20 Strategies for Rural Hospitals to Attract and Retain Staff

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STEPS TO A SAFER CLINICAL LAB

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“one word: plastics.”

A version of that famous scene from *The Graduate* played itself out at a dinner I recently attended. Most of the guests were medical professionals, and I was seated next to a physician. We struck up a conversation about the future of health care. For her, there was one word: immunotherapies.

Targeted immunotherapies are certainly revolutionizing cancer treatment. But, as with other cancer therapies, immunotherapies aren’t right for every patient. Disease heterogeneity and variability among patients mean a drug that works for one might not work for another.

Enter companion diagnostics. These tests can help physicians identify potential candidates for a given therapy. Although the tests are most often associated with cancer, author Raeesa Gupte, PhD, describes other therapeutic areas, including neurology and inflammatory diseases, in which companion diagnostics are coming onto the scene in this month’s feature story “Companion and Complementary Diagnostics in Oncology and Beyond.” Certain areas will inevitably advance quicker than others, she writes: “While infectious diseases and cystic fibrosis may be amenable to rapid progress given their fairly uncomplicated pathogenesis, heterogeneous disease states such as asthma, Alzheimer’s disease, and psychiatric disorders are far more challenging.” Nonetheless, the move away from a one-size-fits-all model of treatment is undoubtedly making inroads outside of oncology.

Another key focus of this month’s issue is laboratory staff. Staffing shortages are among the top concerns on many clinical lab managers’ minds. In “20 Strategies for Rural Hospitals to Attract and Retain Staff,” Denise Bland, MHA, shares firsthand tips on finding and keeping laboratory staff in rural areas. Clinical lab managers also often struggle with people management, particularly keeping their staff motivated. In “Motivating Laboratory Staff,” Sedef Yenice, PhD, outlines theories on motivation and how to apply them in practice in a laboratory setting. Staff safety is an ever-present concern in the clinical lab. To kick off our new Safety section, Mari Ishak Gabra, MS, highlights relevant OSHA regulations in “Steps to a Safer Clinical Lab.”

There’s plenty more in this month’s issue. I sat down with Kristi Kuper, PharmD, BCPS, senior clinical manager of infectious diseases at Vizient’s Center for Pharmacy Practice Excellence, to discuss the ins and outs of implementing a successful antimicrobial stewardship program. Our technology feature showcases exciting applications of single-cell genomics in disease research and diagnostics. And this month’s thought leaders offer their insights into quality management tools and certainty in drugs of abuse screening.

Enjoy!

**Erica Tennenhouse**  
*Erica Tennenhouse, PhD, Managing Editor*
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Artificial Signaling Centers to Grow Embryonic Tissues

Scientists have succeeded in stimulating human embryonic stem cells to grow and differentiate in culture similar to a real-life developing embryo. Mimicking the early developmental processes of human embryos \textit{in vitro} has been challenging. Embryos differentiate into specific cell types when they encounter signaling molecules, called morphogens, at precise times and in accurate concentrations during development. In the study published in \textit{Nature Methods} in June 2019, researchers used a microfluidic chip for controlled delivery of concentration gradients of various morphogens to human embryonic stem cells. Based on the morphogen concentration released by these spatiotemporally controlled artificial signaling centers, embryonic stem cells developed and organized into patterns of specific cell types, similar to embryos that develop \textit{in utero}. This technique may find applications in regenerative medicine to develop human tissues or organs and in drug testing to reduce the use of laboratory animals.


Distinguishing Mutations That Drive Tumor Growth

According to new research published in \textit{Science} in June 2019, recurring mutations (mutation hotspots) may not always promote cancer progression. Recurring errors at the same DNA base pairs across the genomes of several patients have long been used as the gold standard to identify cancer-driving mutations. However, whether tumor-specific functional benefits bestowed by the mutations are solely responsible for their recurrence...
is not known. In the new study, researchers examined over 9,000 patient tumors to determine how specific structural elements may influence recurring mutations caused by the enzyme APOBEC3A. They found that cytosines present in DNA stem-loops, or hairpin structures, were particularly susceptible to being mutated by APOBEC3A. These hairpin sites were “passenger hotspots” for recurring mutations in noncancer-causing genes. In contrast, APOBEC3A-mediated recurring mutations in cancer-driving genes were not restricted to any specific genomic features. The ability to discriminate between mutations that drive cancer progression and those that do not is essential for developing novel cancer therapies.


**Impact of Gold Nanoparticles on B Lymphocytes**

Polymer-coated gold nanospheres do not elicit an immune response in human B lymphocytes in vitro, according to a study published in *ACS Nano* in May 2019. Although nanoparticles are promising vehicles for targeted drug delivery, their interaction with the immune system needs to be adequately characterized. Previous studies have shown gold nanoparticles (GNPs) to be compatible with immune cells such as macrophages and dendritic cells. This is the first study to determine the impact of GNPs on human B lymphocytes—the antibody-producing immune cells. Researchers exposed B lymphocytes to GNPs for 24 hours and examined the immune response by measuring the expression of activation markers and inflammatory cytokines. Polymer-coated and spherical GNPs did not stimulate an immune response, whereas uncoated and rod-shaped GNPs impaired B lymphocyte function. This methodology could be used to test the biocompatibility of nanoparticles and to develop safer therapies, particularly in the field of oncology.


**The Etiology of Childhood Pneumonia in Africa and Asia**

Viruses were identified as the leading cause of severe childhood pneumonia in a June 2019 study published in *The Lancet*. Although antibiotics and vaccines have reduced pneumonia deaths over the past few decades, continued progress is hindered by limited information on other common pathogens. The Pneumonia Etiology Research for Child Health (PERCH) study characterized disease-causing microorganisms in non-HIV-infected children who were hospitalized in seven low- and middle-income countries because of severe pneumonia. The study used 33-target multiplex quantitative PCR to obtain pathogen data from multiple body fluid specimens collected from 4,232 test subjects and 5,119 controls. They found that viruses accounted for 61.4 percent of severe pneumonia cases and 54.5 percent of very severe pneumonia cases, while bacteria were implicated in 27.3 percent of severe and 33.7 percent of very severe cases. Respiratory syncytial virus was responsible for
one third of the viral pneumonia cases. The findings suggest that developing vaccines to target these pathogens may significantly reduce childhood pneumonia mortality in these countries. The rigorous analytical approach of the PERCH study can also be used by other studies to guide policies for the prevention and treatment of other diseases.


**High-Resolution Imaging of Subcellular Drug Reservoirs**

Recently, a new method was developed to visualize the distribution of antibiotics within cells infected with tuberculosis. Since accumulation of antibiotics within infected cells is not an accurate indicator of drug efficacy, it is important to determine whether the drug reaches its pathogenic targets within the cell. In a study published in *Science* in June 2019, scientists used a combination of light, electron, and ion microscopy to visualize the intracellular localization of an antitubercular antibiotic at high resolution. They infected human macrophages with *Mycobacterium tuberculosis* and treated them with the drug bedaquiline after two days. The researchers found that the drug accumulated in lipid droplets within infected macrophages. The lipid droplets served as drug reservoirs, eventually transferring the accumulated antibiotics to the pathogens that consumed them. These findings enhance our understanding of how antibiotics work. This method can also be used in future research to screen novel drug candidates for other infectious diseases based on their subcellular properties.


**Machine Learning to Personalize Radiotherapy Dose**

A study published in *The Lancet Digital Health* in July 2019 reported that machine learning could be applied to medical images to individualize radiotherapy and reduce treatment failure to less than five percent. The generic approach currently used in clinical practice, wherein the radiation dose is not optimized based on individual tumor and patient characteristics, leads to high rates of treatment failure in some patient subgroups. The researchers leading this study applied a deep learning framework to computerized tomography (CT) images of lung cancer patients to identify radiomic features that could predict treatment outcomes. These characteristic image signatures were combined with other clinical variables from patients’ electronic health records to predict treatment failure rate and to estimate the
radiation dose required for effective tumor control. The algorithm could predict treatment failures across diverse clinical settings and CT scanners with high accuracy. This approach can be implemented for risk stratification and dose optimization in clinical trials and, subsequently, in clinical practice.


