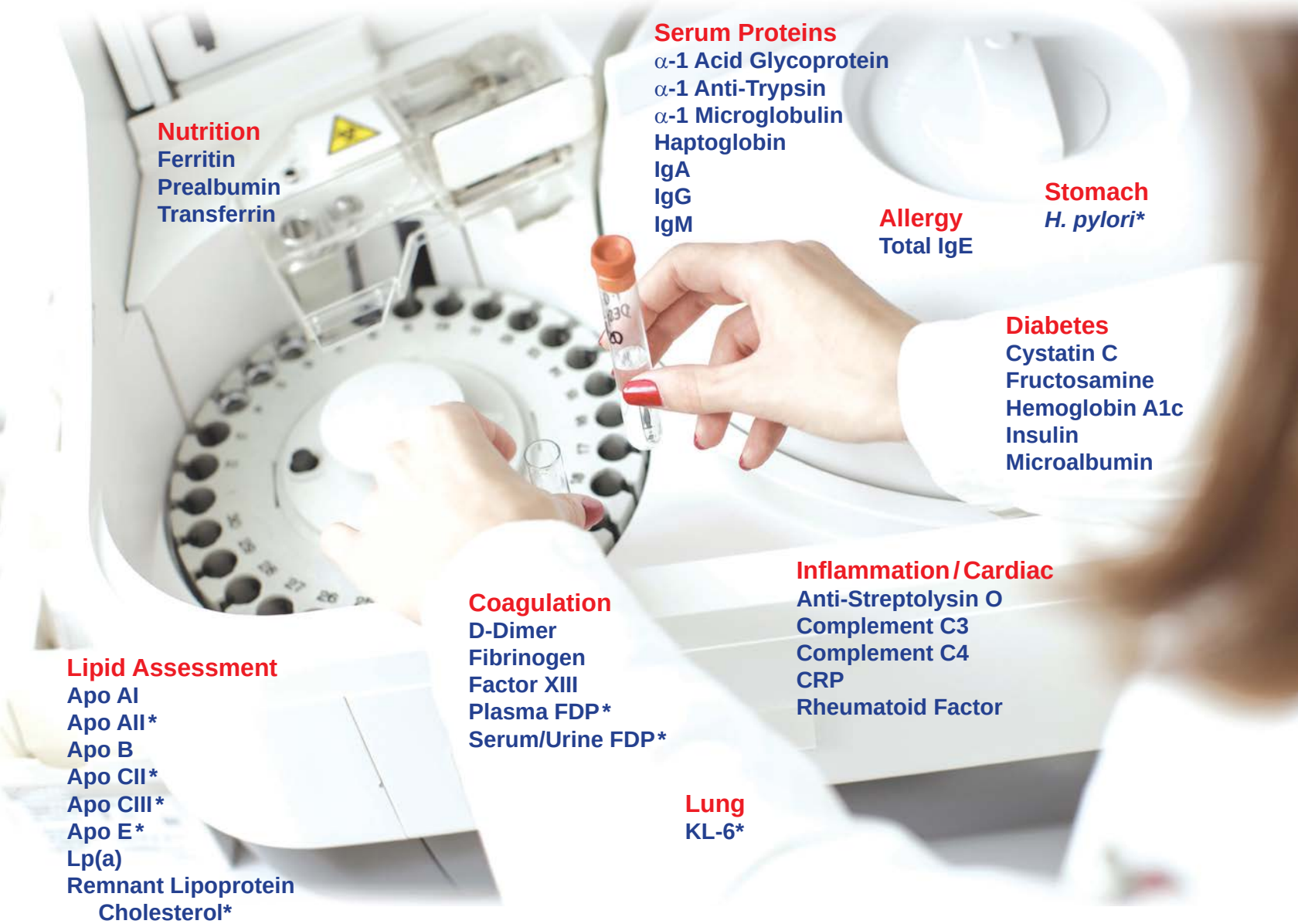

Nutrition
Ferritin
Prealbumin
Transferrin

Serum Proteins
α-1 Acid Glycoprotein
α-1 Anti-Trypsin
α-1 Microglobulin
Haptoglobin
IgA
IgG
IgM

Allergy
Total IgE

Stomach
*H. pylori**

Diabetes
Cystatin C
Fructosamine
Hemoglobin A1c
Insulin
Microalbumin

Inflammation / Cardiac
Anti-Streptolysin O
Complement C3
Complement C4
CRP
Rheumatoid Factor

Coagulation
D-Dimer
Fibrinogen
Factor XIII
Plasma FDP*
Serum/Urine FDP*

Lipid Assessment
Apo AI
Apo AII*
Apo B
Apo CII*
Apo CIII*
Apo E*
Lp(a)
Remnant Lipoprotein Cholesterol*

Lung
KL-6*

New Products Now Available!!

