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CLINICAL LM Lab Manager

Better Tumor Boards

BOOSTING THE CLINICAL UTILITY OF LIQUID BIOPSY

THE DIAGNOSTIC ANSWER TO THE SUPERBUG CRISIS

NEW REPORTING REQUIREMENTS FOR HOSPITAL OUTREACH LABS

THE FINANCIALLY STABLE LAB

CLINICAL LM Lab Manager

April 2019

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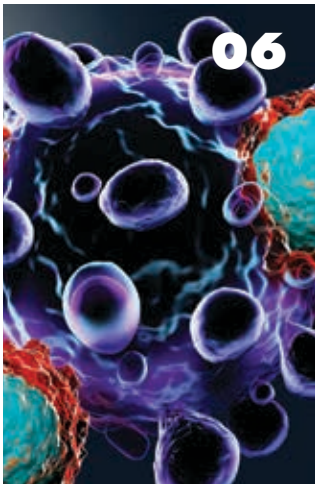

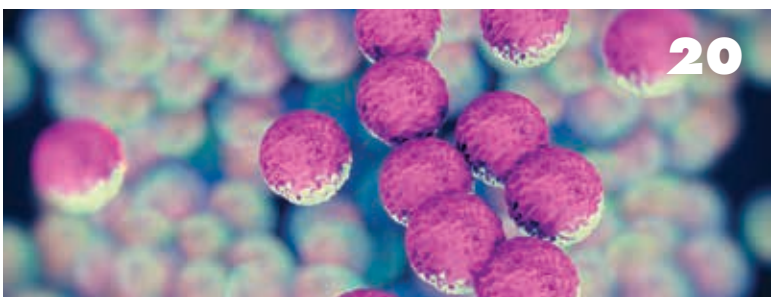

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harnessing data

Healthcare is being rattled by an information explosion, fueled primarily by data from the clinical laboratory. "It is commonly stated that more than 70 percent of data in the patient medical record comes from the laboratory," Jane M. Hermansen writes in this month's Business feature, "The Financially Stable Lab."

When it comes to data, conventional wisdom has been that more is better. But in reality, more data can be messy.

In our cover story, members of the Markey Cancer Center Molecular Tumor Board discuss how data abundance can give way to information overload: "Clinical sequencing of many cancers is now a routine part of care; however, the volume and complexity of sequencing data generated can be overwhelming to practicing oncologists." The authors go on to reveal the crucial role tumor boards play in making sense of the data at hand.

While many informatics tools are available to help diagnostic laboratories manage and interpret their data, some laboratories have been reluctant to adopt them, Rajeev Sehgal writes in his Thought Leadership piece, "A Growing Need for Informatics Tools in Clinical Diagnostics." He believes that's poised to change with the availability of newer informatics platforms that do a better job of centralizing and aggregating data from across lab networks.

It's not just obtaining and analyzing data that pose challenges to laboratories—reporting data is also an issue. The rules keep changing, Kimberly Scott explains in her Regulatory feature, "New Reporting Requirements for Hospital Outreach Labs," and many labs are still unaware of the new data reporting requirements they face as of this year. She outlines what data must be reported by which labs and when.

There are no two ways about it: In the information age, data rules. Clinical laboratories are now tasked with gaining greater control over the vast amounts of data they generate, with the ultimate goal of improving patient care.

Erica Tennenhouse

Erica Tennenhouse, PhD, Editor

editor
Erica Tennenhouse, PhD
etennenhouse@labmanager.com

editor-in-chief
Pamela Ahlberg
pam@labmanager.com

associate editor
Lauren Everett
leverett@labmanager.com

director of creative services
Trevor Henderson, PhD
thenderson@labmanager.com

contributors
Jane M. Hermansen, MBA, MT(ASCP)
Kimberly Scott
Eric Stern, PhD
Marissa Schuh
Rachel Stewart, DO, PhD
Riham El Khouli, MD, PhD
Rachel Miller, MD
Justine Pickarski, MS, LGC
Eric Durbin, DrPH, MS
Susanne Arnold, MD
Jill Kolesar, PharmD, MS
Masha G. Savelieff, PhD
Christoph Pedain, PhD
Rajeev Sehgal, MBAD

production manager
Greg Brewer
gregb@labmanager.com

art director
Danielle Gibbons
danielleg@labmanager.com

business coordinator
Andrea Cole
andreac@labmanager.com

digital media coordinator
Catherine Crawford-Brown
ccrawford-brown@labmanager.com

senior account manager
Alyssa Moore
Mid-Atlantic, Southeast & International
amoore@labmanager.com
610.321.2599

advertising account managers
June Kafato
Canada / Key Accounts
junek@labmanager.com
705.812.2332

Larry Frey
Midwest/West
larry@labmanager.com
845.735.5548

Reece Alvarez
Northeast
ralvarez@labmanager.com
203.246.7598

Published by LabX Media Group
president
Bob Kafato
bobk@labmanager.com

managing partner
Mario Di Ubaldi
mariod@labmanager.com

general manager
Ken Piech
kenp@labmanager.com

publisher
Edward Neeb
edwardn@labmanager.com
203.448.0728

custom article reprints
The YGS Group
labmanager@theygsgroup.com
800.290.5460
717.505.9701 x100

subscription customer service
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Advances

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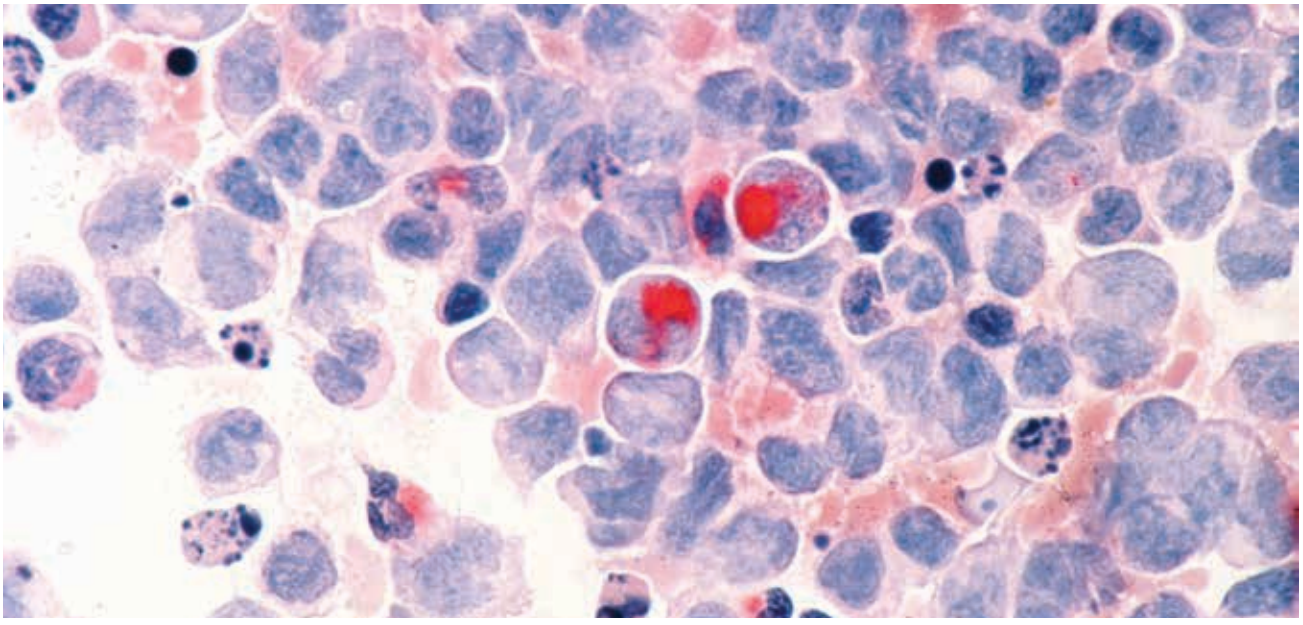


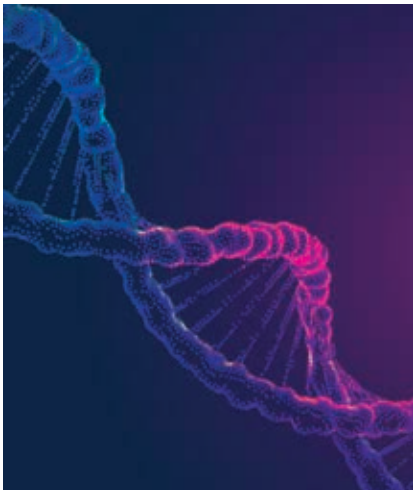
Leukemia Classifications Refined

Investigators have identified new subtypes of B-cell acute lymphoblastic leukemia (B-ALL)—the most common childhood cancer. Using whole-transcriptome analysis by RNA sequencing on nearly 2,000 patients, in addition to whole-genome sequencing and whole-exome sequencing on a subset thereof, they classified more than 90 percent of patients into 23 subtypes, including eight newly identified subtypes. Genetic alterations to the transcription factor PAX5 accounted for almost a third of newly identified B-ALL subtypes and resulted from rearrangements, sequence mutations, focal intragenic amplifications, or point mutation (PAX5 P80R). More than 90 percent of B-ALL cases can now be categorized by subtype. The findings were reported in January 2019 in *Nature Genetics*. A more-refined B-ALL classification scheme could advance precision oncology and improve B-ALL patient survival.

Gu, Zhaohui, et al. "PAX5-driven subtypes of B-progenitor acute lymphoblastic leukemia." *Nature Genetics* 51 (2019): 296-307.

Genetic Testing for Kidney Disease

For the first time, researchers have used whole-exome sequencing (WES) to identify genetic mutations associated with chronic or end-stage kidney disease. Researchers performed WES on patient-derived tissue and analyzed diagnostic variants—mutations in any of 625 nephropathy-associated genes. Out of 3,315 patients, WES detected a genetic cause in 9.3 percent of cases comprising 66 distinct monogenic disorders, 39 of which were present in just one patient, the authors reported in the *New England Journal of Medicine* in January 2019. The low frequency of 39 of the detected mutations underscores the ability of WES to detect rare mutations, which is not possible with conventional diagnostics. Furthermore, WES identified a mutation in 17.1 percent of patients for whom



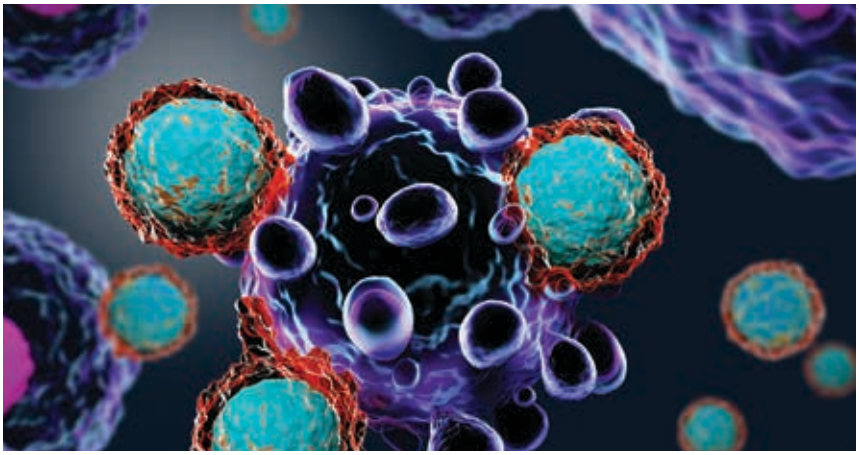
the cause of kidney disease had not been clinically determined. Out of 2,187 patients with clinical data, WES identified a medically actionable mutation in 1.6 percent of cases for a condition unrelated to the patients' kidney disease but that nevertheless impacted kidney care and necessitated attention from another specialist. Chronic kidney disease affects around 10 percent of adults and is associated with significant morbidity, mortality, and socioeconomic burden. The possibility of identifying the underlying genetic cause could help physicians more accurately advise personalized care and deliver better treatment.

Groopman, Emily E., et al. "Diagnostic utility of exome sequencing for kidney disease." *New England Journal of Medicine* 380.2 (2019): 142-151.

Improved Immuno-Oncology Trial Reporting

The Trial Reporting in Immuno-Oncology (TRIO) working group released its guidelines for immuno-oncology (IO) trial reporting in October 18 in the *Journal for ImmunoTherapy of Cancer*. The TRIO consortium, composed of medical oncologists, immunologists, clinical researchers, biostatisticians, and government and industry officials, was convened by the American Society of Clinical Oncology and the Society for Immunotherapy of Cancer. The goal of TRIO was to make proposals to improve the reporting of IO clinical trials, enabling more accurate, evidence-based assessment of the relative benefits and risks of IO. The group made 12 specific reporting recommendations, which fell into three broad categories: efficacy reporting standards, toxicity reporting standards, and combination or sequencing of immunotherapies reporting standards. The reporting guidelines are stringent in order to facilitate comparison between diverse IO trials, and they will be regularly revised by TRIO as IO evolves. Due to the demonstrated efficacy of IO to date, an ever-increasing number of IO trials are being launched. It is anticipated that the TRIO guidelines will help standardize reporting practice and lead to improved trial design and better interpretation of the efficacy and adverse effects of IO.