Do Dentists Overprescribe Antibiotics?

Despite guidelines narrowing the use of prophylactic antibiotics prior to dental procedures, dentists constitute the leading antibiotic prescribers in the US. Currently, prophylactic antibiotics are recommended only in patients with a cardiac condition at high risk of secondary infection. However, a study published in JAMA Network Open in May 2019 suggests that approximately 81 percent of dental antibiotic prescriptions are unnecessary. The retrospective cohort study analyzed 91,438 patients who received prophylactic antibiotics for 168,420 dental visits from 2011 to 2015. Although 90 percent of visits involved an invasive dental procedure, only 20 percent of patients had a cardiac condition with high risk of adverse outcomes from infective endocarditis. Patients most likely to be prescribed unnecessary antibiotics were those with prosthetic joint devices, women, and patients in the western US. These findings suggest that implementing antibiotic stewardship strategies in dental practice is likely to have a major impact on public health in the face of growing antibiotic resistance.


Relevance of Measures Estimating Reduction in Low-Value Care

A systematic review published in the Journal of General Internal Medicine in June 2019 found that most studies assessing the impact of interventions on the prevalence of low-value care focused on reducing resource utilization rather than on clinically meaningful benefits to patients. Low-value care includes efforts that do not benefit patients, waste limited resources, or lead to unnecessary expenses. Although interventions to reduce low-value care are fairly common, robustness of the criteria used to quantify the effects of such interventions has not been studied. Therefore, this study classified the measures used in 101 published studies and 16 ongoing trials. Of the published studies, 68 percent focused on change in utilization of a test or treatment, but only 41 percent measured the consequences of altered usage. Even fewer studies measured unintended consequences of the intervention (34 percent) or included patient-reported outcomes (8 percent). The analysis highlights the need to incorporate more clinically relevant patient-centered measures into the study design of interventions to reduce low-value care.

Motivating Laboratory Staff

PRACTICAL TIPS TO HELP YOUR EMPLOYEES FIND MEANING IN THEIR WORK by Sedef Yenice, PhD

No matter what it is that we are doing, we have to have the proper motivation if we are going to succeed. This requirement applies not only to our individual pursuits, but also to laboratory management.

Of all the functions a laboratory manager performs, motivating team members is arguably the most complex. This is due, in part, to the fact that what motivates people changes constantly. For example, research suggests that as employees’ incomes increase, money becomes less of a motivator. And as employees get older, interesting work becomes a greater motivator.
Motivation is tricky and multifaceted. Therefore, we have to think carefully about what motivates our team members on a day-to-day basis. Key questions to ask ourselves: Is our team properly motivated? What is it that motivates them in the first place?

**What Is Motivation?**
Motivation is widely regarded as a psychological state that compels an individual to act toward a desired goal; it elicits, controls, and sustains certain goal-directed behaviors. It can be considered a catalytic force or the energy to act upon or toward the desired goal. Motivation is an enormous part of success in work and in life.

**Theories of motivation**
There are two types of motivations one can consider: extrinsic and intrinsic. Extrinsic motivation is driven by external forces such as money or praise. Intrinsic motivation is something that comes from within and can be as simple as the joy one feels after accomplishing a challenging task, e.g., a laboratory technician who spends extra time working for validation of a new analytical method because he or she wants to get better results of internal quality. Importantly, people respond differently to various types of intrinsic and extrinsic motivation.

“Of all the functions a laboratory manager performs, motivating team members is arguably the most complex.”

The major approaches that have shaped our understanding of employee motivation are called “motivation theories.” While different motivation theories prioritize different factors, a common theme among them is the idea that motivation is a function of extrinsic and intrinsic factors.

The earliest theories of motivation are content theories, also called “needs theories.” These theories try to identify what one’s needs are and then relate motivation to the fulfilling of those needs. The major content theories are Maslow’s Hierarchy of Needs, Herzberg’s Motivation-Hygiene, McClelland’s Human Motivation, Alderfer’s ERG (existence, relatedness, and growth), Mayo’s Motivation, and McGregor’s Theory X and Theory Y.

![Maslow’s Hierarchy of Needs](image)
According to Maslow’s Hierarchy of Needs theory, a need is defined as a physiological or psychological deficiency that requires satisfaction. Employees have five levels of needs: physiological, safety, social, self-esteem, and self-actualization. Maslow argued that lower-level needs must be satisfied before the next higher-level need will motivate employees.

**Theory X and Theory Y**
Theory X and Theory Y are two contrasting sets of assumptions about workforce motivation that form the basis for two managerial styles.

Theory X stresses the importance of strict supervision, external rewards, and penalties. This management style supposes that the average employee has little to no ambition, shies away from work or responsibilities, and is individual-goal-oriented.

Theory Y highlights the motivating role of job satisfaction and encourages workers to approach tasks without direct supervision. This management style assumes that people in the workforce are internally motivated—they enjoy their labor and will work to better themselves without a direct reward in return.

In the laboratory, it might be best to take a blend of the two approaches. With employees who fit into the motivated and self-reliant categories, a hands-off approach is best. This might apply to tasks that are focused on being creative, such as your team members engaging in research studies or quality improvement projects. On the other hand, if you have a routine clinical laboratory service or some other repetitive-task area—such as that of a phlebotomy unit—it is likely the staff in that setting are not particularly self-driven. So with that part of the business, you may need to keep managers or supervisors in close contact with the subordinates at all times in order to keep operations on schedule.
Process theories are concerned with how motivation occurs and what kinds of processes can influence our motivation. Adam’s Equity, Victor Vroom’s Expectancy, Taylor’s Motivation, Bandura’s Self-Efficacy, Skinner’s Reinforcement, and Locke’s Goal-Setting are examples of process theories.

Although these motivation theories continue to be important today, no single one explains all aspects of motivation or lack thereof. Nonetheless, each theoretical explanation can serve as the basis for the development of techniques to motivate staff.

**How to motivate employees**

Although money is the most expensive way to motivate employees, it remains the first choice for many leaders. Numerous studies, however, show that big bonuses are less effective than smaller, unexpected gestures because gifts create a relationship while bonuses are purely transactional.

According to Daniel Pink, to motivate team members in the correct way, most people require three major drivers:

1. **Autonomy**
   
   Employees need autonomy over some (or all) of the four main aspects of work: when they do it (time), how they do it (technique), whom they do it with (team), and what they do (task).

2. **Mastery**
   
   Employees need to become better at something that matters to them. Daniel Pink uses the term “Goldilocks tasks” to describe those tasks that are neither overly difficult nor overly simple, allowing the employees to extend themselves and develop their skills further. To foster an environment conducive to mastery, four essentials are required: autonomy, clear goals, immediate feedback, and Goldilocks tasks.

3. **Purpose**
   
   Steps must be taken to fulfill employees’ natural desire to contribute to a cause that is greater and more enduring than they are. Employees who understand the purpose and vision of their organization, and how their individual roles contribute to this purpose, are more likely to be satisfied in their work.

With these drivers in mind, Table 1 summarizes the best practices for laboratory leaders to motivate their employees; it also includes approaches that do not work. The common theme among approaches that do not work is that they serve the leader, not the employee. If we want to direct our good intentions into more meaningful expressions of recognition, we need to consider the alternatives.

Table 2 lists practical ways for laboratory leaders and managers to communicate with their staff in order to increase staff engagement.