- *H. pylori* Test Reagent* for chemistry analyzers
- Remnant Lipoprotein Cholesterol* reagent for chemistry analyzers
- KL-6 (Krebs von den Lungen-6)* reagent for chemistry analyzers

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2018 AACC CLINICAL LAB EXPO EXHIBITORS

BOOTH NUMBER	EXHIBITING AS
1838	A/C Diagnostics LLC
2231	AACC
2131	AACC Middle East
1122	Aalto Scientific, Ltd.
2012	Abbott
3005	Abbott
3139	ABIMO
3140	ABIMO
3239	ABIMO
3240	ABIMO
2185	Abraxis, Inc.
4084	Absolute Antibody, Ltd.
3461	Academy of Instrumentation Science Co., Ltd.
1055	Accel Biotech LLC
3075	Access Bio, Inc.
3943	Access Biologicals, LLC
3653	AccuBioTech Co., Ltd.
1675	Acon Laboratories, Inc.
872	Acro Biotech Inc.
3669	Addcare Biotech Co., Ltd.
1556	Adhesives Research, Inc.
3045	Advanced Instruments
3864	Advanced Microdevices Pvt. Ltd.
3055	Aesku Diagnostics
653	Agappe Diagnostics Switzerland GmbH
3175	Agena Bioscience
4674	Agilent Technologies
3557	Ahlstrom Filtration LLC
4458	Ahram Biosystems, Inc.
4184	Aikang MedTech Co., Ltd.
3776	Aiken Corp.
4648	Aim Lab Automation Technologies Pty Ltd.
4680	Akatsuki Technology Co Ltd
4568	ALCOR Scientific Inc.
1149	Alfa Scientific Designs, Inc.
2471	ALIFAX S.r.l.
4477	ALine, Inc.
3970	All Flex Flexible Circuits
3467	ALPCO
4044	Altran
3180	America Diagnostics
2072	American Proficiency Institute
568	Anaerobe Systems
1641	ANBIOTEC - Brazilian Biotechnology and Life Sciences Companies Association
3480	Andwin Scientific
757	Ansh Labs, LLC
4658	Apacor Ltd.
854	Applied Biocode, Inc.
1174	APTEC Diagnostics NV
3858	Arista Biologicals Inc.
1821	ARK Diagnostics, Inc.
3836	ARKRAY
1022	Arlington Scientific Inc.
1842	Artel
863	Artron BioResearch Inc.
2448	ARUP Laboratories
3561	Asahi Kasei Corporation
1467	ASCO
467	ASCP (American Society For Clinical Pathology)
1372	ASP Lab Automation AG
969	Associates of Cape Cod, Inc.
3482	Athens Research & Technology
459	Atlas Genetics
1886	Atlas Medical
1663	Audit MicroControls, Inc.
4667	Auer Precision Co.
4451	Autobio Diagnostics Co., Ltd.
1248	AutoGenomics
3968	AVE Science & Technology Co., Ltd.
2467	AVIOQ, Inc.
1144	Awareness Technology, Inc.
3642	AWEX
3859	Axxin
4277	Azer Scientific
1470	B&E Diagnostics inc.
3581	Baebies
3385	Balda C.Brewer, Inc.
412	Bangs Laboratories/Polysciences
4076	Bao Ruiyuan Biotech (Beijing) Co., Ltd.
1344	BBI Solutions
2224	BD Diagnostics
2135	Beaufort
1078	Beaver Biomedical Engineering Co., Ltd.
3612	Beckman Coulter
4557	Beijing Bohui Innovation Technology Co., Ltd.