Tsimberidou, Apostolia M., et al. "Trial reporting in immuno-oncology (TRIO): an American Society of Clinical Oncology-Society for Immunotherapy of Cancer statement." *Journal for Immunotherapy of Cancer* 6.1 (2018): 108.



People Using Their Pets' Opioids?

A rise in opioid prescriptions for animals at a veterinary teaching hospital in Philadelphia over the past decade has mirrored escalating prescriptions for human patients, researchers reported in *JAMA Network Open* in January 2019. From

January 1, 2007, to December 31, 2017, the researchers evaluated pharmacy records for dispensed or prescribed codeine sulfate, hydrocodone bitartrate, and tramadol hydrochloride tablets and fentanyl citrate patches at the acute care veterinary referral hospital at the University of Pennsylvania School of Veterinary Medicine. The records included 134 veterinarians with 366,468 patient visits consisting of dogs, cats, and exotic animals. Over the study period, opioid prescriptions rose by 41.2 percent, whereas visits increased by only 12.8 percent. The authors suggest that humans may be using leftover opioids after their pets' treatments, which could contribute to the escalating opioid crisis. Greater regulatory oversight in veterinary practice could help mitigate these concerns.

Clarke, Dana L., et al. "Trends in opioid prescribing and dispensing by veterinarians in Pennsylvania." *JAMA Network Open* 2.1 (2019): e186950-e186950.

Top 10 CCU Tests That Predict Death

In a study published in the *Journal of Clinical Pathology* in December 2018, researchers classified critical care unit (CCU) laboratory tests according to how strongly their critical values are associated with imminent death. There is currently no agreed-upon list of tests that must be reported for all CCU patients. On such a list, enough tests must be included to alert the physician that the patient is in critical danger, but too many tests can cause alert fatigue and waste resources. Using machine learning to analyze the Medical Information Mart for Intensive Care-III database, which contains data from around 60,000 patients admitted to the CCU at Beth Israel Deaconess Medical Center in Boston from 2001 to 2012, the researchers found that the 10 tests whose critical values were most strongly correlated with imminent death, in order, were: bicarbonate, phosphate, anion gap, total white cell count, partial thromboplastin time, platelet, total calcium, chloride, glucose, and international normalized ratio. This study employed an unbiased, data-driven approach to generate the top 10 candidates for the critical reporting list, highlighting the benefit of data science in clinical practice.

Yang, Zhutian, et al. "Relative criticalness of common laboratory tests for critical value reporting." *Journal of Clinical Pathology* (2018).

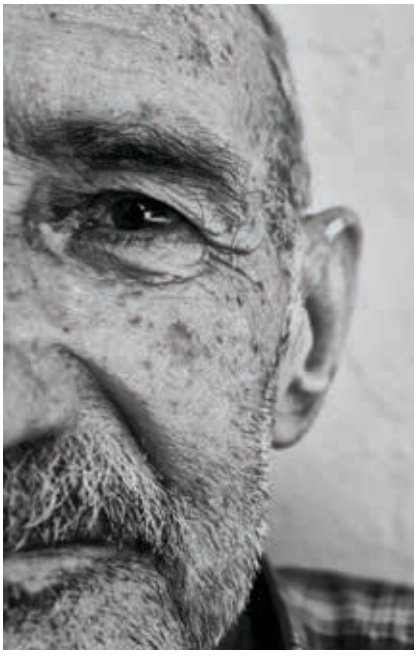
A Call for Improved Evaluation of Penicillin Allergies

Better identification of patients with penicillin allergies could improve antibiotic stewardship, according to a review published in *JAMA* in January 2019. Although β-lactam antibiotics are among the safest and most effective, they cannot be used by around 10 percent of the population due to penicillin allergies. Out of that population, however, only a small percentage of patients have severe Immunoglobin E or T-cell-mediated allergies, while the vast majority of patients can ultimately tolerate this class of antibiotics. Patients whose records indicate penicillin allergies are prescribed suboptimal treatment with broad-spectrum antibiotics, which raises the risk of antimicrobial resistance, including methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus*, and of the patients developing *C. difficile* infection. Currently, penicillin allergies are most frequently reported by patients and included in their healthcare record without actual testing or reaction characteristics. The authors conclude that better evaluation of penicillin allergies is needed, such as by allergy history (low-, medium-, or high-risk history) and skin or oral challenge. Better evaluation of penicillin allergies before prescribing alternative, suboptimal antibiotics could lead to improved antibiotics stewardship.

Pongdee, Thanai, and James T. Li. "Evaluation and management of penicillin allergy." *JAMA* 321 (2019): 188-199.

Predicting Alzheimer's 16 Years Before Symptoms

A blood test could predict Alzheimer's disease (AD) up to 16 years before estimated symptom onset, researchers reported in January 2019 in *Nature*



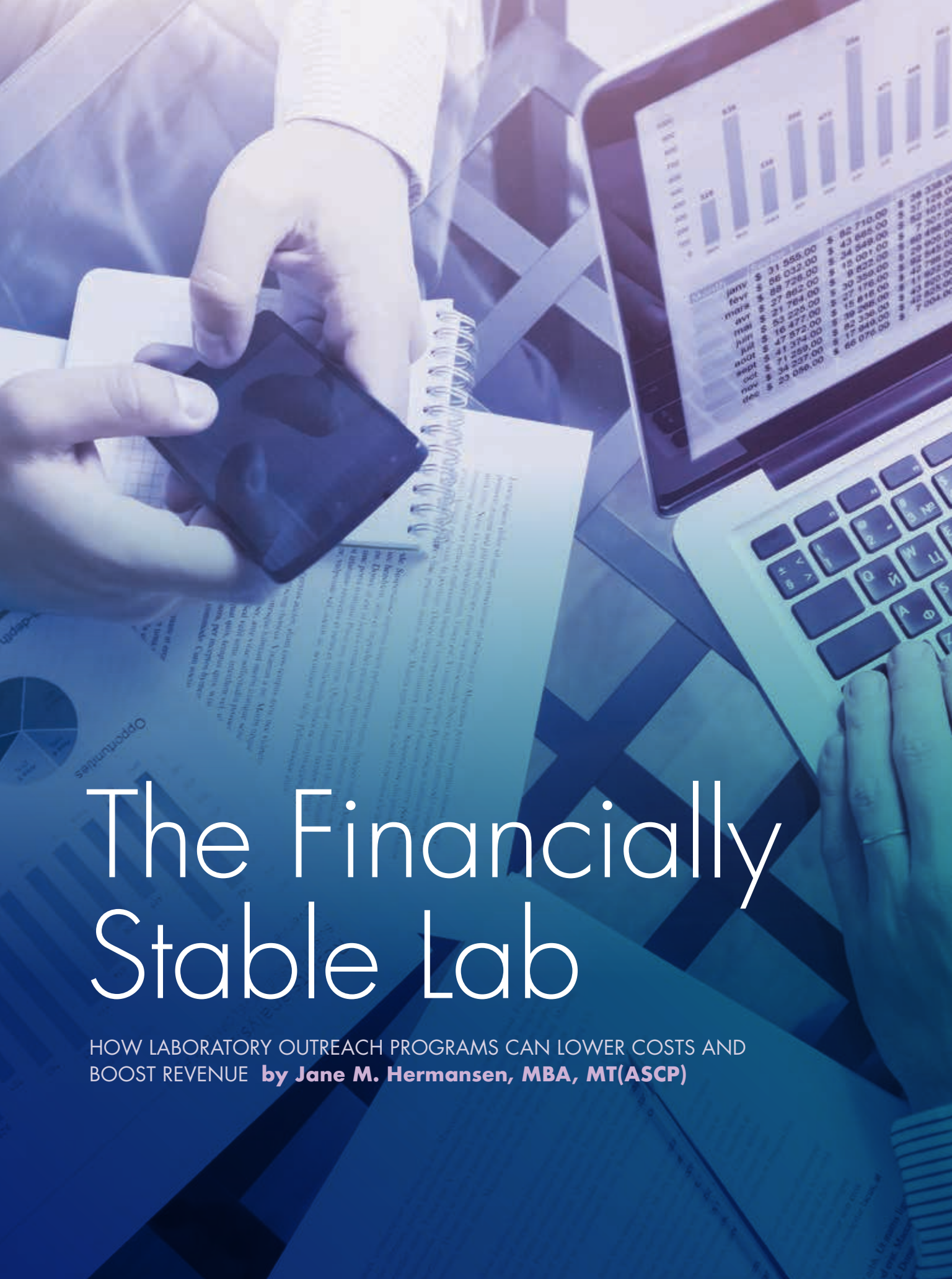
Medicine. Neurofilament light chain (NfL) is a biofluid biomarker linked to neurological proteopathies, like AD. The authors evaluated the biomarker in participants in the Dominantly Inherited Alzheimer Network, an observational study (clinicaltrials.gov identifier NCT00869817) comprising families with a history of AD. Enrolled individuals had a 50 percent chance of possessing a highly penetrant autosomal dominant mutation in one of three familial AD genes: amyloid precursor protein, presenilin 1, or presenilin 2. Family members without mutations served as noncarrier controls. The researchers monitored serum Nfl over time. NfL serum levels differentiated familial AD mutation carriers from noncarriers up to 16 years before estimated symptom onset. Furthermore, the rate of change in serum Nfl correlated more strongly with brain degradation than did buildup of toxic amyloid-β protein. Current diagnostic tests for AD are costly, requiring positron emission tomography for amyloid-β deposition, or invasive, by evaluating cerebrospinal fluid tau levels. A serum test to predict symptom onset and brain atrophy could streamline early AD diagnosis.

Preische, Oliver, et al. "Serum neurofilament dynamics predicts neurodegeneration and clinical progression in presymptomatic Alzheimer's disease." *Nature Medicine* 25 (2019): 277-283.

Clinical Utility of IGRAs for TB Diagnosis

In January 2019, researchers reported in *The Lancet Infectious Diseases* that two commercially available interferon-γ release assays (IGRAs) are inadequate for diagnostic assessment of suspected tuberculosis (TB). IGRAs function by quantifying interferon-γ release from T-cells in patient blood samples in response to two specific and immunogenic *Mycobacterium* tuberculosis antigens or by evaluating the total number of interferon-γ releasing effector T-cells. Second-generation IGRAs incorporate additional antigens. The authors conducted a prospective cohort study that enrolled patients in England with suspected TB. They used two commercial IGRAs and one second-generation IGRA to analyze blood sampled at enrollment. Patients were evaluated by bacterial culture, chest X-ray, and clinical history over six to 12 months to come to a medical diagnosis, which was compared to IGRA results to determine assay specificity, sensitivity, positive and negative likelihood ratios, and predictive values. The sensitivities of the two commercial IGRAs for TB diagnosis were 67.3 and 81.4 percent, respectively, whereas the second-generation IGRA had a sensitivity of 94 percent, giving a negative likelihood ratio of 0.13 for all TB cases. The study concluded that a second-generation IGRA may potentially exclude the possibility of TB in low-incidence settings due to its sensitivity, low-negative likelihood ratio, and high-negative predictive value. While cultures continue to be the gold standard for TB diagnosis, they are time-consuming and occasionally fail to grow from some patients with TB; second-generation IGRAs represent a possible alternative.

Whitworth, Hilary S., et al. "Clinical utility of existing and second-generation interferon-γ release assays for diagnostic evaluation of tuberculosis: an observational cohort study." *The Lancet Infectious Diseases* 19 (2019): 193-202.



The Financially Stable Lab

HOW LABORATORY OUTREACH PROGRAMS CAN LOWER COSTS AND BOOST REVENUE **by Jane M. Hermansen, MBA, MT(ASCP)**

Health system and hospital leaders are facing tremendous challenges in today's healthcare environment: they must deal with tough competition, strict regulatory requirements, staff shortages, and financial pressures. A recent survey of hospital CEOs cited financial challenges as their top concern.[1] What if the laboratory could be part of a financial solution by providing hospitals with a revenue stream and cost savings?

Successful laboratory outreach programs provide mechanisms to enable health systems to achieve their integration goals, deliver excellent quality of care, and improve patient outcomes. Importantly, laboratory outreach programs can also serve as a key source of income.