<table>
<thead>
<tr>
<th>What doesn’t work</th>
<th>What works</th>
<th>How to do it</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apply pressure; Demand accountability</td>
<td>Encourage autonomy</td>
<td>• Invite choice; illuminate boundaries; explore options within boundaries</td>
</tr>
<tr>
<td>Ignore feelings</td>
<td>Deepen relatedness</td>
<td>• Show empathy and caring; acknowledge and validate people’s emotions</td>
</tr>
<tr>
<td>Discount learning</td>
<td>Develop competence</td>
<td>• Emphasize learning goals, not just performance goals</td>
</tr>
<tr>
<td>Enable sabotaging behaviors</td>
<td>Promote mindfulness</td>
<td>• Encourage self-reflection</td>
</tr>
<tr>
<td>Rely on power</td>
<td>Align with values</td>
<td>• Help individuals align goal(s) to their work-related value(s)</td>
</tr>
<tr>
<td>Focus on metrics without meaning</td>
<td>Connect to purpose</td>
<td>• Help individuals connect the goal to their work-related or life purpose</td>
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</table>

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When motivation is lacking

A lack of motivation can manifest itself as a decrease in productivity, e.g., someone who was once productive stops producing consistent results. Studies have shown that focusing on negatives in this situation tends to create fatigue and resistance, whereas looking for opportunities to build on strengths leads to inspiration, motivation, and overcoming challenges.5

As depicted in the motivational cycle (below), the laboratory manager will first need to determine the cause of this decrease in productivity. Is it an interpersonal problem in the laboratory? An experimental obstacle? A personal crisis? Next, the manager should discuss the problem with his or her staff member to try to jointly develop a strategy to address the issue or minimize the impact of the team member’s actions.7

According to Gallup’s 2017 State of the American Workplace Report, using data collected from more than 31 million respondents, only 21 percent agree their performance is managed in a way that motivates them to do outstanding work.6 Seemingly, many employers fail to understand the significance of motivation in accomplishing the mission and vision of the organization. Even when they understand the importance of motivation, they lack the skill and knowledge to provide a work environment that truly fosters employee motivation and organizational health. Hence, employers and laboratory managers should remain up to date with the latest and most useful motivation methods and techniques, but also be brave enough to experiment with new ways of motivating their workforce.

“Many employers fail to understand the significance of motivation in accomplishing the mission and vision of the organization.”

References:

Sedef Yenice, PhD, is a professor of biochemistry and clinical chemistry and has been in the field of laboratory management for over 27 years. She works at the Gayrettepe Florence Nightingale Hospital in Istanbul, Turkey. She has served as chair of the International Federation of Clinical Chemistry and Laboratory Medicine, Committee on Clinical Laboratory Management, since 2014.
20 Strategies for Rural Hospitals to Attract and Retain Staff

RURAL HEALTH CARE FACILITIES OFTEN STRUGGLE TO FIND AND KEEP TALENT by Denise Bland, MHA

The demand for health care professionals is not limited to one area of the country, but rural areas are certainly beleaguered by the deficits. Many rural hospitals have an existing staff recruitment and retention problem. Several organizations have invested in virtual career fairs, built partnerships with medical schools, and developed systemwide marketing efforts to address the serious nature of the problem. The extensive geography of the issue emphasizes the market condition and suggests that staff recruitment and retention will continue to be an obstacle for the foreseeable future. The following are some creative tactics that rural hospitals can apply to recruitment and retention:

RURAL UPBRINGING
Some physicians and health care professionals desire a return to their community roots. It is advisable for hospitals to promote scholarship programs for students from the area, with obligations to return to the area upon school completion.

NETWORKING
An often undervalued resource is existing staff. Many excellent candidates originate from in-house employee recommendations. Also, do not underestimate the leverage of local societies and the power of relationship-building at other hospitals in the vicinity.

RÉSUMÉ FILE
Keeping a résumé file and a spreadsheet of candidate abilities, along with interview notes, is essential. You will often find that going back to these references helps you recover your original thoughts on whether the potential candidate is the right fit for the job.

TRAIN YOUR OWN
Online schooling and on-site internship opportunities can go a long way. They enable employees to develop their careers, thereby encouraging employee retention. Show your employees that you care about their continued growth through a program for tuition assistance. Many companies get significantly discounted rates through community and state colleges. Consider a partnership with colleges and universities nearby and through distance learning.
CONSIDER OTHER SKILLED WORKERS FOR ASSOCIATED TASKS

Look at the job description and make sure it is accurate regarding the qualifications for the position. Remind yourself of the reasons those qualifications exist. Do all of the tasks require an advanced skilled worker? Perhaps modifying the job description will allow the advanced skilled worker to handle additional volume while a lab assistant assumes the responsibilities that were not essential to the job description. Such job task changes can have a high impact.

AUTOMATE

Consider how software and instrumentation can help your existing staff focus on higher-quality tasks for patient care rather than mindless repetitive tasks that are amenable to automation.

SOCIAL MEDIA

While you are not interested in the volume of candidates as much as the quality, social media sites get significant traffic. Consider having managers advertise positions on their professional LinkedIn pages or other platforms.

MARKET YOUR AREA

Entice candidates with the aspects of your community that are attractive. Allow candidates to bring their families when they visit and get to know the area. Ask existing employees to provide information on local schools and daycares or other tips about the area. Consider presenting this information on a blog associated with your career page.

FOCUS ON COST OF LIVING

Those in rural communities should point out the low cost of living in their area. Candidates sometimes turn down positions in bigger cities because added pay ends up going toward daily survival.

BEHAVIORAL INTERVIEWING

Using situational questions and asking candidates to give examples to answer questions helps ensure the candidate is the right fit for the job. Physical task completion during interviews is advisable for laboratory roles to demonstrate competency.

Behavioral Interview Sample Questions

“Describe a stressful situation you have been in at work and how you handled it.”

“Give an example of how you’ve worked effectively as part of a team.”

“How have you handled difficult situations with coworkers?”

“Tell me about a time when you took initiative at work.”

“Give an example of a time you made a mistake and how you handled it.”

BENEFITS

Certain companies have started expanding benefits to include student loan repayment. The longer staff members stay in their jobs, the more repayment they get on their loans.
PRESENT AN IT STRATEGY
Have a comprehensive IT strategy to present to the candidate. The perception is that rural communities and small health care facilities are behind the times; you want to convince the candidate that your facility is technologically up to date.

CONSIDER REMOTE WORKERS
With telehealth, it may not be necessary to have all employees in your community. This option would be especially appealing to candidates who place a premium on work/life balance.

SUPPORT CONTINUED LEARNING
Budget cuts often mean that educational support for continuing education, travel to seminars or conferences, and registration fees to local conferences for existing staff are cut first. This is shortsighted when considering employee retention.

COMPETITIVE SALARY
A market salary adjustment should be a top consideration. Perform a market salary adjustment for existing staff and incoming candidates at least annually.

ON-SITE DAYCARE
Consider what benefits on-site daycare would bring to all staff and ask employees for suggestions on how it would be maintained. If employees would like to creatively staff an on-site daycare, it is worth discussing.

MULTIPLE JOB STRATEGY
Consider that some employees may want opportunities for overtime and would like to fill other part-time positions.

HIRE FAMILY MEMBERS
It has been a strategy at some institutions to hire spouses with appropriate backgrounds. This package deal approach encourages employee retention.

ACTIVE RECRUITING
Keep a constant goal of attracting new employees. In some situations, you may consider slightly overstaffing to keep a buffer on difficult-to-fill positions; it is likely that you need additional full-time equivalents in key role areas anyway. Creative budget strategies and shared duties across job functions will help achieve this goal.