3470	Beijing DDM Technology Co.,Ltd
4339	Beijing Diagreat Biotechnology Co., Ltd
3770	Beijing Expert Medical Technology Co., Ltd
1279	Beijing Key-Bio Biotech Co., Ltd.
1063	Beijing Leadman Biochemistry Co., Ltd.
4662	Beijing MarrBio-Pharmaceutical Co.,Ltd
3777	Beijing O&D Biotech Co., Ltd.
4443	Beijing Unidiag Technology Inc.
3645	Belgian Volition sprl
3278	Benchmark Electronics
2044	Binding Site, Inc.
1679	BioActs
1058	BioAssay Works, LLC
4081	BIOBASE
4280	Biocartis
773	BioChain
4605	Bio-Chem Fluidics Inc.
4243	Biocross S.L.
3844	BioDot, Inc.
3905	BioFire Diagnostics, LLC
4144	Biofortuna Ltd.
1177	BioHit OYJ
4358	BioIVT
4582	BioLegend, Inc.
752	Biological Dynamics, Inc.
2882	BIOLYPH, LLC
3771	Biomat srl
4176	Biomatrica, Inc.
1158	BioMedica Diagnostics Inc.
362	BioMedomics, Inc.
3605	bioMérieux Inc.
1251	Bioneer Corporation
569	BioNex Solutions
4654	Biopharma Technology LLC
2031	Bio-Rad Laboratories
631	Bio-Rad Laboratories
1070	Bioresource Technology, Inc. (US)
4353	Bioscience (Tianjin) Diagnostic Technology Co., Ltd.
3786	BioSoft Integrators, Inc.
1459	BiosPacific
4660	BioSynex
3281	BIOSYNTH International
1044	Bio-Techne
357	BioTek Instruments
444	BioVendor Group
3248	BIT Group
3849	Block Scientific
3286	BMT USA, LLC
4460	Boditech Med Inc.
3753	Bomi Group
1484	BONRAYBIO CO., LTD.
3081	Boule Diagnostics AB
770	Brandwidth Solutions
1578	Broad (Shanghai) Exhibition Business Co., Ltd.
4563	BUHLMANN Diagnostics Corp
3648	Burkert Fluid Control Systems
2075	Byline Financial Group
4168	Byron-Diagnostics (Shanghai) Co., Ltd.
756	CalBioreagents
2363	Calzyme Laboratories, Inc.
3578	Cangzhou Shengfeng Plastic Product, Co., Ltd.
4139	Canon BioMedical
3414	Caplugs / Evergreen Labware
4167	Capralogics Inc.
1651	Capricorn Products LLC
415	Carolina Liquid Chemistries
352	Carville Ltd
4349	Cedarlane
636	CellaVision AB
3100	Centers for Medicare & Medicaid Services
556	Cerba Specimen Services
448	CERTEST BIOTEC S.L.
367	CGM LABDAQ
4369	Changzhou Prefluid Technology Co., Ltd.
857	Chemtron Biotech, Inc.
4572	ChemWare
4444	Chengdu Zen Bioscience Co.,Ltd
1275	Chroma Technology Corp.
1922	Chromsystems GmbH
4054	Cibernética de Mexico
1653	CKD USA Corp.
1642	Cleveland Clinic Laboratories
3520	Clinical and Laboratory Standards Institute
4378	Clinical Genomics
3300	Clinical Laboratory Products
4270	Clippard Instrument Laboratory, Inc.
645	CLTech Corp.
1375	Cognex Corporation
417	COLA
2026	College of American Pathologists
751	COMTRON CORPORATION