The laboratory balance sheet

A laboratory can achieve financial stability by increasing revenue, decreasing costs, or both. Financial performance is demonstrated through a balance sheet or profit-and-loss statement, which is calculated simply by subtracting cost from revenue. In order to accurately project these data, it is important to understand the variables and how they impact the calculations. Simply stated, revenue is the money that the organization receives in payment for performing laboratory testing. Costs can be variable or fixed, and direct or indirect [see glossary]. At the simplest level of accounting, total revenue minus total cost equals profit (or loss) for the department. However, when considering laboratory outreach testing, it becomes more complex to calculate a bottom line or profitability. At the service line level, outreach revenue is usually separate from other hospital outpatient revenues, not capitated or bundled, and the only costs that should be applied are variable and direct. It is important to note that fixed and indirect costs for the hospital laboratory will exist with or without the laboratory outreach program and should not be loaded fully onto the outreach program.

How outreach programs can help labs achieve financial stability

1 Reduce revenue rejections and delays

Rejected laboratory claims can result in lengthy delays in payment, or in lack of payment entirely, ending in write-offs or bad debt. If laboratory managers are not directly involved in the billing process, they may not be fully aware that they are not getting paid for the testing that is performed. If claims are getting rejected, it is necessary to identify the following: 1) the number of claims rejected, 2) the payer type (e.g., government, health plan), 3) the reason for rejection (e.g., failed medical necessity, missing modifiers), and 4) the source of rejections (specific ordering location or type of testing).

Once the reasons for rejections are known, the laboratory can focus on reducing them. It may require working with provider offices to ensure that they are supplying appropriate diagnosis codes with the test request; working with payers to actually understand why they are rejecting claims; or working internally to apply modifiers to specific tests prior to submitting the claim for payment. Timely and responsive attention to rejections will ensure more timely payment for laboratory services.

Glossary

Net revenue: Revenue that is collected for performing laboratory testing.

Gross revenue: Revenue that is charged for performing laboratory testing. Gross revenue is rarely the same as net revenue.

Variable cost: Cost that varies with the number of tests performed (e.g., reagent cost).

Direct cost: Cost that can be fully attributed to the performance of a test (e.g., reagent cost and staff time).

Fixed cost: Cost that does not change with an increase or decrease in the number of tests performed (e.g., instrument cost and rent).

Indirect cost: Cost that is not directly related to test production, such as overhead (e.g., institutional allocations).

Capitated revenue: Fixed, prearranged payment received per patient enrolled in a health plan.

Bundled revenue: Payment based on a patient episode. It does not vary based on services provided.

Bottom line: Calculation of profit or loss for a department.

Service line: A single set of attributes, providing flexibility and consistency across an enterprise and offering a uniform approach to delivering a limited number of high-quality products or services.

If the hospital's write-off threshold is higher than an average laboratory claim, the entire claim will be dismissed. For example, if the average net revenue for a laboratory outreach requisition is between $50 and $80 and the hospital's write-off threshold is $250, the rejected laboratory claim will not be reconciled and no attempt to collect the revenue will ever be made. The best solution in such cases is to lower the write-off threshold for lab testing. Successful labs have write-off limits of $10 or even $5—this ensures that they are collecting everything they can. Even if write-off thresholds are lower but working laboratory claims are not high-priority, there may still be substantial delays in collecting, and revenue may never be recovered.

Another source of lost or delayed revenue may be clients who receive bills directly from the laboratory. Delayed payments or unpaid bills impact laboratory revenue unless there is a concerted effort to collect payment from clients. Managing Part A (first 100 days) and Part B billing of skilled nursing facility patients on Medicare is a frequent concern for laboratories. It is necessary to monitor the census daily to identify when patients transition from Part A to Part B, and to change their billing accordingly.

2 Improve billing practices

Another way to increase revenue is to ensure that the laboratory customers pay at a favorable reimbursement rate. If the laboratory is serving governmental payers (Medicare and Medicaid), it is possible to increase revenue by including third-party health plan patients into the mix, thereby billing other payers. In some US states, laboratory markup remains an acceptable and common practice. In this practice, the laboratory creates a discounted fee schedule for a client, and the client rebills the testing—at a higher fee—to the patient's health plan. As state regulations change and physician practices reduce the hassle of issuing additional bills for laboratory testing, the laboratory outreach program may have an opportunity to bill the health plans directly, thereby increasing revenue.

CAP's Position on Direct Billing

In 2015, the College of American Pathologists (CAP) released a position statement in support of direct billing for anatomic and clinical pathology services for all payers, public and private. The practice of client billing involves a physician turning a profit by charging a patient full price for a laboratory service on which the physician received a discount, or even by marking up the service. CAP notes that the practice incentivized the physician to do the following two things: 1) choose a laboratory based on price rather than quality and 2) order more tests than necessary, in order to gain more profit. With direct billing, on the other hand, payment for services is made directly to the person or entity that performed or supervised the service. Ordering physicians can benefit from direct billing, CAP writes in its position statement, as the practice helps ensure compliance with federal laws that prohibit unlawful economic arrangements between physicians and clinical laboratories.

3 Expand laboratory service

Although it may seem obvious, it's worth noting that an effective way to increase revenue is to expand your laboratory service. Hospital-based laboratories typically send between three and five percent of their tests to a reference laboratory. Such tests may be highly complex, infrequently ordered, or in need of technical expertise and equipment that do not exist within the laboratory. However, when volumes exceed a threshold or technological improvements make select testing more accessible within the hospital laboratory, it may be appropriate to add those tests to the internal testing menu. The laboratory should routinely evaluate the tests that it sends to a reference laboratory and identify the feasibility of insourcing those tests. Part of the evaluation should include a "make versus buy" analysis, which considers immediate revenue opportunities, potential growth in volumes from existing laboratory outreach customers, and the financial impact of not having to purchase a given test from another laboratory. Increasing the esoteric nature of the test menu by including more expensive, specialized tests will also increase test revenue.

4 Manage costs

Lowering costs can improve a laboratory's financial performance. In most laboratories, salaries comprise a large portion of the budget; thus, one way to lower laboratory cost is to create efficiencies for staff. Many laboratories are investing in automation to replace technologists' manual work. Laboratory information systems enable bidirectional interfacing with instruments and allow for automatic verification and release of normal test results. Robotic specimen handling, transport, and

storage and retrieval allow laboratory scientists to focus their efforts on the technical tasks that are aligned with their education and skill set.

Laboratories also have opportunities to streamline processes by using management engineering principles and implementing lean manufacturing concepts. By eliminating unnecessary steps throughout the testing process, a laboratory may be able to increase throughput, reduce waste, and improve turnaround time. Each of these efficiencies has the opportunity to reduce cost.

Lastly, increasing volumes can lower overall cost per test. If a laboratory is functioning at only 60 percent capacity and the outreach program provides additional volumes to bring the laboratory to 90 percent capacity (a 50 percent volume increase), its efficiency will go up. It is unlikely that the laboratory will have to purchase additional equipment or hire substantial staff to test the additional specimens, and the primary cost will be the supplies and reagents to perform the test.

Looking beyond the laboratory

Finally, when considering financial performance, it is important to look beyond the laboratory itself. It is commonly stated that more than 70 percent of data in the patient medical record comes from the laboratory, and that data is used to drive patient care decisions. Diagnosis, treatment, monitoring, and preventive care all rely upon accurate laboratory testing for effective patient care. With the increase in companion diagnostics and pharmacogenomics, the correct laboratory test could save tens of thousands of dollars in pharmaceuticals.

As healthcare payment models shift toward value-based reimbursement, it will be important to retain focus on the importance of performing the right laboratory test for the right reason at the right time. Even an inexpensive test that adds no value to the care of the patient is an unnecessary cost. Diagnostic labs should help guide clinicians in ordering the right test and reducing waste. Nationally, campaigns such as Choosing Wisely[2] provide evidence-based and peer-reviewed guidelines developed by professional associations. As a laboratory industry, we have a responsibility to ensure that our testing is used correctly and managed efficiently.

The laboratory and its successful outreach program can contribute to organizational goals overall by providing financial stability. Effectively managing costs, maximizing revenue opportunities, and demonstrating value beyond the laboratory will ensure long-term success.

Lean Manufacturing

Lean manufacturing is a comprehensive set of techniques, derived from the Toyota Production System, that allow manufacturers to reduce waste. The following are a few of the key concepts behind lean manufacturing:

5s

The 5s system aims to eliminate waste by continually sorting items and moving things into places where they'll have greater value.

Cellular manufacturing

Equipment and workstations are arranged to reduce material handling and setup time and to improve productivity.

Jidoka

In this form of automation with human intervention, workers have the authority to stop the process when an abnormality occurs.

Kanban

This is a system in which manufacturers can control inventory by producing only what the customer asks for.

References:

1. Knowles, Megan. "ACHE: 10 most concerning issues for hospital CEOs," *Becker's Hospital Review.* (2019).
2. "Choosing Wisely," *The ABIM Foundation.* (2019), http://www.choosingwisely.org/.

***Jane Hermansen**, MBA, MT(ASCP), has nearly 35 years of clinical laboratory experience, but she knew she was going to be a laboratory scientist when she was eight years old. She started her career working in the hospital laboratory in International Falls, Minnesota and has been at Mayo Clinic since 1988. She currently directs the outreach consulting program for Mayo Clinic Laboratories. Jane holds a B.A. in Medical Technology from Concordia College in Moorhead, Minnesota and an MBA from the New York Institute of Technology.*

Jane is also a busy volunteer. She is currently the president of the international Clinical Laboratory Management Association. She has contributed to the laboratory industry by presenting at over 125 state and national professional meetings, has written more than 25 articles for industry publications, and has personally trained over 1,800 laboratory professionals in the art of customer service. Her experience includes clinical research, process engineering, consulting, training and facilitation, and project management.

New Reporting Requirements for Hospital Outreach Labs

HOSPITAL OUTREACH LABS ARE NOW CHALLENGED TO COLLECT AND REPORT PRIVATE PAYER PRICING, BUT THERE MAY BE AN UPSIDE **by Kimberly Scott**

Hospital outreach laboratories are facing an enormous challenge this year: Beginning Jan. 1, almost all outreach labs are required to collect and report their private-payer rates to Medicare as part of the lab test repricing initiative mandated by the Protecting Access to Medicare Act of 2014 (PAMA).

PAMA essentially overhauled the previous system for determining how Medicare would pay for laboratory testing under the Clinical Laboratory Fee Schedule (CLFS). Beginning in 2016, applicable laboratories were required to report their private-payer rates to the Centers for Medicare and Medicaid Services (CMS) on a test-by-test basis, along with associated test volumes. Applicable laboratories were defined as those that received more than 50 percent of their total Medicare revenues under the CLFS and Physician Fee Schedule and that received at least $12,500 in Medicare revenues for CLFS services. CMS then calculated a "weighted median" for each billing code for tests paid under the CLFS beginning Jan. 1, 2018. That payment system resulted in Medicare cuts of up to 10 percent for many lab tests.

Hospital outreach labs were largely excluded from the data collection and reporting in the first PAMA reporting cycle, which began in 2016. Under criteria set by CMS, only outreach labs that had their own National Provider Identifier (NPI) were required to report, resulting in only 21 outreach labs reporting.

But under a final rule published Nov. 1, 2018,[1] CMS expanded the reporting requirement[2] to include hospital outreach labs that bill through their hospital's NPI under bill type 14x on Form CMS-1450, which many hospital outreach labs use to bill for laboratory services provided to non-patients. This means that any hospital outreach lab that receives at least $12,500 in Medicare payments under the CLFS in the first six months of 2019 must now report its private-payer volume and rates to CMS.

The new data collection period runs from Jan. 1, 2019, to June 30, 2019. Labs are required to report this data to CMS in the first quarter of 2020, and the agency will use it to calculate new rates that will take effect Jan. 1, 2021.

Challenges for outreach labs

Because most outreach labs were not required to participate in the first data collection and reporting process, many do not have the necessary systems in place to accurately identify private payor reimbursement rates at the CPT level, notes Lale White, executive chairman and CEO of XIFIN Inc., a health information technology company based in San Diego. What's more, many are still unaware they need to be collecting data and will be required to report.

"There are numerous land mines in the PAMA data-collection process and hospital labs have an even steeper hill to climb in most cases, being further removed from the actual lab billing process and lacking the detailed financial reports to facilitate ease and accuracy in reporting," explains White. "Oftentimes, hospitals do not retain source documents—ERAs—once payment is posted, and the ERAs are essential to audit the data for accuracy and to appropriately calculate allowables. Where posting is performed in bulk at the patient level, the ERA is also the only source that provides the CPT-level data needed for reporting."