Denise Bland has been in the field of histopathology for over 28 years. She works at a Boston hospital. Her days are spent striving to bridge the gap between laboratory protocols and best patient outcomes.
Human diseases often affect specific cell types within organ systems. In some disorders, such as amyloid lateral sclerosis (ALS), the disease impacts a single cell type representing a minor population of all cells in the tissue, as is the case for the motor neurons in ALS. Because tissues are composed of heterogeneous cell types, studying cell-type-specific features of human pathological conditions demands alternatives to conventional genomics approaches, such as bulk tissue RNA sequencing. Recent advances in single-cell genomics, in particular single-cell RNA sequencing, are opening new avenues for identifying the exact molecular changes that are associated with pathology in specific cell types. New research utilizing single-cell genomics to better understand human disease conditions is already providing novel insights and promises to help identify highly specific and diagnostic biomarkers and therapeutic targets.

Dissecting roles of immune cells in cancer and tumor heterogeneity

The immune system was one of the first systems to be analyzed in detail using single-cell genomics techniques. The availability of immune cells, which can be readily purified from the blood, along with historically well-established panels of markers of immune cell types, served to simplify the analysis of single-cell genomics data. Results of these efforts to apply single-cell RNA sequencing to human immune cells led to characterization of novel subtypes of lymphoid and myeloid cells as well as dynamic molecular events underlying differentiation of megakaryocyte and myeloid progenitors. Importantly, single-cell transcriptomics can be used not only to characterize unbiased subtypes of immune cells and their differentiation but also to obtain the repertoire of T and B cell clones mediating adaptive immune response. To this end, researchers recently developed a computational method to utilize single-cell RNA-seq data to reconstruct full-length sequences of T cell receptors (TCR). Combined single-cell gene expression and TCR analysis has since been applied to profile T cell repertoires in liver carcinoma and to document changes in T cell clonal composition after checkpoint inhibitor therapy in carcinoma patients. In these ways, single-cell genomics is currently being applied to measure the detailed cellular characteristics of the immune response to tumor growth in cancer patients.

Besides profiling populations of immune cells infiltrating the tumor, single-cell genomics approaches recently helped to tackle one of the biggest challenges of cancer biology: tumor heterogeneity. It has been increasingly recognized that tumors consist of a number of interacting cell types, derived both from tumor-initiating cells and infiltrating immune and endothelial cells. Tumor heterogeneity is thought to underlie mechanisms of tumor drug resistance. Single-cell transcriptomics studies of various cancer types such as glioblastoma, metastatic melanoma, and myeloid leukemia have identified novel potential drug targets expressed in specific tumor cell types (e.g., cancer stem cells) and genes that may be responsible for drug resistance.

Currently, single-cell approaches to studying cancer have been moving closer to the bedside. For instance,
single-cell RNA sequencing has been used to analyze single circulating tumor cells (CTCs), the cells that are shed by the tumors into the patient's bloodstream. Profiling of CTCs in melanoma and pancreatic cancer holds promise of early diagnosis and dynamic monitoring of cancer recurrence,1 which could dramatically reduce patient mortality in the future.

Analyzing disorders of the human brain

While single-cell analysis of the immune system and tumors is made possible by the accessibility of the patient tissue, which can be obtained through a blood draw, biopsy, or surgical resection, these options are not available when it comes to brain disorders. For most neurological diseases, except for epilepsy, the only time to access the patient's brain tissue is postmortem. Until recently, single-cell genomics tools required a suspension of live cells to work. However, a novel technique termed single-nucleus RNA sequencing (snRNA-seq) can analyze the RNA of a single cell nuclei isolated from frozen postmortem human brain tissue.4 Nuclear gene expression profiles have been shown to accurately match whole-cell transcriptional profiles, and snRNA-seq has recently been used to identify cell-type-specific gene expression changes in a number of psychiatric and neurological diseases.

In one study, the technique was applied to profile cortical brain tissue of patients with autism spectrum disorder (ASD) and compare the profiles of neuronal and glial subtypes in ASD with those from donors without any brain disorder.5 The authors observed that ASD-associated pathological changes converge on specific cell types, such as the projection neurons in the upper layers of the cortex that are responsible for information flow between cortical regions in the brain. In another study, snRNA-seq was applied to examine the prefrontal cortex of Alzheimer's disease patients with varying degrees of disease progression.6 The authors were able to dissect changes in specific cell types that underlie progression of Alzheimer's pathology, highlighting changes in excitatory neurons and oligodendrocytes related to regulation of myelination. Another group utilized snRNA-seq to profile cell-type-specific changes in the brain white matter of patients with multiple sclerosis (MS), observing changes in subpopulations of oligodendrocytes in MS patients.7 Overall, an increasing number of studies of human brain disease are successfully adopting single-cell genomics to investigate how pathology affects specific brain cell types.

The dawn of personalized diagnostics

Single-cell genomics techniques offer unprecedented resolution of cell types affected by pathological disease conditions. Multi-institutional projects, such as the BRAIN Initiative and Human Cell Atlas, aim to construct a census of cell types of the human brain and the body. The idea is to catalog all of the cell types in the human body and identify sets of marker genes that can be used to distinguish them. At the same time, studies of human pathology on the single-cell level aim to identify genes and pathways that are dysregulated in specific cell types in human disease. Building upon these efforts, it is expected that single-cell analysis of tissue samples from individual patients using techniques like spatial transcriptomics8 will soon become feasible, which will help shift the approach to disease diagnostics and treatments toward personalized medicine.

References


Dmitry Velmeshev, PhD, is a postdoctoral researcher at the University of California, San Francisco. His research is focused on applying single-cell genomics techniques to study human brain development and disease.
Single-Cell Sequencing Techniques to Overcome the Challenge of Tumor Heterogeneity

Developments in single-cell sequencing enable scientists to study disease pathology in individual cell types. These techniques may be especially useful to overcome several challenges in cancer treatment, including tumor heterogeneity.

Cancer Challenge: Tumor Heterogeneity

Tumors demonstrate high heterogeneity, as they consist of multiple cell subpopulations. This presents a significant challenge to oncologists, as clinical decisions are often based on the presence of biomarkers and genetic mutations. Further, tumor heterogeneity is thought to contribute to drug resistance. Single-cell transcriptomics may be useful for the identification of novel drug targets expressed in specific tumor cell types. Two models have emerged to describe tumor development: Clonal evolution and cancer stem cells.

Clonal Evolution Model

First proposed by Peter Nowell in 1976, the clonal evolution model describes the positive selection and expansion of certain cell lineages and depletion of others.

A single cell becomes neoplastic

Cell lysis, DNA and RNA release

Certain mutant cells have selective advantages and become precursors to the new subpopulations

The tumor consists of multiple cell subpopulations and has unique metabolic characteristics and antigens

Cancer Stem Cell Model

It is proposed that only a small number of cells, termed cancer stem cells, are tumorigenic and possess the ability to initiate tumor growth. The heterogeneity of tumor cells is therefore the result of their cancer stem cell predecessors.

Within a tumor, a single or multiple progenitors (cancer stem cells) occur.

Cancer stem cells initiate subsequent tumor growth and contribute to heterogeneity.

No tumor growth

Cancer stem cell

No tumor growth
Tackling Tumor Heterogeneity and Drug Resistance with Single-Cell Sequencing

Prior to sequencing, cells must be isolated from the specimen. Fluorescence Activated Cell Sorting (FACS), microfluidics, or laser capture microdissection may be used to isolate target cells.

Following cell isolation, a single cell undergoes whole cell lysis to release DNA and RNA. DR-seq (gDNA-mRNA sequencing) or G&T-seq (genome and transcriptome sequencing) strategies may be used for DNA and RNA sequencing. These techniques enable comparison of genomic and transcriptional variation within a single cell.