3751.....Conductive Technologies, Inc.
2035.....Cone Bioproducts
4205.....Copan Diagnostics, Inc.
4245.....Core Technology Co., Ltd.
3742.....Coris Bioconcept
3635.....Cosmo Biotechnologies LTD
4238.....Cowin Biosciences Co., Ltd.
3878.....CPC Colder Products
4570.....CRYSTAL Technology & Industries, Inc.
1244.....CTK Biotech, Inc.
3463.....CTK Biotech, Inc.
1121.....Curetis USA
3185.....Currier Plastics, Inc.
749.....DAAN Gene Co., Ltd. of Sun Yat-sen University
1751.....Data Innovations LLC
3452.....DCN Diagnostics, Inc.
3048.....Denka Seiken Co., Ltd.
664.....DenLine Uniforms, Inc.
414.....Desert Biologicals/Omega Biologicals
457.....Dexter Magnetic Technologies
1175.....DFI Co., Ltd.
4171.....DiaCarta
3746.....DIAGAM S.A.
3744.....DIAGENODE DIAGNOSTICS
1861.....Diagnostic Automation/Cortez Diagnostics
1224.....Diagnostica Stago, Inc.
4263.....Diagnostics Biochem Canada Inc.
337.....DiagnostikNet-BB e.V.
349.....DiagnostikNet-BB e.V.
2364.....DIALAB GmbH
3941.....Diamond Diagnostics Inc.
4241.....Diamond Technologies Inc.
3053.....DIARECT AG
2853.....DiaSorin Inc.
3642.....DIAsource ImmunoAssays s.a.
4041.....DiaSys Diagnostic Systems GmbH
2275.....Diatron MI Zrt
1014.....Diazyme Laboratories
3555.....DIBA Industries, Inc.
4409.....Diener Precision Pumps
4442.....Dier Biotech Co., Ltd.
4422.....DIESSE Diagnostica Senese S.p.A
1478.....Dino-lite Scopes (BigC)
3426.....Dirui Industrial Co., LTD
4357.....Dr. Fooke Laboratorien GmbH
3438.....DRG International, Inc.
1151.....Drucker Diagnostics
3972.....Drugdu Technology Co., Ltd.
748.....Drummond Scientific Co.
1981.....DSM Pentapharm
1684.....DWK Life Sciences
3954.....Dxgen Corp.
3977.....Dx-Sys, Inc.
4352.....Dynamiker Biotechnology (Tianjin) Co., Ltd.
3441.....Dynex Technologies Inc.
967.....EastCoast Bio, Inc.
3778.....Eastern Business Forms Inc
1985.....EasyDx Inc.
4405.....Edan Instruments, Inc.
3880.....EKF Diagnostics Inc.
1670.....ELGA Labwater
4131.....ELITech Group
2062.....Ellkay
1476.....ELMI North America
4371.....Enplas Corporation
1839.....Envigo Bioproducts, Inc.
3280.....Enzo Life Sciences
3673.....Enzyme Research Laboratories, Inc.
469.....ePath Logic, Inc.
4663.....Epitope Diagnostics, Inc.
3419.....Eppendorf North America
3971.....Equitech-Bio, Inc.
639.....Era Biology
325.....ERBA Diagnostics
1852.....Eudipia Co., Ltd.
1040.....Euroimmun US
1178.....Eurospital S.p.A.
3841.....Eurotrol, Inc.
649.....Express Diagnostics
3632.....EZLife Bio, Inc.
3285.....Fabrico Medical
959.....Fapon Biotech Inc.
3577.....Ferrotec (USA) Corp.
462.....Festo Corporation
4178.....Finger Lakes Instrumentation, LLC
1363.....Fitzgerald Industries Int'l
2142.....Fluid Metering, Inc.
4281.....Flytech Technology Co., LTD
1482.....Follett LLC
4377.....Fralock
2272.....FUJIFILM Medical Systems USA, Inc.
2839.....Fujirebio
3684.....FUSION BIOTEC, Inc.
2085.....GBF, Inc
4255.....GE Healthcare
3667.....Gems Sensors & Controls
1784.....GENBODY, INC.
1074.....GENEALL BIOTECHNOLOGY
3563.....Genereach
4622.....GenMark Diagnostics, Inc.
3076.....Genolution
4261.....GenomeWeb LLC
4159.....GenPrime Inc.
957.....Genrui Biotech Inc.
4559.....Gentian AS
1458.....GenWay Biotech, Inc.
1741.....GeSiM mbH
652.....Getein Biotech, Inc.
3631.....Ginolis Ltd
1020.....Globe Scientific Inc.
3340.....GNA Biosolutions
3956.....Gold Colloid, Co.
4612.....Gold Standard Diagnostics
4653.....Golden Biotechnologies Corp.
3457.....Golden West Biologicals, Inc.
4338.....GoldMag Nanobiotech
1440.....Greiner Bio-One, Inc.
4457.....Grenova, LLC
2444.....Grifols
3855.....Guangdong Uniten Biotechnology Co., LTD
3784.....Guilin Royalyze Medical Instrument Co. LTD
3885.....GVS North America
4275.....Haematologic Technologies, Inc.
1369.....Haemonetics Corporation
4686.....Hahn-Schickard
4554.....Haier Medical and Laboratory Products Co., Ltd.
4219.....Hamilton Company
3656.....Hangzhou Biotest Biotech Co., Ltd
4546.....Hangzhou Clongene Biotech Co., Ltd.
1176.....Hangzhou Gene Era Biotech Co., Ltd
3585.....Hangzhou Lifereal Biotechnology Co., Ltd.
4646.....Hangzhou Realy Tech Co. Ltd
3384.....HANGZHOU ROLLMED CO., LTD
4536.....Hangzhou Safecare Biotech Co., Ltd.