During the last data collection period, many labs hired consultants, segregated internal-focused staff, and spent untold hours and expense gathering the data and analyzing it to provide a meaningful and accurate data set to CMS, says White. Even so, there was still a significant amount of questionable data received by CMS, as well as a number of unintended errors in reporting made by labs that lacked the reporting and analytical sophistication to find simple remittance errors made by payers and payment posting clerks.

Hospital labs are likely to face these same challenges, although there may actually be an upside to being required to report private payer data: The exercise will likely lead to stronger financial systems and improved insight into profit and loss as labs are forced to retain detail-level transactional data.

"There is no question that the PAMA exercise can be costly in time and resources for all labs, and that hospital labs may have an even higher burden due to inadequate systems," says White. "However, PAMA also provides the most instructive exercise in highlighting the financial reporting shortcoming of the business unit and requirements for future systems decisions. After all, the financial data and analytical requirements essential for accurate PAMA reporting are no different from those required for the strategic management of any business unit, and are even more critical for the management of a laboratory whose responsibility is to provide not just a result on a report, but actionable information from which critical patient therapy decisions are made."

WHAT DATA ARE LABS REQUIRED TO REPORT?

The PAMA regulations require all applicable reporting labs, including hospital outreach labs, to report the following:

- The specific HCPCS code for each test on their test menu, excluding unlisted/NOC codes.
- The private-payer rates received by all private payers, including commercial plans, Medicare Advantage and Medicaid Managed Care, after all price concessions and discounts are applied.
- The volume of tests for each code paid at each private-payer rate.
- Non-reportable tests excluded from reporting requirements, including those subject to an unresolved appeal and tests with final payment of zero dollars.

PAMA DATA COLLECTION AND REPORTING SCHEDULE

Jan. 1, 2016 – June 30, 2016: Labs collected the private payer amount and volumes for all their tests.

Jan. 1, 2017 – May 30, 2017: Labs reported their private payer amounts and volumes to CMS.

Late Summer/Early Fall: CMS published the draft 2018 Medicare rates.

Jan. 1, 2018 – Dec. 31, 2020: New Medicare rates in effect. Rates are equal to the median weighted private payer's rate (limited to a 10 percent year-over-year decline).

Jan. 1, 2019 – June 30, 2019: Round 2 – Labs will collect the private payer amount and volumes for their tests.

Jan. 1, 2020 – March 31, 2020: Labs will report the private payer amounts and volumes to CMS.

Jan. 1, 2021 – Dec. 31, 2023: New Medicare rates will go into effect. Rates are equal to the weighted median private payer's rate (limited to a 15 percent year-over-year decline).

**The data collection and reporting periods will repeat every three years indefinitely.*

Kimberly Scott *is a freelance writer specializing in health care and medical diagnostics.*

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Fluorescence-Activated Cell Sorting for Cell-Based Therapies

FLOW CYTOMETRY APPLICATIONS IN DEVELOPMENT AIM TO ISOLATE CELLS FOR IMMUNOTHERAPY AND REGENERATIVE MEDICINE **by Masha G. Savalieff, PhD**

Flow cytometry has become a mainstay in the clinical laboratory as a reliable, rapid, and sensitive immunodiagnostic method. At present, its uses in the clinic have been limited to diagnostics. However, flow cytometry's many strengths and advantages, which include single-cell resolution and multiplexed biomarker identification by a powerful instrument with a suite of analysis software, make the technique ideal for other potential clinical applications. Indeed, flow cytometry methods for therapeutic applications are emerging.

FACS, or fluorescence-activated cell sorting,[1] is a specialized flow application that, in addition to analyzing the fluorophore content and biomarkers on single cells, can sort them based on the desired phenotype. One potential therapeutic application is for collected cells to be expanded *ex vivo* and reinfused into the patient as cell-based therapies.

The ability to perform multiplex biomarker analysis using flow cytometry is significant because it enables the identification and isolation of immune cells to a very specific phenotype.[2] In addition, the ability to serially analyze single cells can lead to a high purity of sorted cells.[2] This is important for cell-based therapies, which must be free of contaminating harmful cells, e.g., cancer cells, or therapeutically ineffective cells, e.g., over-differentiated T-cells. Despite its great potential for cell-based therapies, FACS is presently limited to preclinical and early-phase studies for such applications. However, intensive research aims to translate these findings to the clinic, particularly for sorting immune and stem cells for immunotherapy and regenerative medicine.

Isolating immune cells for immunotherapy

FACS can be employed to enrich hematopoietic stem cells (HSCs) from a patient's blood for autologous reimplantation after high-dose chemotherapy, which ablates the process of hematopoiesis from the patient's bone marrow. In a study of 22 patients with metastatic breast cancer enrolled in a phase I/II trial,[2] FACS was employed to purify HSCs bearing a $CD34^+Thy\text{-}1^+$ signature for autologous mobilized peripheral blood (MPB) infusion, a process generally considered suboptimal due to contaminating circulating cancer cells. However, adding a FACS sorting step after enrichment of HSCs on an apheresis $CD34^+$ column resulted in a 250,000-fold reduction in cancer cells. Moreover, patients receiving FACS-sorted MPB had longer progression-free survival and overall survival compared with patients who received regular MPB. Although limited in sample size, the study demonstrated the ability of FACS to purify HSCs to a high level for autologous MPB.

Autologous adoptive cell transfer[3] is a process of purifying immune cells from a patient's blood sample, expanding them *ex vivo*, and reinfusing them into the patient for therapeutic benefit. In cancer patients, this could involve reinfusion of cancer-specific antigen (Ag)-activated T-cells or tumor-infiltrating lymphocytes (TILs) to combat hematological or solid cancers. TILs exhibit a range of phenotypes,[2] from the immature and least-differentiated stem cell memory T-cells (T_{SCM}s) to the terminally differentiated effector T-cells. Studies have shown a correlation between clinical outcome and

reinfusion of less-differentiated cells, suggesting that sorting TILs to enrich them in T_{SCM}s or other less-differentiated forms prior to reinfusion could improve survival outcomes for patients. FACS could potentially accomplish this task, although the application is still in the preclinical phase.

The FDA has recently approved a novel therapy called chimeric antigen receptor-modified T-cells (CAR-Ts)[4] to treat relapsed or refractory diffuse large B-cell lymphoma and B-cell precursor acute lymphoblastic leukemia. The treatment process involves obtaining T-cells from the patient and modifying them genetically to express a surface antibody specific to a cancer Ag fused to a protein domain that activates the T-cell. The CAR-Ts are then expanded and reinfused into the patient as an immunotherapy to target cancer cells. Various T-cell subsets differ in their efficacy and lasting effects *in vivo* as CAR-Ts; consequently, sorting T-cells by FACS prior to their genetic manipulation could boost their efficacy in patients, although this is still in the research stages. Additionally, flow cytometry can be used to characterize CAR-Ts and their expression of Ag receptors.[5,6]

Selecting stem cells for regenerative medicine

Stem cells retain the ability to transform into a variety of different cell types and are therefore of potential use in regenerative medicine to treat degenerative diseases, congenital conditions, or tissue damage from injury. The list of potential applications for stem cells (embryonic, induced pluripotent, neural, placental, or mesenchymal) is staggering, with numerous ongoing clinical trials testing stem cell therapies for bone, cardiovascular, immune, and neurodegenerative diseases, to name a few.[7,8] FACS is well-suited to sorting stem cells[9] and is extensively employed in research, but its clinical applications are still in the nascent stages of development. Presently, flow cytometry can be used to verify the phenotype of cultured or isolated stem cells.[10]

Limitations and potential solutions

FACS is an antibody-dependent technology and is therefore limited in its clinical applications by the availability of antibodies conforming to good manufacturing practices. Cells sorted by FACS can also suffer shear- or electrically induced damage. Newer formats of cell sorting, such as microelectromechanical systems in tandem with a flow cytometer, can mitigate these problems. A general issue facing all cell-based therapies is the labor intensity of culturing cells, which limits production volume. A potential solution would be to integrate existing automated cell culturing systems with sorting machines for a seamless transition from automated culturing to automated sorting.[10] Overall, many of these limitations are technical in nature. Improvements could increase the applicability of FACS to cell-based therapies.

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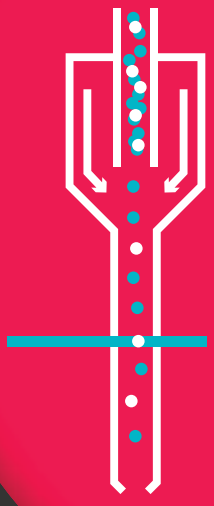
***Masha G. Savelieff**, PhD, is a full-time science writer and co-founder of SciGency Science Communications. She obtained her PhD in chemistry at the University of Illinois at Urbana-Champaign, and performed research in medicinal chemistry, Alzheimer's disease, and cancer biology before becoming a full-time writer.*

FLOW CYTOMETRY



VS

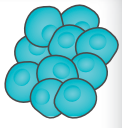
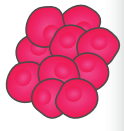
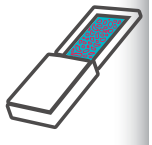
FLUORESCENCE MICROSCOPY

Flow cytometry is a powerful technology that allows researchers and clinicians to perform complex cellular analyses quickly and efficiently by measuring the intensity of scattered or emitted light from individual cells as they pass before a laser.

Fluorescence microscopy is a type of enhanced light microscopy that uses a higher-intensity light source to excite fluorophores in the sample. The fluorphores in turn emit a lower energy light with a longer wavelength that produces the magnified image.

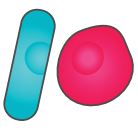
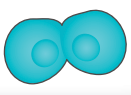
While many of the same cellular analyses can be performed using fluorescence microscopy and flow cytometry, these methods differ in key ways in terms of the applications they support, compatible sample types, complexity, cost, the number of parameters they can detect, sensitivity, and throughput.

SAMPLE TYPE

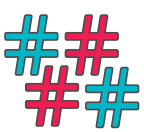
FIXED CELLS	Yes	Yes	
LIVE CELLS	Yes	Yes	
TISSUE	To analyze solid tissues, a single-cell suspension must be prepared	May require tissue sectioning, but enables detection of *in situ* characteristics	

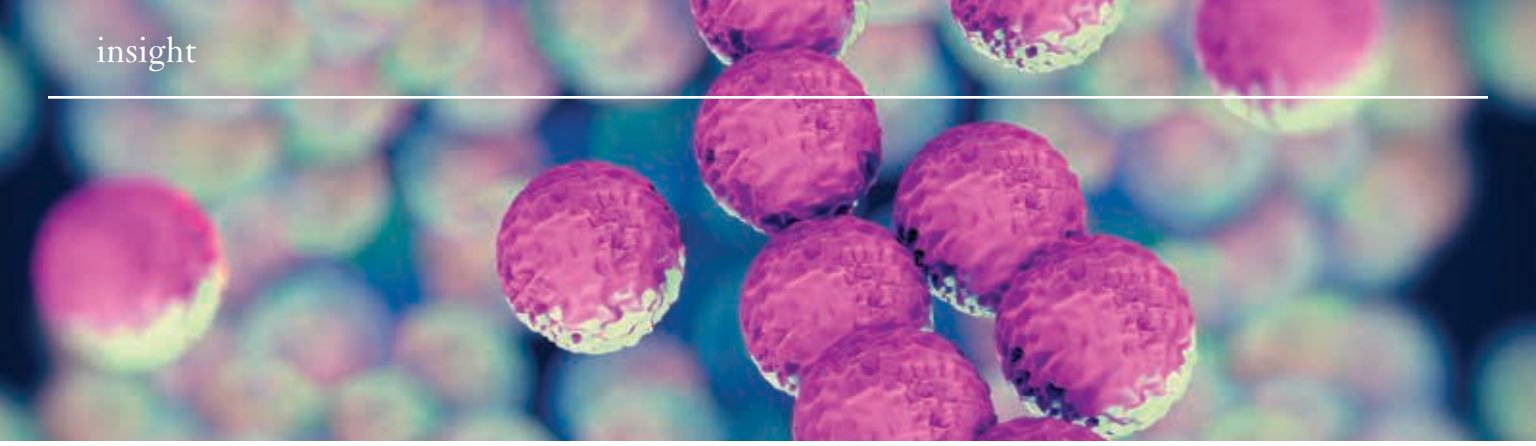
Flow Cytometry Fluorescence Microscopy

APPLICATION

CELL SORTING	Requires a fluorescence activated cell sorter (FACS)	Not possible	
TIME-LAPSE DATA	Challenging	Routinely performed	
RARE CELL DETECTION	Easily done	Requires a highly trained operator scanning visual fields for long periods of time	
RNA DETECTION	Requires specialized assays that detect RNA and protein expression	Easily visualized	
STRUCTURAL/ MORPHOLOGI-CAL DATA	Imaging cytometers are available for this purpose	Easily acquired	
CELLULAR INTERACTIONS	Rarely provides this information	Provides this information	