**DR-sequencing**

1. Isolate single cell
2. Cell lysis, DNA and RNA release
3. RNA reverse transcription to synthesize single stranded cDNA
4. gDNA amplification by PCR
5. cDNA-specific-second strand synthesis + in vitro transcription
6. Sequencing

**G&T-sequencing**

*(Adapted from Trends in Genetics, February 2017, Vol.33, No.2)*

1. Isolate single cell
2. Cell lysis, DNA and RNA release
3. Separate polyadenylated mRNA and DNA using oligo-dT-coated magnetic beads
4. mRNA to cDNA conversion + amplification
5. DNA precipitation + amplification
6. Sequencing

Single-cell RNA sequencing may potentially be applied to single circulating tumor cells shed from tumors, early diagnosis, and disease monitoring.

Single-cell transcriptomics may be used to guide the selection of targeted therapies through determination of potential drug targets within cells and tumors.

Drug resistance may arise as a result of specific subclones present prior to treatment or as a result of new mutations. Single-cell sequencing provides insight into factors contributing to drug resistance.
The Occupational Safety and Health Act of 1970 marked Congress’s creation of the Occupational Safety and Health Administration (OSHA) to ensure the safety of workers by setting and enforcing standards and providing necessary training, resources, and assistance. To ensure their safety, all clinical laboratory workers, and especially clinical lab managers, should have basic knowledge of the regulations set by OSHA that directly affect clinical laboratories.

Laboratories in the US employ more than 500,000 workers, who can be exposed to a myriad of potential hazards in the workplace. Finalized in 1990, OSHA regulation for laboratory safety was designed to protect workers from chemical, biological, physical, and other safety hazards. Compliance with OSHA laboratory safety regulations starts with implementing a written Chemical Hygiene Plan (CHP) and a designated officer. This article aims to highlight the steps clinical lab managers should take to cover the major OSHA requirements and the resources available to prevent workplace injuries and illness.
Lab Manager Safety Summit will focus on key management and safety issues affecting lab managers and safety specialists. Expert speakers will offer practical tools to help laboratory leaders guide their teams to higher levels of safety engagement and commitment. Based on a keen knowledge of our readers and multiple readership studies, we know that our Safety Summit will be relevant, timely, lively, and on target.
STEP ONE: Familiarize yourself with relevant standards and requirements

The first step toward a safe laboratory environment is understanding the various OSHA standards that directly apply to many health care and clinical laboratories. The following are the most important and relevant regulations:

Hazard Communication Standard (29 CFR 1910.1200):3 This standard is based on the simple concept that employers need a written plan to inform their workers of all hazardous chemicals on-site. This is achieved by maintaining an inventory of all chemicals, ensuring all containers are properly labeled, and confirming all safety data sheets (SDSs) are current and accessible.

Bloodborne Pathogens Standard (29 CFR 1910.1030):4 OSHA initiated this standard to protect employees whose jobs put them in direct contact with blood and other infectious materials. The Center for Disease Control and Prevention (CDC) indicates that HIV and hepatitis B and C viruses are the main concern and employers should provide controls to prevent exposure to biological samples.7 This standard also requires a written Exposure Control Plan (ECP). The ECP must document possible routes of exposure to bloodborne pathogens, the implementation of various controls (such as universal precautions, engineering controls, and good work practices), hepatitis B vaccination, and recordkeeping of training and incidents.

Personal protective equipment (PPE). Although not a standard, PPE is a requirement under the OSHA laboratory safety guidance. Clinical lab managers or safety officers must perform an assessment of their workplace and determine all the required PPE for each task. PPE is the final protective barrier between clinical laboratory workers and the hazard, after implementing engineering controls (such as the use of biosafety cabinets) and work practices (including limiting time of exposure to hazardous material).

STEP TWO: Recognize hazards in clinical laboratories

In addition to those outlined in step one, there are several other potential safety and health hazards at a clinical laboratory. Here are some examples of these hazards and the resources to assist in compliance with OSHA requirements:

Chemical hazards. Hazardous chemicals, including carcinogens, irritants, and corrosives, can pose a threat to the health of clinical laboratory workers.5 As specified by federal regulation, employers are required to limit the exposure of all workers handling hazardous chemicals at or below permissible exposure limits specified in the standard on air contaminants (see CFR 1910.1000, Table Z). Therefore, employers and clinical lab managers must use the written CHP to identify criteria to reduce employees' exposure to chemicals used in the laboratory. The written CHP should also include requirements to ensure that chemical fume hoods function properly and that other protective measures are in place such as certification, instructions for proper use, waste management, and routine cleaning. Additionally, employees must be trained to recognize hazardous chemicals, know the inventory of the types of hazardous chemicals in the workplace, and know which measures to use to protect themselves from exposure. They must be provided with information about who to contact in the case of a medical emergency.

Ergonomic hazards. According to OSHA, laboratory work can pose several ergonomic stressors, which include static or awkward postures and repetitive motions.9 Tasks such as examining slides under the microscope, pipetting several samples, or even using the biological safety cabinets can result in injuries or repetitive stress disorder. Thus, employers should provide their workers with general tips to prevent these injuries.

QUICK TIPS ON ERGONOMICS

• Wear hard, closed toe shoes in the laboratory for comfort
• Keep items such as waste containers, pipettes, pipette tip boxes within reach
• When using the microscope, ensure that you can use the eyepiece while sitting or standing in an upright position
• When possible, use an electronic pipette or ergonomic pipettes for intensive pipetting
• Keep head and shoulders in an upright position while pipetting
• Use low-profile tubes and containers inside fume hoods or biological cabinets to avoid bending or twisting the wrists and neck
STEP THREE: Survey workplace for additional hazards

A clinical lab manager or safety officer must identify any additional types of hazards and proper controls through a job-hazard analysis or risk-evaluation checklist. This will allow laboratories to identify potential risks associated with all techniques used by their employees and to devise the most suitable way to reduce chances of injury. The OSHA website provides a wealth of resources and templates on how to perform this type of assessment and ways to customize reports for any workplace.11

STEP FOUR: Train your employees

OSHA requires employers to provide updated training to workers exposed to any type of hazard to perform their job in order to prevent illness and injury. Inspectors will often test workers’ knowledge of hazards and safety. Training can be in the form of online modules or in-person workshops. There are also different types of continuing education material available through the OSHA website,12 including booklets, fact sheets, and posters to keep employees up to date on safety information. All employee training documentation should be saved in order to satisfy the first question typically asked by an incident investigator: “Did the employee receive adequate training to do this job?”

STEP FIVE: Recordkeeping, reporting, and posting

Unless the laboratory has 10 or fewer employees, all employers are required to keep record of workplace injuries and illnesses (29 CFR 1904). All incidents, from needlestick and sharps injuries to bloodborne pathogen exposures, should be logged by the laboratory manager or environmental health and safety officer. A new rule by OSHA requires certain employers with 250 workers or more to submit incidents electronically. In addition, all employers are required to report to OSHA within eight to 24 hours all work-related fatalities, hospitalizations, amputations, and losses of an eye. Finally, an OSHA poster or state plan equivalent should be posted in a prominent location in the workplace.

All managers and laboratory workers should recognize that violating any safety laws poses risks to their employers and can lead to serious consequences. Thus, it is important to keep up to date with regulations and standards as required by OSHA, as well as other clinical regulatory institutions. Getting involved in the regulatory process and hiring or designating safety officers are the best ways to ensure compliance.

References


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Disease heterogeneity and interpatient variability contribute to differences in drug efficacy and safety. This variability initiates a cycle of trial and error that continues until a suitably safe and effective drug is identified for each individual patient. Personalized medicine promises to eliminate the trial-and-error method by incorporating predictive biomarkers into therapeutic decision making.

A cumulative understanding of disease mechanisms and advances in molecular diagnostics in recent years have spurred a rise in the number of predictive biomarker assays being developed. These assays may be categorized as companion or complementary diagnostics, and a number of them are currently approved by the US Food and Drug Administration (FDA). While most are used in conjunction with oncology therapies, other therapeutic areas can also benefit from these predictive assays.