4341.....Hangzhou Zheda Dixun Biological Gene Engineering Co.,Ltd.
968.....Hardy Diagnostics
3848.....hc1.com
848.....Healgen Scientific LLC
2279.....Health Gene Technologies Ltd.
353.....Hebei Xinle Sci. & Tech Co., Ltd.
3514.....Helena Laboratories Corporation
1874.....Helmer Scientific
4208.....Hemosure / WHPM
572.....Hettich
3418.....HiberGene Diagnostics Ltd
4340.....HICOMP Microtech (Suzhou) Co., Ltd.
3773.....Higuchi Inc. USA
3574.....Hipro Biotechnology Co., Ltd
4657.....Hitachi Chemical Diagnostics
3176.....Hochuen International Corp
1831.....Hologic, Inc.
4059.....Hoover Precision Products, LLC
3205.....HORIBA Medical
4606.....HORIBA Medical
640.....HTI Medical
2875.....Hycor Biomedical
3948.....HyTest
3874.....I.W. Tremont
4462.....IBL-America
3978.....ICA Corporation
3078.....Icosagen Cell Factory
4519.....IDEX Health & Science
3242.....IDG Sanzay Corp
4531.....IDS Co, LTD
1049.....Iline Microsystems
3434.....IMEGEN
3651.....IMI Precision Engineering
1648.....Immucor, Inc.
3421.....Immundiagnostik AG
3151.....Immuno Concepts
1640.....ImmunoChemistry Technologies
1743.....Immunodiagnostic Systems Plc (IDS)
656.....Immunology Consultants Laboratory, Inc.
3686.....ImmunoReagents, Inc.
1667.....Improve Medical
3676.....IMRA America Inc.
3576.....IMT Masken und Teilungen AG
540.....InBios International, Inc.
3181.....Indigo BioAutomation
651.....Innova Biosciences
4558.....INNOVITA (TANGSHAN) BIOTECH CO.,LTD.
648.....Innovize
2238.....Inpeco S.A.
1778.....INSTANT NanoBiosensors Co., Ltd
422.....Instrumentation Laboratory (IL)
623.....Instrumentation Laboratory (IL)
3962.....Integra Biosciences (ViaFlo)
4342.....International Equipment Trading Ltd.
2800...International Federation of Clinical Chemistry and Laboratory Medicine (IFCC)
667.....InterSystems Corporation
1448.....Invetech
4343.....iQ Valves
363.....i-SENS, Inc.
440.....ITL BioMedical
1876.....ITL Group
4276.....IVD Research, Inc.
3850.....IVD Technologies
3772.....IVD Vision
3580.....IVEK Corporation
567.....Iwaki America Inc.
3086.....iXensor Co., Ltd.
3882.....J. Mitra & Co. Pvt. Ltd.
3951.....Jackson ImmunoResearch Laboratories
4607.....JADAK
1975.....Japanese Association of Clinical Laboratory Systems (JACLaS)
3677.....JENOPTIK Optical Systems, LLC
4376.....Jiangsu Kangjie Medical Devices Co., Ltd
4438.....JIANGSU SKYRAY INSTRUMENT CO., LTD.
3177.....Jiangsu ZECEN Biotech Co., Ltd.
1672.....J-Pac Medical
3277.....JSR Life Sciences
4419.....KAMIYA BIOMEDICAL COMPANY
4078.....KANANI BIOLOGICALS
3142.....KANGJIAN MEDICAL
1780.....Kawasumi Laboratories America, Inc.
3143.....Kem-En-Tec Diagnostics
1980.....Kepler Diagnostics
4252.....Key Tech
743.....Kikkoman Biochemifa Company
4655.....Kinbio Tech. Co., Ltd
3445.....Kinematic Automation Inc
3637.....KMC Systems Inc.
1161.....KNF Neuberger Inc.
3462.....KOAMTAC
3974.....Koco Motion US LLC
3485.....KOGANEI International America, Inc.
1075.....Korchek Technologies
2384.....Kova International, Inc.
3245.....KRONUS, Inc.
3339.....KSS Co., Ltd. (Japan)
3634.....Kurin, Inc.
1880.....Kyowa Medex Co., Ltd.
3200.....LabMedica International
3674.....Labnovation Technologies, Inc
4361.....Labor Diagnostika Nord GmbH&Co. KG
1067.....Labroots, Inc.
2284.....LabWare, Inc.
4242.....LAMEDITECH
3256.....Lampire Biological Laboratories, Inc.
3610.....Lampire Biological Laboratories, Inc.
4067.....LasX /MicroMed Solutions
1475.....Leinco Technologies
641.....LGC
1272.....LGP Consulting, Inc.
3961.....Liferiver Bio-Tech (United States) Corp.
851.....LifeSign
3079.....Lifotronic Technology Co., Ltd.
3486.....LigaTrap Technologies
3253.....LightIntegra-ThromboLUX
455.....LIN ENGINEERING
3982.....Lite-On Technology Corp.
2256.....Liuyang SANLI Medical Technology Development Co., Ltd
4355.....Lohmann Precision Die Cutting
2076.....LPS Industries, LLC
1854.....LRE Medical, an Esterline Company
1673.....LSI International Inc.
4038.....LTS Health
3967.....Lumigenex
1867.....Luminex Corporation
1584.....LumiQuick Diagnostics, Inc.
3672.....Lumos Diagnostics
4335.....LW Scientific
4350.....M.A. Industries, Inc.
4516.....Maccura Biotechnology
862.....MagArray, Inc.
739.....Maine Standards Company (LGC Maine Standards)
4069.....Market Diagnostics International
1377.....Martel Instruments Ltd.
771.....Maxim Biomedical, Inc.
1863.....Mayo Medical Laboratories
3275.....MBL International
3346.....McKesson Medical Surgical
4234.....Medcaptain Medical Technology Co.,Ltd
4464.....MediaLab, Inc.
1742.....MEDICA 2018/Messe Duesseldorf North America
860.....Medica Corporation
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Industry Playbook