OTHER CONSIDERATIONS

COMPLEXITY AND COST	The more parameters needed, the more complex and costly instruments and software will be	More complex experiments require more expensive instruments and software	
NUMBER OF PARAMETERS DETECTED	Up to 30 on a single cell	Up to six on a single cell with special instruments	
STATISTICS	Statistics are easy to obtain with embedded software	Time-consuming if done manually, but statistics are easy to obtain with software	
SENSITIVITY	Depends on the fluorochromes, experimental design, and instrumentation	Depends on the fluorochromes and exposure time	
THROUGHPUT	Up to 100,000 cells per second	Several hundred cells per second with automated microscopy coupled with automated image analysis	



The Diagnostic Answer to the Superbug Crisis

NEXT-GENERATION PHENOTYPING HOLDS PROMISE FOR RAPID ANTIBIOTIC DE-ESCALATION **by Eric Stern, PhD**

Antibiotic resistance has emerged as a global medical crisis, perhaps the biggest public health challenge of our time. Each year, according to the Centers for Disease Control and Prevention, at least two million people in the US alone get infections that are resistant to antibiotics. More than 23,000 of these infections result in death.[1]

One of the most significant factors driving the antibiotic resistance crisis is the widespread use, and overuse, of broad-spectrum antibiotics.[2] The more frequently antibiotics are deployed, the more likely it is that pathogenic microbes will evolve resistance. Under the current paradigm of clinical care, septic patients are prescribed broad-spectrum antibiotics for a minimum of three days[3]—and often five or more days. This overreliance on some of the best drugs currently available directly fuels the rise of multidrug-resistant organisms (MDROs).

> "To combat the rise of multidrug-resistant organisms, patients must be transitioned to personalized, targeted therapies as quickly as possible."

To combat the rise of MDROs, patients must be transitioned to personalized, targeted therapies as quickly as possible. Recent investments in rapid bacterial identification (ID) and resistance marker platforms have aided clinical microbiology laboratories in their quest to help clinicians better target therapies. While these platforms rapidly differentiate viral from bacterial infections, doctors will prescribe a targeted antibiotic therapy only if they can be certain that the drug will effectively target a patient's infecting pathogen. In the absence of rapid antimicrobial susceptibility testing (AST) platforms, infectious disease doctors will continue to over-rely on broad-spectrum therapies.

A new prescription paradigm

The era of personalized medicine effectively originated in infectious disease departments, thanks to microbial ID and AST serving as the companion diagnostics that directed therapies. The first automated ID/AST platforms enabled virtually all clinical microbiology laboratories to provide consistent, reliable results to infectious disease doctors.

While revolutionary in their time, these automated platforms now fail to meet clinical needs in two critical dimensions. First, results arrive too slowly, and sample preparation requires too many days to keep pace with cutting-edge ID techniques. Second, antibiotic menus are limited, which prevents most hospitals from having panels matching their formularies and means that patients infected with MDROs require additional reflex testing. Limited test menus are particularly insidious because the patients with the most difficult-to-treat infections end up receiving the most delayed, least effective care. A new diagnostic paradigm is therefore needed to improve patient care and maintain antibiotic potencies and efficacies.

The ID-to-AST gap

Over the past decade, advances in genetic and proteomic techniques have created a new gold standard for

clinical microbiology laboratory ID. These platforms are more accurate and faster than traditional biochemical methods, which has resulted in a new clinical microbiology laboratory paradigm where ID results are known at least one to two days before AST results are available. This ID-to-AST gap accentuates the slow pace of AST and creates an agonizing delay for doctors who need the AST results in order to select the safest and most effective treatment for their patients.

Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS, or MALDI) is not only better and faster, but also—depending on laboratory volumes—sometimes cheaper than traditional biochemical ID methods.[4] As a result, nearly two-thirds of the clinical laboratories in the US have already adopted MALDI as their primary ID platform.[5] These laboratories' original ID/AST platforms now perform only half their originally intended service, as their biochemical ID approaches are obsolete.

For all its considerable strengths, MALDI suffers one major weakness: it requires isolated microorganism colonies because it cannot consistently detect more than one species at a time. This inability to reliably differentiate polymicrobial from monomicrobial samples is a result of the core physics of matrix ionization coupled with the time-of-flight detector. Thus, laboratories cannot rely on MALDI IDs from positive blood cultures to de-escalate therapies.

Genetic multiplex (gen-plex) technologies, both PCR- and hybridization-based, have found a powerful niche providing rapid ID from positive blood samples as well as directly from some patient samples, such as nasal swabs and respiratory and stool samples. Like MALDI, gen-plex platforms have dramatically impacted clinical microbiology laboratories. Using PCR, Cepheid set a new infection control standard by rapidly differentiating methicillin-resistant *Staphylococcus aureus* (MRSA) from methicillin-susceptible *S. aureus* (MSSA) infections from nasal swab samples. BioFire® (acquired by bioMérieux) then significantly expanded PCR's multiplexing capabilities with the FilmArray® platform. Nanosphere's VERIGENE® platform (acquired by Luminex) offers similar performance from positive blood cultures with its hybridization-based approach.

Since gen-plex platforms do not require isolated colonies, they typically provide IDs one day faster than MALDI does, exacerbating the ID-to-AST gap. But gen-plex speed is expensive: per-test prices are 10 to 25 times higher than those of MALDI. Nonetheless, clinical microbiology laboratories have rapidly adopted these platforms because they improve patient care and decrease lengths of stay.

In addition to providing IDs, gen-plex platforms provide information on known resistance genes in their multiplex assays. Because thousands of documented mutations confer resistance—even the utility of *mecA* to exclusively determine MRSA vs. MSSA is now under question—these fast antibiotic resistance tests are limited to providing information about which antibiotics will *not* work. Thus, resistance tests prove useful if there happens to be a known marker that requires therapy escalation, but they provide limited actionable de-escalation information.

Next-generation phenotyping (NGP) challenges

The rapid ID platforms have exacerbated the slow speed of AST, and infectious disease doctors are clamoring for earlier susceptibility results. To change infectious disease patient care, an AST platform must offer 1) a rapid time to results and 2) a comprehensive, expandable antibiotic menu. Furthermore, it is essential that such an NGP platform meets the throughput requirements of laboratories and the cost structures of infectious disease care.

> NGP platforms provide rapid, comprehensive AST results that enable targeted therapies to be delivered to patients, including those infected with MDROs, within a day of sample collection.

The key technological challenge of rapid AST is performing accurate microorganism quantification while accounting for antimicrobial-induced morphological changes. This is particularly critical for beta-lactam agents, which account for approximately two-thirds of US antibiotic prescriptions.[6] Bacteria susceptible to beta-lactams often filament or swell (forming spheroplasts or protoplasts) before lysing at antibiotic concentrations around the minimum inhibitory concentration (MIC).

Because they utilize bulk optical density (OD) measurements to assess microorganism growth, traditional, first-generation automated AST platforms cannot differentiate filamented or swelled susceptible cells from truly replicating resistant cells. Since filament, spheroplast, or protoplast lysis requires 7.5 hours for the fastest-replicating strains, traditional platforms are limited by the speed with which they can make accurate AST calls. This limitation

leads many clinical laboratories to perform AST overnight, since standard clinical laboratory shifts are eight to 10 hours and AST results must typically be reviewed and interpreted by first-shift personnel before being reported.

In order to close the ID-to-AST gap, an NGP platform must therefore be capable of determining bacterial morphologies. The need for same-shift AST is further driven by the increasing shortage of trained medical technologists and the difficulty of filling second and third shifts—another harsh reality faced by many laboratory directors.

The menu limitation of first-generation AST platforms derives from their measurement paradigms. To provide AST results as early as possible, these machines take OD measurements of every reservoir on every card/plate every 15-20 minutes. These are combined to create growth curves, which are assessed by computer algorithms to determine MICs.

Though these platforms are powerful in concept, their reliance on growth curves limits the number of drugs that can be tested in parallel and creates system trade-offs that decrease result accuracies. The need for repeated measurements imposes a significant engineering constraint. The time required to take each measurement and shuttle cards/plates from the incubator to the optical reader is compounded by the fact that the machines hold ~100 cards/plates at a time. Thus, the addition of a new test reservoir must come at the cost of either throughput or accuracy. Since no lab can afford to compromise throughput or accuracy, the number of test reservoirs is locked for each platform.

As a result, directors are faced with a zero-sum game when new drugs gain FDA approval: to accommodate a new drug, they must sacrifice a generic mainstay already on the panel. Adding meropenem-vaborbactam, for example, requires the sacrifice of piperacillin-tazobactam. Because Kirby-Bauer diffusion disks suffer no such trade-off, these disks are available shortly after drugs gain FDA approval.

The limit on the number of test wells on traditional AST platforms also prevents laboratories from performing actual quality control (QC) tests for many drugs. This has created such significant accuracy issues that the FDA no longer grants clearances for agents that do not include on-scale QC. Thanks to this new FDA requirement, all newly cleared drug-bug combinations on traditional AST platforms, as well as all drug-bug combinations on new AST platforms, must provide on-scale QC.

The NGP hunt continues

The hunt continues for a rapid, broad-menu, cost-effective NGP platform that brings AST into the 21st century. Results should be available within five to six hours to enable the same-shift reporting necessary to keep pace with rapid ID technologies and eliminate the ID-to-AST gap.

Furthermore, the distribution of the time to results should be minimal in order to allow hospitals to establish structured workflows for antibiotic stewardship team reporting. In addition, the system should not only provide results from a broad menu of antibiotics but also should have the capability to easily accommodate new drugs as they are developed. While meeting these requirements, the new platform must also remain more affordable than rapid gen-plex ID systems.

NGP Platform Wish List

The ideal NGP platform for AST should:

- Offer a rapid, broad test menu that can accommodate new drugs.
- Enable same-shift reporting.
- Eliminate the ID-to-AST gap.
- Allow hospital to establish structured workflows.
- Be more affordable than rapid gen-plex ID systems.

Though companion diagnostics began with AST, current AST platforms' slow speeds and incomplete results have considerably dulled AST's sheen. Since susceptibility results are more important than ever due to the rise of MDROs, companies and investigators are now trying to find ways to emulate phenotypic results with genetic technologies. These approaches, such as next-generation sequencing, face considerable technical and cost challenges but must be considered real competitors to NGP.

Multiple companies and investigators are now racing to develop AST platforms based on new detection paradigms. The winning NGP technologies will solve the AST speed and menu issues cost-effectively while addressing the medical technologist shortage plaguing clinical microbiology laboratories.

The need has never been greater; time will tell whether the current generation of diagnostic developers can create an NGP platform that allows AST to reclaim its companion diagnostic throne.