Companion and complementary diagnostics in oncology

Oncology has spearheaded the development and growth of the companion and complementary diagnostics industry. Predictive biomarker assays were first developed in the 1970s when the efficacy of tamoxifen was found to correlate with estrogen receptor status in patients with advanced-stage breast cancer. Subsequently, when Genentech developed the HER2 receptor antagonist trastuzumab, it collaborated with Dako to develop an in vitro diagnostic assay to screen breast cancer patients for HER2 overexpression. In 1998, this immunohistochemistry (IHC) assay, known as the HercepTest, became the first companion diagnostic to be approved by the FDA. Since then, several oncology products have adopted the drug-diagnostic codevelopment model, although the FDA also permits companion diagnostics and their corresponding drugs to be approved at different times.

COMPANION VERSUS COMPLEMENTARY DIAGNOSTICS

The FDA defines a companion diagnostic as “a medical device, often an in vitro device, which provides information that is essential for the safe and effective use of a corresponding drug or biological product.” Companion diagnostics are meant to identify patients most likely to benefit from a particular therapeutic product or, conversely, those most likely to suffer serious adverse effects due to the product. Notably, the companion diagnostic assay is identified on the corresponding drug or biological product’s label under Indications and Usage or Patient Selection.

Although there is not yet an official definition of complementary diagnostics, the FDA has presented a draft definition. It states that complementary diagnostics “identify a biomarker-defined subset of patients that respond particularly well to a drug and aid risk/benefit assessments for individual patients, but that are not prerequisites for receiving the drug.”
Currently, 32 drugs are linked to 33 oncology companion diagnostics that have been cleared or approved for use by the FDA. These assays help identify relevant patient populations based on the drug’s mechanism of action. For instance, *in vitro* diagnostics such as the EGFR pharmDx Kit (Dako), cobas KRAS Mutation Test (Roche Molecular Systems), Praxis Extended RAS panel (Illumina), and FoundationOne CDx (Foundation Medicine) help identify colorectal cancer patients eligible for treatment with the EGFR inhibitors cetuximab and panitumumab based on EGFR receptor expression or absence of *KRAS* mutations. Similarly, IHC, fluorescence *in situ* hybridization, and next-generation sequencing assays have been developed by Ventana Medical Systems, Abbott Molecular, and Foundation Medicine, respectively, to identify non-small cell lung cancer patients who can undergo treatment with ALK inhibitors (ceritinib, crizotinib, and alectinib). These assays qualitatively determine ALK expression and gene rearrangement. Companion diagnostics have also been approved for ovarian, gastric, urothelial, and cervical cancers, as well as melanomas.

In 2015, the FDA approved Dako’s PD-L1 IHC 28–8 pharmDx as the first complementary diagnostic for the oncology drug nivolumab in patients with non-small cell lung cancer. Currently, two oncology drugs (nivolumab and atezolizumab) have complementary diagnostics whose indications are expanded to include melanoma and urothelial carcinoma. The IHC assays by Dako and Ventana measure PD-L1 protein expression to identify patients who may demonstrate a better response to the PD-1 receptor inhibitors, but the assays are not prerequisites for receiving the drug.

Oncology comprises approximately 87 percent of the companion diagnostics market in North America and 95 percent in Europe. With nearly 60 percent of drugs in late-stage clinical development relying on biomarker data, oncology is expected to continue to lead the field of personalized medicine.

### Companion and complementary diagnostics beyond oncology

Taking a cue from oncology, biopharmaceutical companies are also developing companion and complementary diagnostics in other disease areas. Some estimates suggest that nearly half the therapies currently in Phase 3 clinical trials are associated with a non-oncology biomarker assay. Major therapeutic areas for companion and complementary diagnostic development are discussed below.

#### Diagnostic Name | Manufacturer
---|---
BRACAnalysis CDx | Myriad Genetic Laboratories
therascreen EGFR RQ PCR Kit | Qiagen Manchester
cobas EGFR Mutation Test v2 | Roche Molecular Systems
PD-L1 IHC 22C3 pharmDx | Dako North America
Abbott RealTime IDH1 | Abbott Molecular
ARIDx BCR-ABL Test | MolecularND Corporation
FoundationOne CDx | Foundation Medicine
VENTANA ALK (D5F3) CDx Assay | Ventana Medical Systems
Abbott RealTime IDH2 | Abbott Molecular
Praxis Extended RAS Panel | Illumina
Oncomine Dx Target Test | Life Technologies Corporation
LeukoStrept CDx FLT3 Mutation Assay | Invitrogen Technologies
FoundationFocus CDxBRCA Assay | Foundation Medicine
Vysis CLL FISH Probe Kit | Abbott Molecular
KIT D816V Mutation Detection by PCR for Gleevec Eligibility in Aggressive Systemic Mastocytosis (ASM) | ARUP Laboratories
PDGFRB FISH for Gleevec Eligibility in Myelodysplastic Syndrome / Myeloproliferative Disease (MDS/MPD) | ARUP Laboratories
cobas KRAS Mutation Test | Roche Molecular Systems
therascreen KRAQ PCR Kit | Qiagen Manchester
Dako EGFR pharmDx Kit | Dako North America
FemrScan | Resonance Health Analysis Services
Dako c-KIT pharmDx | Dako North America
INFORM HER-2/neu | Ventana Medical Systems
PathVysion HER-2 DNA Probe Kit | Abbott Molecular
PATHWAY antiHer2/neu (4B5) Rabbit Monoclonal Primary Antibody | Ventana Medical Systems
InSite Her-2/neu KIT | Biogenex Laboratories
SPOT-LIGHT HER2 CISH Kit | Life Technologies Corporation
Bond Oracle HER2 IHC System | Leica Biosystems
HER2 CISH pharmDx Kit | Dako Denmark A/S
INFORM HER2 Dual ISH DNA Probe Cocktail | Ventana Medical Systems
Hercutest | Dako Denmark A/S
HER2 FISH pharmDx Kit | Dako Denmark A/S
THX10 Braf Kit | bioMeineux
Vysis ALK Break Apart FISH Probe Kit | Abbott Molecular
cobas 4800 BRAF V600 Mutation Test | Roche Molecular Systems
VENTANA PD-L1 (SP142) Assay | Ventana Medical Systems
therascreen FGFR RQ PCR Kit | Qiagen Manchester
therascreen PHL3CA RQ PCR Kit | Qiagen GmbH B
Neurology

In 2012, the FDA approved Quest Diagnostics’ Stratify JCV—an immunoassay to aid risk stratification in multiple sclerosis patients receiving natalizumab. The companion diagnostic detects anti-JC virus antibodies that are associated with an increased risk of development of a rare but serious brain infection in patients undergoing prolonged natalizumab therapy. Of the 261 FDA-approved drugs with pharmacogenomic labeling information, 54 are used in the treatment of psychiatric or neurological disorders. This therapeutic area is therefore a viable candidate for the development of companion and complementary diagnostics. Although there are currently no FDA-approved pharmacogenomics-based companion or complementary diagnostics for neurological disorders, several CLIA-certified laboratory-developed tests are available. For instance, Assurex Health’s GeneSight Psychotropic test and Admera Health’s PGxPsy test evaluate the influence of several individual gene variants to predict patient response to 38 to 60 neuropsychiatric medications. Recently, Adial Pharmaceuticals announced plans to begin Phase 3 studies of their alcohol use disorder drug AD04 in subjects with target genotypes. The company has partnered with Eurofins Scientific to develop a quantitative polymerase chain reaction-based companion diagnostic to help identify the appropriate patient population.

As the global population of individuals aged 65 years and older continues to grow, it is essential to develop drugs and companion diagnostics for age-related neurodegenerative disorders such as Alzheimer's disease (AD). CSF levels of Aβ or tau and positron emission tomography (PET) neuroimaging biomarkers are being evaluated as potential companion diagnostics in a Phase 3 clinical trial of Roche’s gantenerumab in patients with prodromal AD. Other clinical trials that contemporaneously evaluated AD drugs (Merck’s verubecestat and Eli Lilly’s solanezumab) and diagnostics failed to show significant benefits.