PATH and Mologic Develop New Test to Support Malaria Elimination

PATH, a Seattle-based global health nonprofit, is partnering with the U.K. firm Mologic to advance a new rapid diagnostic test (RDT) to support treatment and elimination of malaria caused by *Plasmodium vivax (P. vivax)*. *P. vivax* is especially difficult to eliminate because the parasite can lie dormant in the liver and re-emerge, causing relapsing periods of illness. Treatment with 8-aminoquinolines, a class of drugs that includes primaquine, is currently the only means to kill the liver form of the *P. vivax* parasite. However, 8-aminoquinolines can cause serious side effects in patients with severe glucose-6-phosphate dehydrogenase (G6PD) deficiency, a hereditary condition common to areas where malaria is found. The World Health Organization recommends testing patients for G6PD deficiency before administering treatment with primaquine, but the diagnostic tests currently on the market for G6PD deficiency are not robust nor simple enough for widespread use in the hot, humid, and low-resource areas where malaria is endemic.

PATH is therefore advancing a portfolio of tests for G6PD deficiency that meet requirements for use in settings where *P. vivax* malaria is close to elimination. As part of this effort, PATH is working with Mologic to develop a novel qualitative point-of-care G6PD RDT. PATH and Mologic optimized the Mologic RDT for use in environmental conditions typical in malaria-endemic countries and for use in communities where malaria is commonly diagnosed and treated. The test also provides simple results (positive or negative) that test users can easily interpret to determine if a patient has severe G6PD deficiency.

"[This test] will help to fill critical gaps in G6PD testing experienced by elimination programs, and will complement quantitative tests for G6PD deficiency being advanced by PATH and partners," said Gonzalo Domingo, PhD, scientific director and malaria diagnostics lead at PATH.

Dennis Kunkel Microscopy/Science Photo Library

BIOMÉRIEUX BUYS ASTUTE MEDICAL

BioMérieux has acquired Astute Medical, the manufacturer of the NephroCheck test, which is a Food and Drug Administration-cleared diagnostic for the early risk assessment of acute kidney injury based on the level of two biomarkers, insulin-like growth factor-binding protein-7 and tissue inhibitor metalloproteinases-2. This acquisition builds upon a partnership between the two companies developed in 2015 when Astute granted bioMérieux a license to develop and market the NephroCheck test for the Vidas automated immunoassay system. Following this, bioMérieux has been a licensed distributor with Astute since 2017 for the NephroCheck test on the Astute140 Meter in the U.S. With this acquisition, bioMérieux now intends to continue to invest in health economic and outcome studies for NephroCheck, explore the other promising biomarkers in the Astute pipeline, and work with Astute's current license and distribution partners in order to expand patient access to the NephroCheck test worldwide.

ILLUMINA, BRISTOL-MYERS SQUIBB TEAM ON IMMUNOTHERAPY CO-DIAGNOSTICS

Illumina and Bristol-Myers Squibb have partnered to use Illumina's next-generation sequencing (NGS) technology to develop and globally commercialize in vitro diagnostic assays in support of Bristol-Myers Squibb's oncology portfolio. Bristol-Myers Squibb's clinical development program includes 24 clinical-stage molecules designed to target different immune system pathways across more than 50 types of cancers, and through its translational capabilities, the company has identified a number of potentially predictive biomarkers for these oncology therapeutics, including programmed death-ligand 1, tumor mutation burden, microsatellite instability-high or mismatch repair deficient, and lymphocyte-activation gene 3. The companies will develop a diagnostic version of the Illumina TruSight Oncology 500 assay to measure these biomarkers. "With [Bristol-Myers Squibb's] leading position in immunotherapy development, we see tremendous promise in this partnership to co-develop next-generation sequencing-based diagnostics that can identify effective therapeutic combinations and provide global access

to these targeted drugs," said Garret Hampton, PhD, executive vice president of clinical genomics at Illumina.

PERKINELMER, HELIX JOIN FORCES ON DIRECT-TO-CONSUMER TESTS FOR GENETIC CONDITIONS

PerkinElmer is collaborating with Helix, a personal genomics company, to develop and commercialize exome sequencing-based tests that will be made available to consumers through Helix's online marketplace for DNA-powered products. The initial targeted product offering will return results for 59 genes that the American College of Medical Genetics and Genomics identifies as highly penetrant genetic conditions with established interventions aimed at significantly reducing morbidity and mortality. A clinician will review all orders placed for these products through the Helix store to ensure that the test is medically appropriate before the order is completed. All DNA sequencing data for these products will then be generated using Helix's proprietary Exome+ assay in its CLIA- and College of American Pathologists-certified next-generation sequencing laboratory. In turn, PerkinElmer Genomics' medical genetics team will provide data analysis and interpretative services to individuals who purchase the product. Upon request, genetic counseling will also be available free of charge to people using PerkinElmer Genomics products on the Helix platform.

RTI INTERNATIONAL TO SUPPORT PIERIANDX'S CLINICAL GENOMICS INITIATIVES

The research institute RTI International has joined forces with PierianDx with the aim of solving the problem of translating complex genomic data into actionable clinical information. The collaboration will include investment and other strategic support to help advance PierianDx's growth plan. Since 2014, PierianDx has focused on providing solutions to accelerate molecular testing and advance precision medicine. The company has built the Clinical Genomics WorkSpace (CGW), a comprehensive clinical genomics platform that creates streamlined, accurate analysis, interpretations, and reporting for clinical labs. By integrating cloud-based software and clinical lab enablement services, the CGW helps to simplify the process of translating genomic data into patient-specific diagnosis and treatments. PierianDx also founded the PierianDx Partner Sharing Network, which has more than 50 members—including leading academic medical centers, cancer centers, and health systems—that use shared genomic data to personalize treatments for cancers and hereditary diseases.