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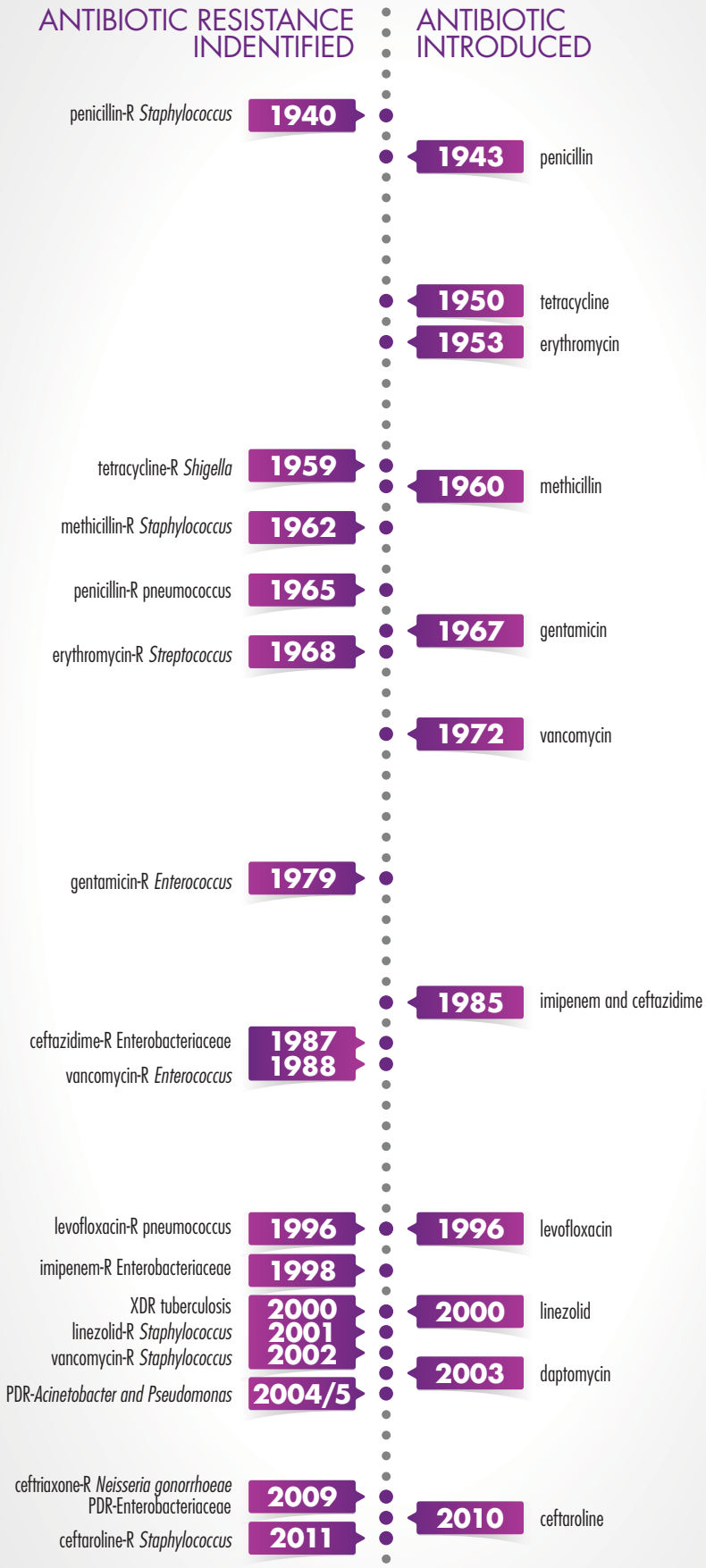
***Eric Stern**, PhD, is chief technology officer and co-founder of SeLux Diagnostics, a Boston-based biotechnology company that is addressing the global crisis of antibiotic resistance by developing a next-generation antimicrobial susceptibility test system aimed at transforming the treatment of patients with infectious disease. Prior to co-founding SeLux, he served as director of cell technology at the solar firm 1366 Technologies and as a senior scientist at Nano-Terra, an innovation and product development company. He completed a postdoc at Harvard and earned his BS (chemistry), MS (electrical engineering), and PhD (biomedical engineering) from Yale. He is also the adoring father of two little girls and dedicates his work in loving memory of Alan Stern.*

Timeline of Antibiotic Resistance Events



Note: Penicillin was in limited use prior to 1943.
Source: Centers for Disease Control and Prevention

How to Run an Effective Tumor Board

A GUIDE TO THE ROLES, PROCESSES, AND DATA MANAGEMENT

by Marissa Schuh; Rachel Stewart, DO, PhD; Riham El Khouli, MD, PhD; Rachel Miller, MD; Justine Pickarski, MS, LGC; Eric Durbin, DrPH, MS; Susanne Arnold, MD; Jill Kolesar, PharmD, MS

Oncology is unique in that somatic mutations can both drive the development of a tumor and serve as a therapeutic target for treating the cancer. Clinical sequencing of many cancers is now a routine part of care; however, the volume and complexity of sequencing data generated can be overwhelming to practicing oncologists. Molecular tumor boards (MTBs), typically multidisciplinary and disease agnostic, have emerged as a method for analyzing sequencing data and providing clinically relevant recommendations to the treating physician. A number of factors contribute to the effective implementation of an MTB.

Key considerations

MTBs should evaluate their scope by considering the needs of the constituency, the population, and the institution, and the research interests of the team. The focus should be on providing the highest-quality analysis, with broad intellectual support across multiple disciplines. Creating a set of guidance documents and levels of evidence for decision making will place all decisions into context, allowing individual practitioners who receive the MTB reviews to easily understand the data that support recommendations. These measures also give third-party payers and institutions confidence in the decisions of the MTB, and mediate medicolegal risks, while supporting the provision of targeted therapy by insurers.

"MTBs should evaluate their scope by considering the needs of the constituency, the population, and the institution, and the research interests of the team."

Members and roles

Identifying the leadership team of an MTB is a critical first step. At our institution, the University of Kentucky Markey Cancer Center, the co-leaders are a clinical pharmacologist and a gynecologic oncologist. The co-leaders have complementary expertise in the clinical care of cancer patients and the molecular pharmacology of anticancer agents, and provide scientific, administrative, and clinical leadership to the MTB.

A pathologist with board certification and/or subspecialty expertise in molecular genetic pathology should be included on an MTB in order to assist with variant interpretation, discussion of clinically actionable variants, and questions regarding test methodology and quality assurance practices. Input from a pathologist can also be useful for prioritizing molecular testing in the setting of small or limited tumor samples. The clinical significance of variants and resulting treatment recommendations are best discussed within the context of the primary site and histopathologic diagnosis. A pathologist with expertise in surgical pathology can add valuable information to the discussion by presenting histopathologic findings, staging information, and interpreting the results of immunohistochemical stains and other ancillary tests.

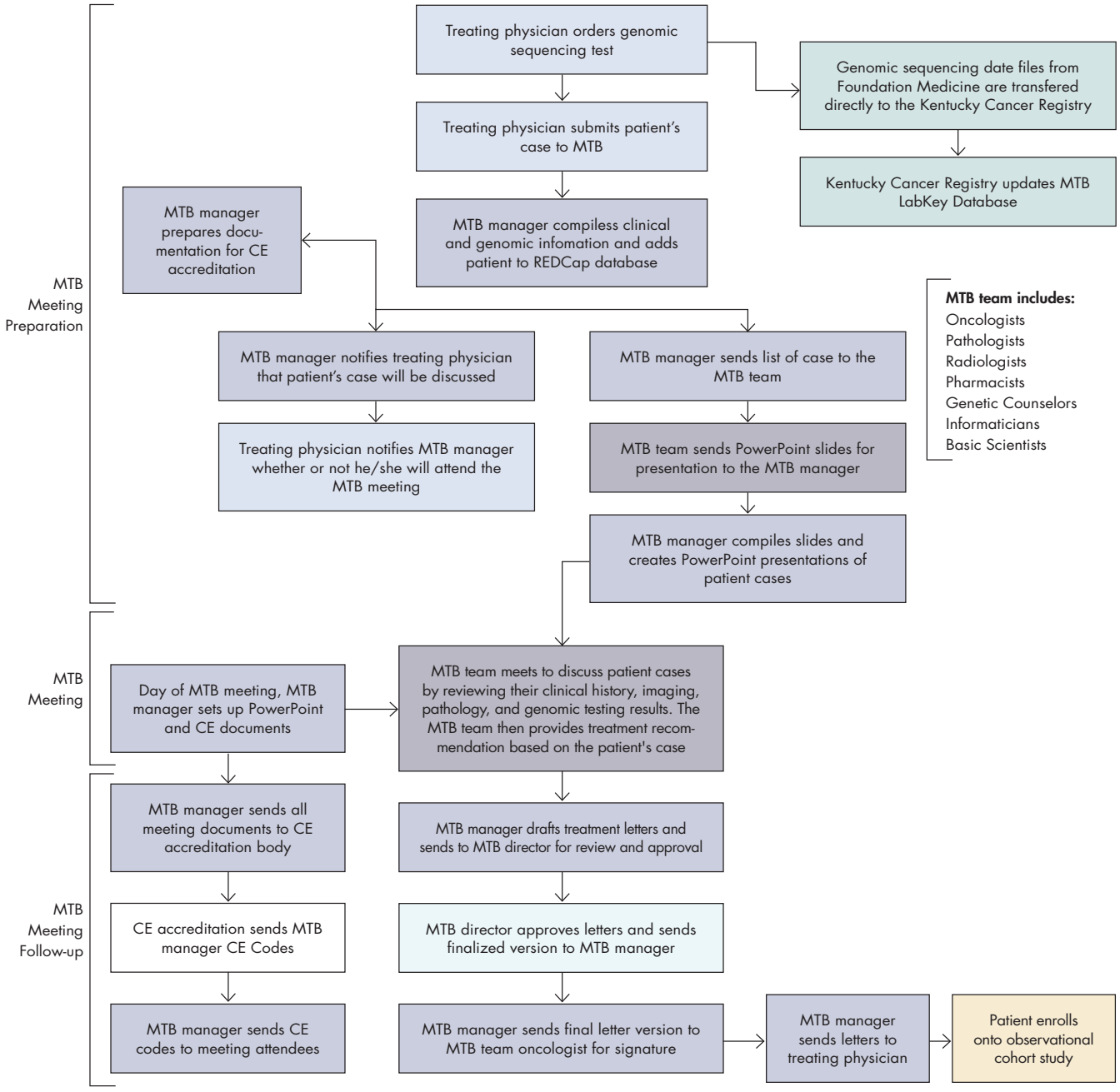
Patients referred for MTB consultation are typically refractory or relapsing patients who have exhausted all clinical standard of care options, which makes review of imaging a critical component of the process. Board-certified, fellowship-trained radiologists are key members of the MTB and provide expertise regarding disease extent and progression. Careful review and comparison of all prior imaging studies using the standard treatment response metrics—including the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) and Positron Emission Response Criteria in Solid Tumors (PERCIST 1.0)—is valuable. Additionally, selection of representative images for presentation during the MTB session helps the group understand the disease behavior and the multidisciplinary assessment of each patient.

Our clinical team is composed of physicians, clinical pharmacologists, and genetic counselors. Input from surgical and medical oncologists with broad clinical expertise for the most common tumor types seen by the MTB, and with experience in therapeutic decision making in the era of targeted therapies, is essential. Clinical trialists are also valuable, as they not only review cases for clinical recommendations but also identify potential candidates for clinical trials with biomarker entry criteria. Clinical pharmacologists provide a critical assessment of the drugability of identified mutations, potential treatment strategies, and pharmacological differences within a drug class. A genetics counselor is also present at all MTB meetings to identify candidates for germline testing. Our clinical team reviews the clinical case history, evaluates the targetability of identified mutations, and develops a patient-specific recommendation for either standard of care therapy, off-label therapy, a clinical trial, or additional testing.

The MTB process

The MTB manager oversees all aspects of MTB operations [see flowchart on next page]. The manager uses standard operating procedures to set the meeting agenda, disseminate cases to reviewers, return recommendations to treating physicians, develop documentation, and provide continuing medical education. Guidance documents serve to objectify the decisions of the group, maintain consistency, and provide structure to the review process.

University of Kentucky Markey Cancer Center's Molecular Tumor Board Process



▲ *Overview of the University of Kentucky Markey Cancer Center's MTB process, including the steps that occur before, during, and after the MTB meeting.*

Recommendation (based on color)	Evidence Level
FDA-indication therapy; substantial evidence supporting use	Meta-analysis, RCTs, etc. OncoKB level 1
Off-label use; substantial evidence supporting use	Phase II studies and above OncoKB level 2 and above
Off-label use; low to moderte evidence supporting use; MTB recommends, clinical trial preferred	Phase I, case studies and reports OncoKB level 3 and below
Off-label; no evidence supporting use: enrollment in clinical trail recommended; report experience to MTB if used outside clinical trial	Little to no evidence (pre-clinical, animal/cellular models), mechanistically plausible
Not recommended	Phase II studies or above recommending against therapy

▲ *The University of Kentucky Markey Cancer Center's MTB evidence grading scale.*

Prior to the initiation of the MTB, we received approval of our initial guidance documents by the university's policy and administrative bodies. We continuously review the guidance documents as the science changes to incorporate new findings, new technologies, and new therapeutic options for patients. Levels of evidence do not change, however, and that is the context in which we report all results.

Data management

MTB data must be properly managed to support clinical decision making, to enable the evaluation of the MTB's performance, and to support downstream research. At a minimum, an MTB requires the ability to track patients through the MTB process. A data management system should capture patient demographics, consents, details about the cancer diagnosis and stage, prior treatments and responses, and clinically relevant variants, as well as the final recommendations made by the MTB. Information about disease progression and response to treatment post-MTB review are also critical for evaluating the impact of the MTB on patient outcomes. Our center utilizes a clinical trials management system for this purpose.