Inflammatory diseases

Over the past two decades, biologics such as anti-TNF-α drugs have revolutionized the management of inflammatory disorders, including rheumatoid arthritis. However, with a third of the patients failing to respond adequately to these agents, relying on trial and error alone to identify the appropriate biologic can become expensive. Therefore, single nucleotide polymorphisms in TNF-α or its receptor and other gene variants may be used as predictive biomarkers in the development of companion and complementary diagnostics to stratify patients into potential responders and nonresponders. Additionally, other protein biomarkers involved in immune regulation have been incorporated into the Vectra DA test panel by Crescendo Bioscience to classify patients based on disease severity and to measure changes in response to drug treatment.

Inflammatory molecules are also being evaluated as potential biomarkers for asthma. An assay to measure serum levels of periostin was used as a companion diagnostic in Phase 3 trials of two IL13 inhibitors (Genentech’s lebrikizumab and AstraZeneca’s tralokinumab). Elevated serum periostin levels are indicative of severe asthma. Despite promising Phase 2 data, neither drug caused significant improvements in patient subgroups with high periostin levels.

Infectious diseases

Companion diagnostics that test HIV tropism identify patients suitable for treatment with the antiretroviral drug maraviroc. Maraviroc specifically inhibits the entry of the CCR5 receptor-dependent HIV virus but not the CXCR4 receptor-dependent or dual tropic viruses. Therefore, HIV tropism testing is a prerequisite for use of the drug.

Pharmacogenomic studies suggest that individuals with specific gene variants may be at an increased risk of adverse effects in response to two antiretroviral drugs—abacavir and efavirenz. Although there is no FDA-approved test to confirm this, several laboratory-developed test panels are available. Additionally, hepatitis C-infected patients carrying specific gene variants may be resistant to the antiviral agents mericitabine and daponprevir.

Growing antimicrobial resistance presents considerable challenges in the treatment of infectious diseases. In 2012, Cempra Pharmaceuticals collaborated with Curetis to use the latter’s PCR-based molecular diagnostics platform to aid pathogen diagnosis during the Phase 3 trial of its pneumonia drug. Although the drug was not approved by the FDA, the trial paved the way for drug-diagnostic codevelopment in the field of infectious diseases. Earlier this year, the FDA issued a guidance document to promote the coordinated development of antimicrobial drugs and antimicrobial susceptibility test devices.

Cystic fibrosis

Cystic fibrosis is an autosomal recessive disease characterized by mutations in the CFTR gene that encodes an ion channel. Nearly 2,000 disease-causing mutations have been identified and classified based on the nature of the defect
they cause. Cystic fibrosis drugs currently available on the market are effective against specific \textit{CFTR} mutations. For instance, ivacaftor is not effective in patients who are homozygous for the F508del mutation; however, combinations of lumacaftor and ivacaftor or tezacaftor and ivacaftor are beneficial in such patients. Therefore, a \textit{CFTR} mutation test is recommended prior to treatment initiation.

Several nucleic acid-based \textit{CFTR} mutation detection tests have been cleared for use by the FDA. These include the Cystic Fibrosis Genotyping Assay (Celera Diagnostics), InPlex CF Molecular Test (Third Wave Technology), Verigene CFTR and Verigene PolyT (Nanosphere Inc.), and xTAG Cystic Fibrosis 39/60 Kit (Luminex Molecular Diagnostics), among others. The most recently approved test is Illumina’s MiSeqDx Cystic Fibrosis 139-Variant Assay based on next-generation sequencing technology.

**Challenges and future directions**

Although oncology currently dominates the field of companion and complementary diagnostics, discovery of predictive biomarkers and technological advances are enabling progress in other therapeutic areas. While infectious diseases and cystic fibrosis may be amenable to rapid progress given their fairly uncomplicated pathogenesis, heterogeneous disease states such as asthma, Alzheimer’s disease, and psychiatric disorders are far more challenging. Gaps in knowledge about disease progression and lack of predictive biomarkers limit the development of companion and complementary diagnostics for these polygenic diseases. Additional challenges are the difficulty in sample collection and the paucity of blood biomarkers.

Despite these challenges, the companion and complementary diagnostics market is estimated to exceed $7 billion by 2024. The industry is witnessing a shift away from the “one drug, one test” paradigm, with companies now formulating high-throughput systems and multibiomarker panels to test for several drugs at once. This flux calls for regulatory bodies to formulate policies for complementary diagnostics and laboratory-developed tests to ensure patient safety.

### References:


Raeesa Gupte, PhD, is a freelance science writer and editor specializing in evidence-based medicine, neurological disorders, and translational diagnostics.
Q: Can you tell me a bit about Vizient and its activities related to antimicrobial stewardship?

A: Vizient is the nation’s leading health care performance improvement company. We serve more than half of the health care organizations across the United States—from large integrated delivery networks and academic medical centers to community hospitals, pediatric facilities, and non-acute care providers.

Because of the large diversity of our organization, we have the ability to interact with hospitals in a variety of ways around stewardship. This ranges from one-to-one engagements through our advisory solutions teams (i.e., consulting services) where our consultants work directly with individual hospitals and health systems to manage antibiotic use, to one-to-many engagements where we deliver educational programs to hundreds of hospitals on key topics related to antibiotic stewardship and work with smaller groups as part of our performance improvement collaboratives.

Finally, we also have an antibiotic stewardship committee that comprises 30 infectious diseases physicians and pharmacists who meet monthly and are working on programs and conducting research on antibiotic stewardship. This group is composed of our Vizient University HealthSystem Consortium members, who represent 95 percent of the nation’s academic medical centers.

Q: What are some of the key components of successful antimicrobial stewardship programs?

A: Several years ago, the CDC came out with what they call the Core Elements of Antibiotic Stewardship. They have four sets of elements for hospitals, small and critical access hospitals, nursing homes, and ambulatory care, respectively. These are really the blueprints for what are considered a successful stewardship program. They each vary a little bit, but I think all of them have this basic first tenet, which is that successful stewardship starts at the top—you need good leadership from a physician and pharmacist who have experience in infectious diseases and can influence change among others.

Leadership at the highest levels of the organization is also beneficial because there are times when the program may require financial or senior level medical staff support and this person (usually at the C-suite level) is typically in the best position to enable those resources. I always say it is a good sign when your hospital CEO knows what the term “antibiotic stewardship” means.

It is important to have a set of interventions for improving antibiotic use that are performed consistently and accurately as well as educational programs or resources available that can help educate clinicians and support personnel. Also, antibiotic stewardship should be something that everyone who interacts with a patient thinks about. For example, nurses can be great allies in helping promote antibiotic use. They can perform a simple evaluation about a patient’s antibiotic use that might prompt a physician to look more closely at the patient’s antibiotic regimen.
Finally, you should have a way to track metrics and a process to use these metrics for performance improvement.

Q: How can hospitals measure the success of their antimicrobial stewardship programs?

A: There are many different ways that hospitals can track the success of their antibiotic stewardship programs. Many track antibiotic utilization on a monthly basis by individual drug or drug class and then report this as a function of census. For example, antibiotic days of therapy per 1,000 patient days. In nursing homes, this can be more difficult to track, so it might be easier to look at antibiotic starts instead. About a quarter of the nation’s hospitals can report their antibiotic use data into the National Healthcare Safety Network’s Antibiotic Use and Resistance Module.