MIODX, DIACARTA TO DEVELOP TEST TO GUIDE IMMUNOTHERAPY

MIODx, an early-stage immunogenomics company, has partnered with DiaCarta, a translational genomics and personalized diagnostics company based in the U.S. with significant business operations in China. The two firms plan to develop a diagnostic test to predict patient response to immunotherapy. They will base the test on MIODx's ClonoMap immune sequencing platform, which is designed for the development of diagnostics and immunotherapies, and to interrogate a person's immune system. The new test will be developed and validated at DiaCarta's CLIA labs in both the San Francisco Bay Area and Nanjing, China, followed by manufacturing at DiaCarta's ISO 13485-certified GMP-compliant manufacturing facility. "With the well-established CLIA and ISO manufacturing facility at DiaCarta, also the experienced [in vitro diagnostics] team and sales channels in the U.S., Europe, and China, we are able to speed up our MIODx's ClonoMap technology to the global market, especially the huge market potential in China," said M. Allen Northrup, PhD, CEO of MIODx.

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Ask The Expert

The Re-emergence of Cold-Stored Platelets

EXPERT
Aaron D. Shmookler, MD, FCAP

Why is the medical community (re)-interested in cold-stored platelets?

A: In most healthcare settings, the treatment of choice for hypovolemic shock involves administering individual blood components—red cells, plasma, and platelets (PLTs)—proportionally to reflect their constitution in whole blood. In our practice, we previously abandoned using cold-stored PLTs (CS-PLTs) stored at 4°C, in part because studies show CS-PLTs are cleared from circulation faster than room temperature PLTs (RT-PLTs) stored at 22°C. However, although RT-PLTs may be more useful prophylactically in patients with thrombocytopenia, recent research has revealed that cold-induced storage lesions alter the metabolic and functional profile of PLTs such that they effectively curtail hemorrhage.

In light of these findings, healthcare institutions should tailor two different therapeutic strategies for CS-PLTs and RT-PLTs, respectively, based on specific clinical situations. This shift in transfusion practice could impact laboratory technologists cross-trained to work in both clinical labs and blood banks—a role that is becoming more common as many healthcare organizations move toward increased integration. A rise in CS-PLT usage will also have implications for labs that perform infectious diseases testing for blood banks.

Are CS-PLTs regulated by the Food and Drug Administration?

Yes, the regulatory standards for CS-PLTs are enumerated in the Code of Federal Regulations (CFR, 21, 640.24; CFR, 21, 640.25). These standards apply only to PLTs obtained via the Terumo BCT Trima Accel automated blood collection system. According to this regulation, CS-PLTs may be stored at 1-6°C. They must maintain a pH of at least 6.2 and a PLT count of at least 5.5 x 10^{10} per whole blood-derived unit in at least 75% of tested units, just like RT-PLTs. (As an aside, this last criterion is set at 90% by *Standards for Blood Banks and Transfusion Services*.)

Unlike RT-PLTs, however, CS-PLTs do not require bacterial testing and they may be stored without agitation for a maximum of 3 days. Importantly, their use is also "restricted only to the resuscitation of actively-bleeding trauma patients" (Transfusion 2017;57;2836-44).

How should blood banks manage their CS-PLT inventory?

An acute/non-acute framework is clinically impactful and naturally lends itself to fostering a dual-PLT inventory. Conveniently, CS-PLTs adhere to the same storage and transport conditions as red blood cells, thawed and liquid plasma components, and whole blood. Altogether these products may be sequestered in a refrigerator, cooler, or other means of transport dedicated to emergent or massive transfusions. RT-PLTs, on the other hand, can be part of a general stockpile of blood products for routine transfusions. This split inventory could reduce wastage due to PLTs deviating from their designated storage temperatures. Moreover, it may reduce costs associated with obsolete bacterial testing and by minimizing PLT outdating, since CS-PLTs have been shown to exhibit decreased risk of bacterial contamination and a longer storage interval due to associated pathogen reduction technologies and platelet additive solutions.

What implications does CS-PLT transfusion have for patient testing?

Given the clinical indication for CS-PLTs, providers should perform a global analysis of acute traumatic coagulopathy when determining whether or not to transfuse a patient with CS-PLTs. The best test for this purpose is point-of-care thromboelastography, which interrogates the entire coagulation system and produces a tracing that identifies abnormal parameters that targeted blood component therapy could correct. The latter information is particularly important when making treatment decisions regarding CS-PLTs because PLTs play a central role in hemostasis after injury, yet are especially prone to acquiring both quantitative and qualitative defects in trauma. Thromboelastography could also be used to monitor resuscitation with CS-PLTs, which otherwise demonstrate a relatively normal functional profile.