The way molecular data is reported can impact its usefulness. While the PDF reports generated by molecular testing laboratories are sufficient for clinician review, they are not suited for further analyses such as calculating variant allele frequencies and identifying retrospective cohorts or those needed for research. It is essential to obtain reported variant data (including both significant variants and variants of unknown significance) in a structured format that can be loaded into a query-able database. While no national standards yet exist for structured molecular reporting, many vendors offer reports in an eXtensible Markup Language (XML) or JavaScript Object Notation (JSON) format for this purpose. In addition to the report data, it is important to also obtain the raw sequencing data and metadata that describes the bioinformatics pipelines utilized for the samples. Our center routinely obtains raw data files in the Binary Alignment Map (BAM) format. We store these rather large files on a secure university supercomputer and in public cloud-based resources.

Molecular data is most useful for analyses and research when integrated with other clinical, biomarker, and multi-omics data sources. For example, cancer registry data is often a rich source of standardized clinical, treatment, and long-term outcome information for patients. Our center has partnered with the Kentucky Cancer Registry, a National Cancer Institute Surveillance, Epidemiology and End Results (SEER) registry, to build a Cancer Research Data Commons that integrates data from the MTB, SEER registry, electronic pathology reports, clinical trials, biorepositories, and other multi-omics sources as a resource available to clinicians and researchers. A portal has been developed that allows authorized investigators to review patient populations using a combination of data points from the various sources. This provides an excellent source of preliminary data to further enhance research efforts at our academic medical center.

"Molecular data is most useful for analyses and research when integrated with other clinical, biomarker, and multi-omics data sources."

MTBs are an effective way to interpret and synthesize complex clinical sequencing reports, provide actionable treatment recommendations to treating physicians, and develop a database for ongoing research questions. Implementing an effective MTB requires the input and commitment of a large interdisciplinary team, strong administrative support, adoption of standardized workflows, and incorporation of evidence into clinical decision making.

Marissa Schuh *is the project manager of the Markey Cancer Center Precision Medicine Center;* ***Rachel Stewart****, DO, PhD, is an assistant professor of pathology and the scientific associate director of the Markey Biospecimen Core;* ***Riham El Khouli****, MD, PhD, is an assistant professor of radiology and the medical director of research in the department of radiology at the University of Kentucky;* ***Rachel W. Miller****, MD, is an associate professor of obstetrics and gynecology and co-director of the Markey Cancer Center Molecular Tumor Board;* ***Justine Pickarski****, MS, LGC, is a genetic counselor supervisor at the Markey Cancer Center;* ***Eric B. Durbin****, DrPH, MS, is an assistant professor of biomedical informatics and director of the Kentucky Cancer Registry and the Cancer Research Informatics Shared Resource Facility;* ***Susanne Arnold****, MD, is a professor of medicine and associate director of clinical translation at the Markey Cancer Center;* ***Jill Kolesar****, PharmD, MS, is a professor of pharmacy and co-director of the Markey Cancer Center Molecular Tumor Board.*

Maximilian Diehn, MD, PhD

ASK THE EXPERT

Boosting the Clinical Utility of Liquid Biopsy

by Masha G. Savelieff, PhD

Maximilian Diehn, MD, PhD, is an associate professor of radiation oncology at Stanford University. He received his bachelor's degree in biochemical sciences from Harvard College and his MD/PhD in biophysics from Stanford University. He is a board-certified radiation oncologist and specializes in the treatment of lung cancers. Dr. Diehn's research program spans laboratory, translational, and clinical studies. His areas of interest include cancer genomics, liquid biopsies, and lung cancer biology.

Q: What are liquid biopsies?

A: Liquid biopsies refer to biomarker assays that query evidence of cancer cells in biological fluids. In particular, the most commonly studied liquid biopsies are circulating tumor cells (CTCs), which are intact cancer cells in the circulation, and cell-free DNA (cfDNA) or circulating tumor DNA (ctDNA), which are fragments of DNA that are outside of cells and present in the circulation.

Q: What advantages can liquid biopsies offer over pre-existing testing technologies? What disadvantages do they suffer from?

A: There's a lot of excitement about liquid biopsies because they provide tumor genotype information through a simple blood draw, without requiring an invasive biopsy. Since an ever-increasing number of drugs target specific tumor mutations, having a way to identify these non-invasively is an exciting new opportunity. Additionally, because biological fluids are relatively easy to obtain, we can perform these assays repeatedly, allowing us to monitor how tumor burden and a tumor's molecular properties change with treatment.

A disadvantage is the amount of cancer DNA present in a blood draw, which is very small compared with that in a tumor biopsy. This represents a challenge from an analytical standpoint. Also, liquid biopsies, particularly the next-gen sequencing assays, can be quite expensive. However, taking into account the cost of surgical tumor biopsies, liquid biopsies can actually be quite cost effective.

Q: Can you tell me a little bit about your research focus in liquid biopsies?

A: Our focus has been on developing novel methods of detecting ctDNA, such as CAPP-Seq (CAncer Personalized Profiling by deep Sequencing), and on applying these technologies in the clinic. We're also interested in measuring aspects of a tumor from a blood draw that go beyond the presence of specific mutations. One particular area I'm very excited about is using ctDNA to measure minimum residual disease (MRD), which refers to a small amount of tumor cells that can remain in a patient after treatment. Currently, we can't distinguish patients with MRD from those who are cured. But if we could do that, we could better personalize treatment. Patients who are cured could be spared the toxicity and cost of additional treatment, whereas patients with detectable MRD could likely benefit from further treatment to try to eliminate the residual cancer.

Q: In what areas have liquid biopsies seen the most progress? What's on the horizon?

A: I think the most successful tests have been for ctDNA, which are already in clinical use and part of standard-of-care for certain cancer patients. As for what's on the horizon, I'm most excited about the data emerging on MRD and its potential for personalized treatment for early stages of the disease. I also think there are going to be improvements that will lead to novel applications, including for early cancer detection.

Q: What is the concordance like been between tissue and liquid biopsies?

A: The concordance between liquid and tumor biopsies depends on the method used and specific study—but

ranges from 75 to 95 percent. There are two main reasons for discordance. The first occurs when there isn't enough ctDNA in a blood sample. In this case one may not be able to detect all mutations present in a patient's tumor. Those are the false negatives. On the flip side, you can detect mutations in the blood that you didn't detect in the tumor biopsy. Those are often real tumor mutations that weren't present in the tumor deposit that was biopsied due to tumor heterogeneity.

Q: Do you think liquid biopsies are ready to replace tissue biopsies?

A: I think in certain cases, we're already there. In non-small cell lung carcinomas patients who progress on certain epidermal growth factor receptor tyrosine kinase inhibitors, we routinely do liquid biopsies for resistance mutations to determine whether we can start the patient on the next line of treatment. Only if we don't detect the mutation by liquid biopsy do we perform a tissue biopsy.

For the majority of patients, however, we absolutely still need a tumor biopsy to make the diagnosis and measure things like protein expression and histological subtype. So, I think for most patients, tissue biopsy will continue to be a critical aspect of their initial workup. But I do foresee in the future that we will be able to test more aspects of tumor biology using liquid biopsies, so that more patients will be able to avoid or minimize the number of tissue biopsies.

"I foresee in the future that we will be able to test more aspects of tumor biology using liquid biopsies, so that more patients will be able to avoid or minimize the number of tissue biopsies."

Q: What are the technology's future prospects as a diagnostic tool?

A: I think the prospects are bright and it's likely that we will have clinically useful ctDNA screening tests, at least for some cancer types. It remains to be determined which patient populations will benefit most. Importantly, we need to perform large prospective randomized studies to prove that patients who are screened have better survival outcomes.

Q: How is health insurance coverage for liquid biopsies? What is needed to increase clinical use?

A: Several liquid biopsies have been approved by the Centers for Medicare and Medicaid Services in recent months, so it is possible to get these tests covered, at least for patients with advanced disease. Some of the earlier stage applications such as MRD will require evidence from trials to prove their clinical utility before they will be reimbursed. Therefore, a lot of clinical trial work remains to be done to bring liquid biopsies fully into the standard of care.

CAPP-Seq: An Economical, Ultrasensitive, Broad-Coverage Liquid Biopsy

In 2014, Diehn published a study in *Nature Medicine* on CAPP-Seq—a liquid biopsy technique designed to identify recurrent tumor drivers, including single nucleotide variants and fusions, from ctDNA in patient plasma. Unlike single target liquid biopsies for a specific mutation, CAPP-Seq comprises "selector" biotinylated probes designed to amplify ctDNA at 521 exons and 13 introns from 139 recurrently mutated genes in non-small cell lung carcinomas (NSCLC), with a coverage of approximately 125 kilo base pairs. That means it can detect somatic mutations in over 95 percent of NSCLC patients. When Diehn and his colleagues applied it to patient plasma samples, CAPP-Seq detected ctDNA in 100 percent of patients with stage II–IV NSCLC and in 50 percent of patients with stage I, at a specificity of 96 percent for mutations present at fractions as low as about 0.02 percent. The technique also employs features to minimize false positives from the potential impact of biological variability and stochastic noise. The study's authors found that the levels of ctDNA quantified by CAPP-Seq varied proportionately with the tumor volume and could be used to monitor treatment response. It was also capable of detecting residual disease more accurately than radiographic means. Although originally designed to detect the most frequent mutations in ctDNA from NSCLC patients, the method can be extended to any other type of cancer characterized by established, recurring mutations.

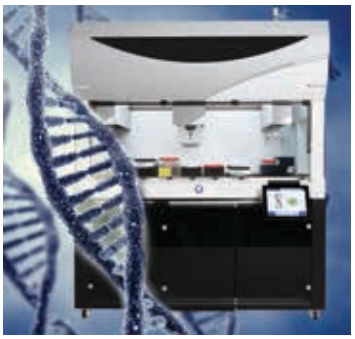
***Masha G. Savelieff**, PhD, is a full-time science writer and co-founder of SciGency Science Communications. She obtained her PhD in chemistry at the University of Illinois at Urbana-Champaign, and performed research in medicinal chemistry, Alzheimer's disease, and cancer biology before becoming a full-time writer.*

solutions FOR THE CLINICAL LAB

From assays to analyzers, these are some of the latest and greatest products for use in the clinical lab

TECAN NGS DREAMPREP™

Tecan has announced the launch of NGS DreamPrep™, a fully-automated approach to next-generation sequencing (NGS) library preparation for research use. This new approach offers quality controlled, sequencing-ready NGS libraries in just a matter of hours, with minimal manual interaction and no sample loss. NGS DreamPrep™ is a full walkaway solution that combines the Tecan Fluent® liquid handler and Infinite® plate reader, together with Celero™ DNA-Seq and Universal Plus mRNA-Seq library preparation kits—an optimized solution that brings significant improvements in speed, flexibility, accuracy, and precision.



DIASORIN MOLECULAR GROUP B STREP ASSAY

The FDA has cleared DiaSorin Molecular LLC's new Simplexa™ GBS Direct assay for diagnostic use. Designed for use on the LIAISON® MDX instrument, the highly sensitive assay enables qualitative detection of Group B Streptococcus (GBS) nucleic acid from 18- to 24-hour Lim broth enrichments of vaginal/rectal specimen swabs obtained from antepartum women. Assay results can be used as an aid in determining the colonization status of antepartum women. The new assay can replace traditional culture testing methods and features an efficient, fast workflow.

BIOCARE MEDICAL VALENT® IVD AUTOMATED STAINING PLATFORM

Biocare Medical, LLC has announced the release of the VALENT IVD automated staining platform, which merges high-throughput and quality staining with a powerful and intuitive user interface. VALENT overcomes the limitations of closed systems with its unique open platform, allowing reagents from multiple sources and providing top-tier IHC results. It provides an easy-to-use fully automated platform, 48-slide capacity, multiplex IHC capability, and high-quality staining. With VALENT, the IHC protocol is completely automated, performing fast, non-toxic online deparaffinization and utilizing a novel, patent-pending, continuous antigen retrieval dispense technology.

SIEMENS HEALTHINEERS ASSAYS FOR INFECTIOUS DISEASE AND ONCOLOGY

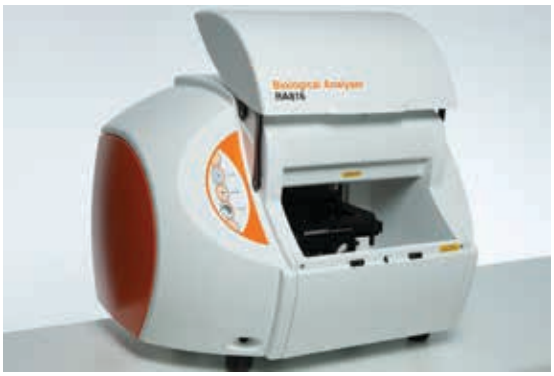
Siemens Healthineers has achieved 12 pre-market approvals from the FDA for its infectious disease and oncology testing menu. This milestone means the company's Atellica® Solution now provides laboratories in the U.S. with a comprehensive menu on a single laboratory platform for patients' in vitro diagnostic testing needs. The infectious disease tests new to the Atellica Solution include HIV (HIV Ag/Ab Combo (CHIV) and HIV 1/O/2 Enhanced (EHIV)) and Hepatitis B and C (Anti-HBs 2, HBsAg II, HBsII Confirmatory, HBc IgM, HBc Total, HBeAg, and HCV), and provide physicians with testing options for hepatitis screening, diagnosis, and monitoring.