Aaron D. Shmookler, MD, FCAP, is assistant professor of pathology and director of the blood bank and stem cell laboratory at West Virginia University, Morgantown.
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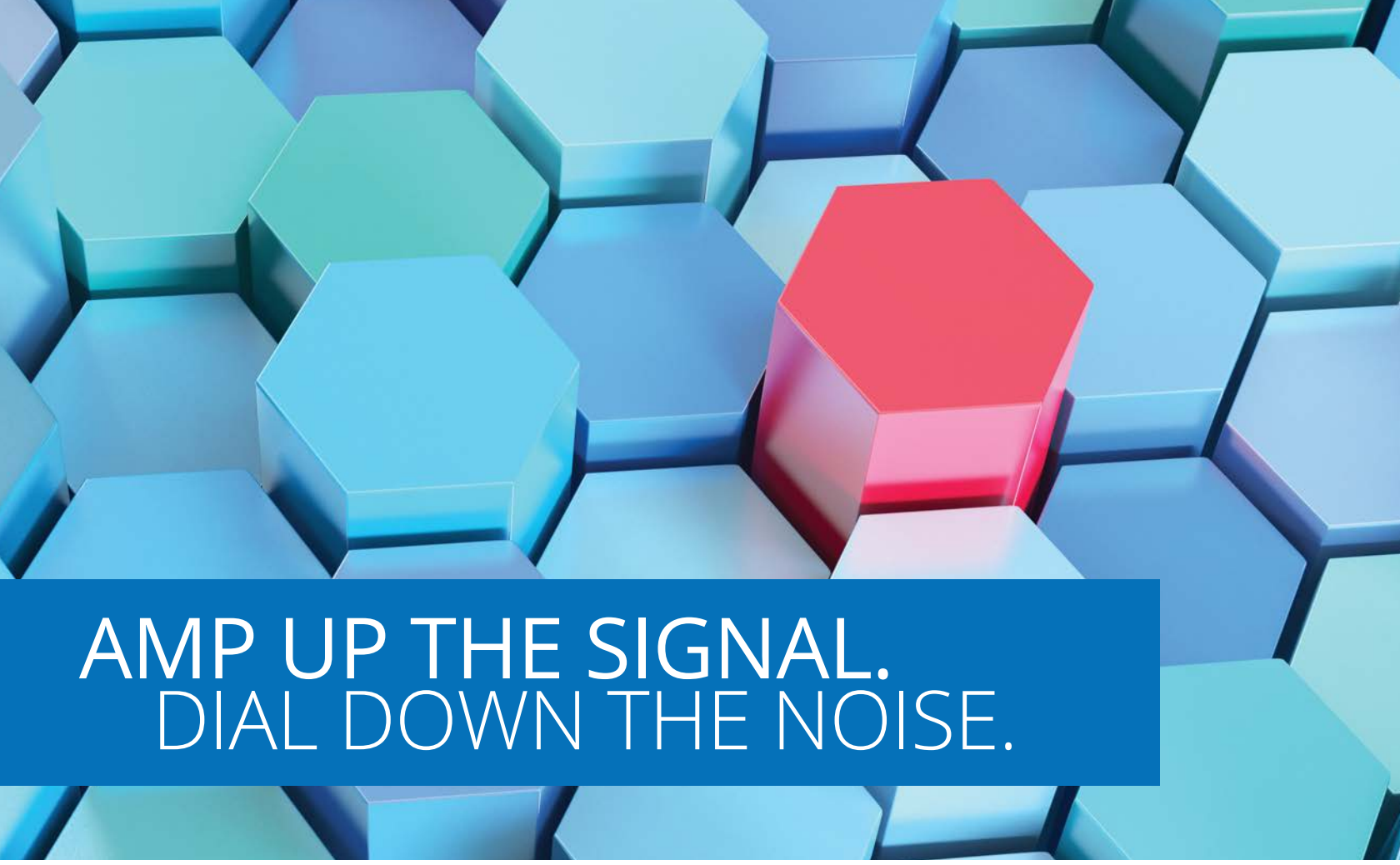

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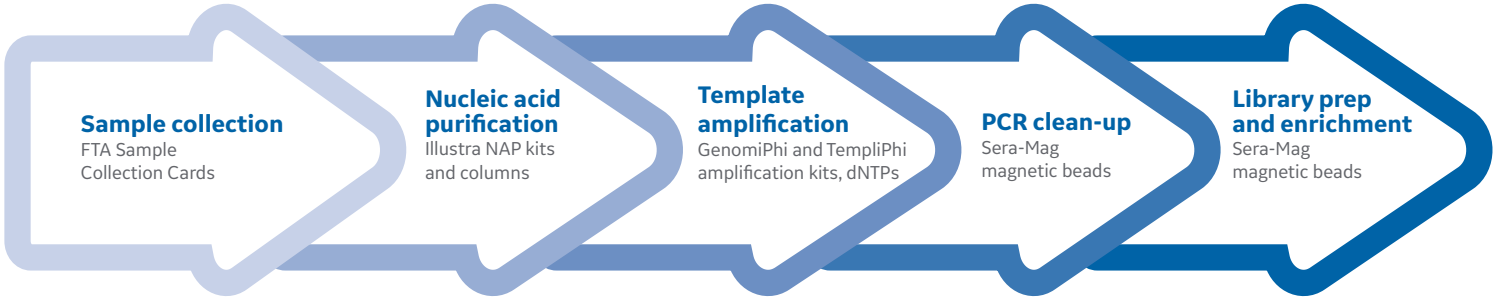

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