BD PHOENIX™ CPO DETECT TEST

Carbapenemase-producing organisms (CPOs) represent a prominent antimicrobial resistance (AMR) threat to public health because these dangerous microbes are often resistant to nearly all available antibiotics. BD (Becton, Dickinson and Company) has received FDA clearance of the BD Phoenix™ CPO detect test, which will allow hospitals to identify infections caused by CPOs. The test may help hospitals contain the spread of AMR by shortening the time it takes to detect CPOs, thereby enabling the earlier implementation of infection control procedures and the initiation of appropriate antibiotic therapies designed for treating these infections. The test streamlines laboratory workflow by routine, concurrent testing of CPO and susceptibility to one panel. Conventional phenotypic methods for CPO detection can take up to 96 hours, whereas the BD Phoenix™ CPO detect test can accurately detect CPOs in under 36 hours.

BECKMAN COULTER DXONE WORKFLOW MANAGER

Laboratories today are under increased pressure to manage costs and resources, while balancing increasing test volumes. Beckman Coulter has announced the U.S. release of its DxONE Workflow Manager, the first and only cloud-based middleware offered by a major in-vitro diagnostics organization, designed to help low-volume laboratories deliver timely results for patient care by enhancing consistency, accuracy, and efficiency. With a limited number of middleware solutions on the market available to support low-volume laboratories, DxONE Workflow Manager fills an industry need to help these laboratories streamline workflow and maximize staff time. The system features an intuitive interface designed for ease of use, with visual cues that facilitate rapid decision making.



RENISHAW RA816 BIOLOGICAL ANALYZER

The new Renishaw RA816 biological analyzer is a compact benchtop Raman imaging system, designed for biological and clinical research. It enables biologists and clinicians to identify and assess biochemical changes associated with disease formation and progression, providing the full range of biochemical information without needing prior knowledge of specific molecular targets, or time-consuming labeling or staining. Users are able to reveal detailed information from biological samples, from the distribution of exogenous and endogenous compounds within tissue, to the detection of protein secondary structure changes due to drug interaction and tissue injury.

ORTHO CLINICAL DIAGNOSTICS VITROS® HIV COMBO TEST

Ortho Clinical Diagnostics has announced that its VITROS® Immunodiagnostic Products HIV Combo Reagent Pack and Calibrator (VITROS® HIV Combo test) received approval from the FDA for use on Ortho's VITROS® ECi/ECiQ Immunodiagnostic Systems. The VITROS HIV Combo test was previously approved for use on Ortho's VITROS® 5600 Integrated System and Ortho's VITROS® 3600 Immunodiagnostic System. VITROS® HIV Combo, a fourth-generation test, detects both HIV-1 and HIV-2 antibodies and the p24 antigen. By detecting the antigen itself, rather than only the antibodies to the antigen, Ortho's VITROS HIV Combo detects HIV-1 acute infection earlier than previous generations of tests.

SPOTLIGHT ON CANCER solutions

BIO-RAD DIGITAL PCR SYSTEM AND TEST FOR MONITORING CHRONIC MYELOID LEUKEMIA TREATMENT RESPONSE

Bio-Rad Laboratories, Inc. has announced that its QXDx AutoDG ddPCR System, which uses Bio-Rad's Droplet Digital PCR technology, and the QXDx BCR-ABL %IS Kit are the industry's first digital PCR products to receive FDA clearance. Used together, Bio-Rad's system and kit can precisely and reproducibly monitor molecular response to treatment in patients with chronic myeloid leukemia. The QXDx AutoDG ddPCR System is designed to be flexible, allowing users to run either FDA-cleared in vitro diagnostic tests or lab developed tests on the platform.

QIAGEN ONCOLOGY AND IMMUNO-ONCOLOGY PANELS

QIAGEN has launched three innovative sample to insight workflows for NGS research in oncology using QIAGEN's GeneReader NGS System and other NGS platforms. Two new GeneRead QIAact panels for use on QIAGEN's GeneReader NGS System deliver more powerful genomic insights, one covering a broad range of cancer-causing variants and the other focusing on genes tied to breast and ovarian cancers. Additionally, a new QIAseq panel was launched for use on any NGS system to measure tumor mutational burden, an emerging biomarker for use in assessing how a patient may respond to checkpoint inhibitors, which are a form of cancer immunotherapy.

ROCHE NAVIFY® CLINICAL DECISION SUPPORT APPS

Roche has launched the first two NAVIFY® clinical decision support apps to help oncology care teams access relevant clinical trial information and publications more effectively. Finding the most relevant up-to-date clinical trials and relevant literature is a cumbersome and labor-intensive process. The two launched apps available on the NAVIFY Tumor Board facilitate this process. The NAVIFY Clinical Trial Match app identifies clinical trial options based on patient-specific attributes such as age, gender, biomarkers, and various tumor information from 11 international registries. The NAVIFY Publication Search app mines publication sources globally for the most recent clinically and therapeutically relevant literature.

THERMO FISHER SCIENTIFIC ONCOMINE DX TARGET TEST

Thermo Fisher Scientific announced that it has CE-IVD marked its NGS-based solution that screens biomarkers across solid tumors. Oncomine Dx Target Test is CE marked as an in vitro diagnostic for detection of 46 cancer-driver gene variants. All biomarkers on the panel are associated with approved and investigative targeted therapies in solid tumors, including EGFR, BRAF, KRAS, and ERBB2 mutations, as well as ALK, ROS1, RET, NTRK, and MET fusions. It is also validated as a companion diagnostic for approved therapies in non-small cell lung cancer, including ALK, ROS1, and BRAF kinase inhibitors, as well as EGFR exon 19 deletions and L858R tyrosine kinase inhibitors.

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Thought Leadership

BIG IDEAS ABOUT THE CLINICAL INDUSTRY

How Point-of-Care Testing Can Add Value to Healthcare Providers

by Christoph Pedain, PhD

In today's healthcare system, the need for quick and accurate medical decision-making calls for the right type of test result to be available at the right time. Given the cost challenges and labor shortages many clinical laboratories face, healthcare providers must find new ways to deliver in vitro diagnostic test results efficiently.

Enter point-of-care testing (POCT). Several large US hospitals have successfully introduced POCT instruments in their sepsis programs. Huntsville Hospital in Alabama is a prime example. Having converted blood gas testing throughout the hospital from benchtop to handheld analyzers a few years back, the hospital began exploring additional areas in which to use handheld devices. One area they had targeted for improvement was sepsis care. For every hour sepsis patients spend waiting for an antibiotic, mortality increases. By implementing handheld blood gas analyzers, clinicians can now check a patient's lactate level in three minutes to help initiate treatment sooner and reduce a patient's risk of complications. The greatest benefit in this hospital was improving the quality of care: The hospital reported that mortality rates dropped by nearly 50 percent in the first six months of implementation. From a financial standpoint, the introduction of POCT also made business sense: savings in workforce efficiency and improved patient flow far outweighed the necessary investments.

Since its inception more than 6,000 years ago with the introduction of "urinalysis" as conceived by Hippocrates, POCT has evolved to include blood gas testing, cardiology, sepsis care, and much more. In addition, parameters for testing have progressed, education for IVD testing has become more specialized, and many qualitative observations have been developed into complex quantitative algorithms.

With POCT, critical tests can be processed quicker, facilitating patient care for emergency situations such as suspected venous thromboembolism or sepsis. Maintaining specimen integrity is another benefit: Instruments are located nearby, and testing is immediate, which reduces

the likelihood of processing delays that could impair sample viability. Also, as health systems are increasingly focused on value-based patient care, POCT can supplement missed or underutilized testing and improve the patient experience by reducing wait times and travel needs.

While the benefits of POCT are clear, some clinicians may be reluctant to introduce new instruments for fear of overloading an already lean workforce with a new technology to learn. To address this challenge, some manufacturers have incorporated safety and quality control measures into the instruments and their corresponding software, such as "intelligent" urine strips that automate quality checks by detecting humidity exposure and automatically identifying the strip type. These features enhance testing accuracy and workforce productivity by automating certain processes, eliminating the subjectivity of visually read tests, and reducing transcription errors.

With a greater number of patients to manage, more stringent regulations to follow, and evolving technologies, clinicians have a full workload. Finding the right balance of POCT combined with laboratory testing is worth the investment in process and equipment innovation. Companies that supply both laboratory and POCT solutions are in a position to offer standardization and correlation across testing sites and along a patient's journey. Using the same technology across multiple settings maximizes efficiency for the clinician, and can therefore expedite and improve diagnosis and treatment for the patient.

***Christoph Pedain**, PhD, is the head of point-of-care diagnostics for Siemens Healthineers. He has worked in the medical device industry for 20 years, and has been with Siemens Healthineers since 2017.*

A Growing Need for Informatics Tools in Clinical Diagnostics

by Rajeev Sehgal, MBA

As is common throughout the healthcare industry, microbiology labs are under pressure to improve output without sacrificing quality or increasing costs. In many cases, microbiology labs are the first line of defense when it comes to mitigating situations that may disrupt hospital workflow and inadvertently place patients in harm's way. One primary example is early, accurate diagnosis and effective communication of results to avoid patient exposure to healthcare-associated infections (HAIs).

Rapid detection of harmful bacteria and viruses can be key to reducing instances of locked-down wards and to keeping HAI rates low, but there is certainly room for improvement. According to the Centers for Disease Control and Prevention (CDC), approximately 722,000 HAIs occur annually in US acute-care hospitals. On any given day, about one in 25 hospital patients has at least one HAI, according to the CDC.

While new diagnostic technologies in microbiology labs can help in identifying and investigating the spread of HAIs, informatics tools are sometimes overlooked as part of the solution to a multifaceted problem. Utilization of informatics solutions can help labs streamline their workflows and reporting, which in turn may help hospitals make progress toward their HAI reduction benchmarks.

Informatics solutions can help clinicians expedite the delivery of diagnostic information, thereby enabling timely clinical decision-making, whether it's isolating a patient colonized with an antibiotic-resistant infection or quickly identifying and determining therapy to treat an HAI. Implementing informatics into a lab workflow could expedite the reporting of results and potentially help reduce human errors. However, informatics solutions are currently underutilized in diagnostic labs.

The reluctance to adopt new informatics technologies may lie in the obsolete informatics systems found in many labs, which can hamper productivity. These outdated and fragmented systems often require labs to process large amounts of work manually or to rely on a variety of middleware systems that may only complete a single stage of analysis. The lack of integration, combined with variable data storage or formatting, makes it almost impossible to achieve a streamlined workflow that allows for easy access across the ever-growing networks of labs and their satellite locations.

The limitations of older informatics systems have been addressed with improved informatics platforms that offer a

single, centralized system that links all instruments to one common middleware solution. Some of these solutions have the flexibility to connect additional instruments over time and can centralize data from operations across multiple sites. Not only can these solutions make it easier to deliver results to clinicians, but they also aggregate data, helping labs gather information needed for compliance reporting.

In some cases, these technologies can extend the reach of key personnel. Informatics can offer lab personnel access to the same information anytime and anywhere via virtual bacteriology and telemicrobiology capabilities, which may reduce or eliminate the need for on-site intervention or consultation. This benefit is especially meaningful in large lab networks with many satellite locations because the added responsibility of visiting multiple sites can reduce productivity and be burdensome for key personnel. Together, these benefits enable labs to provide faster turnaround time, realize cost savings, and improve efficiency. Informatics can also help enable expedited decision-making by the clinical team—pharmacy, physician, infection control, and nurses—to help guide patient care.

A more streamlined informatics approach may also provide other benefits: it can simplify onboarding and lab training and improve ease of use by reducing manual processes and technological redundancies inherent in multiple middleware systems.

These workflow benefits can go a long way toward helping clinicians provide quality patient care. Informatics solutions may assist clinicians in providing more timely diagnoses, and therefore may potentially expedite patient management decisions. In addition, rapid diagnoses may help hospitals prevent the spread of HAIs and antimicrobial-resistant infections by enabling infection-control departments to respond in a timely manner.

***Rajeev Sehgal**, MBA, is the director of informatics at BD (Becton, Dickinson and Company), where he is responsible for strategy creation, roadmap execution, and commercialization for the informatics business.*

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