Other measurements that can be used to track the success of an antibiotic stewardship program include number of interventions (e.g., how many patients have their antibiotic therapy streamlined or narrowed, how many patients had their medications appropriately adjusted for kidney dysfunction, or how many patients were converted from intravenous to oral therapy). Another good metric that is associated with improved antibiotic use is the rate of *Clostridiodes* (*Clostridium*) *difficile* infections. Good antibiotic stewardship use has been directly correlated with a reduction in *C. difficile* infections.

Ideally, we would like to be able to also track metrics such as mortality, hospital readmissions, and antibiotic resistance, but these can be more difficult to track in the acute care setting since these events often happen after the patient leaves the hospital.

Q: What is the most common pitfall that hospitals encounter when implementing antimicrobial stewardship programs?

A: They make it just about reducing costs or they are under-resourced, meaning they don’t have the appropriate pharmacist and physician resources available to support the program. Antibiotic stewardship programs should be seen as having the primary goal of patient safety. As the old saying goes, “If you do the right thing, cost will follow.”

Q: How are technological advances impacting antimicrobial stewardship?

A: Integrating technology into your stewardship program can make a substantial difference in improving the quality of the program and extending the human resources, but it has to be done well.

Technology can extend the reach of the program and can be used to engage other personnel, outside of just the antibiotic stewardship team, to perform antibiotic interventions. For example, alerts can be built into the electronic health record that can prompt a physician to evaluate a patient’s antibiotic therapy at a specific point in time (e.g., 48 to 72 hours). This is referred to as an antibiotic time-out. Alerts can also be built into an electronic health record to prompt a nurse to speak to a physician about converting a patient who has other active oral medications on their profile and is tolerating an oral diet to oral therapy.

Technology can also be used to help communicate the results of rapid or traditional antibiotic-stewardship-testing resources to decision makers so that the benefits of these tests can be realized in a timely manner. Finally, technology can help automate the tracking and reporting of metrics of antibiotic use, which saves a tremendous amount of time.

Q: What advice do you have for hospitals looking to improve their antimicrobial stewardship programs?

A: Start by having the basics in place and doing them well. I always say, “Walk before you run.” It is also important to not only have metrics but to also set goals for those metrics and evaluate them periodically. If you are not meeting those metrics, conduct an assessment of why, and use these findings to improve quality. Also, take the time to understand what other activities in the hospital are ongoing that the stewardship program could connect with in order to be synergistic. For example, take time to speak with infection prevention, quality, and microbiology specialists to understand what their priorities and programs are and to think about ways that you can support each other’s programs. Finally advertise your program’s successes. I think sometimes we’re focused on what is being done wrong, but it’s important to take time to recognize when people or prescribers are doing the right thing.

Q: What is your outlook for the future of antimicrobial stewardship?

A: Extremely positive! In one way, shape, or form, antibiotic stewardship is now recognized as an important patient safety program in every care area. The interest in stewardship in the ambulatory setting has just been invigorated by the Joint Commission’s Medication Management Standards for Ambulatory Health Care, which goes into effect on January 1, 2020.

Erica Tennenhouse, PhD, is the managing editor of Clinical Lab Manager.
**Q:** What is your vision of the future of health care?

**A:** The future that I see is that when you are born, you’ll get your DNA sequenced, and from that you’ll know you’ve got the propensity for five or six diseases during your lifetime. Some of those will be hereditary and some of those will be just point mutations that arise as mutations do. Once you know that, you will be monitored for traditional wellness markers, whatever they become—vitamins would be a good example, but steroids as well, and probably a number of proteins that are related to a healthy human being. The markers will be different from men to women and they will be different from Caucasians to Africans to Asians, but there will be a set of markers for this wellness. On top of that, there will be a set of markers that will be based on the diseases that it is expected that you might or might not get during your lifetime. But really, once you sequence your DNA, it is largely not going to change from the day that you’re born to the day that you die in every cell in your body (aside from epigenetic changes).

“**I think there is a shift now to disruption in health care, just as we’ve seen other industries get disrupted.**”

Then you’ll have to measure these metabolites, lipids, and proteins monthly most likely. You’ll do that in your home from a drop of blood on a little tube. You’ll snap it off, put it in the post, and send it to a reference lab or a biotech lab. The results you will get back will be a screen—not a diagnostic, but a screen against your baseline that shows how your baseline is changing all the time. Since you’ll then have anonymized populations of these tests, there will be some artificial intelligence or machine learning that says, “Hey, we’ve noticed that people have started changing in this way, started to get these diseases.” Over time, the body of data will get more indicative of smaller changes as you slip from wellness into illness. Then when you slip into illness, maybe you’ll start feeling a bit unwell, or you won’t know and a red flag will come up on your mobile phone that says you’ve got to go to the doctor because something’s about to happen. When you go to the doctor, you will not just use the diagnostic tests that exist at the moment, which are not as precise and accurate as they could be. You’ll have precision tests using mass spectrometry that identify the disease that you’ve got.

Once you know what you’ve got, there will be options of therapies. At the moment, those tend to be small-molecule drugs, though there’s been a shift from small molecules to monoclonal...
antibodies and newer modalities like oligos that can knock down RNA to affect change within your cells, and cell and gene therapies—CRISPR-Cas9 gene editing, for instance, has great potential. Precision therapy will start to make you well again.

**Q:** How would people know they’re getting well if they never get to the point where they feel sick?

**A:** You need to measure that in some way; you need a marker. That is roughly translated as companion diagnostics. At the moment, companion diagnostics really stratify patients to say whether they should take a certain treatment or not. HER2 breast cancer is a good example of this; if a companion diagnostic reveals you have the HER2 gene, you can take Herceptin. But that really just stratifies patients; it doesn’t monitor whether the treatment is improving or not. So you’ve got to have a number of markers that are really more around treatment efficacy—not necessarily companion diagnostics, which are a slightly different subclass—and then to measure those markers until you return to wellness.

**Q:** What hurdles must be overcome before we can move from a system of sick care to well care?

**A:** If you think about how you would meaningfully deploy a program like that, even if you had wellness, even if we could measure all of those things in your body, would you be willing to go once a month and give blood? You need a process; you need to make it more accessible to the consumer. So that’s one thing—accessibility. I think it’s acknowledged whilst you may go once a year to give an armful of blood, most people will not go once a month to do that, and you need to be able to take a pinprick of blood, you need to be able to do that in the comfort of your own home just like you do with the genetic tests at the moment, like Ancestry DNA—spit in a tube and send it off.

The second thing is that you need the technology to do it. We’ve already established that chemistry and immunoassay systems are good at measuring analytes, but you can only measure one thing at a time. You aren’t going to know whether you’re slipping from wellness into illness by just measuring one marker—it’s got to be hundreds of markers. It’s got to be some kind of multiplexing. So the technology is not existent. It’s also that sensitivity and specificity to be able to measure multiple things in small volumes of blood as well, so the technology has not really been there to do that.

And I think the last thing is that the markers are not there. We don’t know what they are just yet. We can guess, we do a little bit of that, we look at vitamins and endocrinology, we look at cholesterol, do some blood pressure testing, Fitbit and things, but it’s going to be a combination of things.

**Q:** What role will mass spectrometry play in the transition to well care?

**A:** Mass spectrometry is becoming increasingly foundational in all of this because the ability to accurately quantify molecules is the basis of well care. If you can’t precisely quantify molecules, you don’t get precision diagnostics. It’s a kind of cascade.

I think if you look at the evolution of mass spec, it’s become more sensitive, more specific, easier to use, and can analyze more things. When mass spec started, you were looking at maybe one or two things at a time in a sample. Now, in proteomics, for example, you can quantify 5,000 proteins in about 25 minutes and you have reproducibility across samples. So I think mass spec technology has come a long way over the last few years.

I think reference labs are the cutting edge of taking mass spec into the clinic. They have very experienced operators of the system and they have totally honed the automation. If you look at the academic medical centers, some of the innovations there are being able to find the new markers of disease. When you think about any kind of experiment you need to do, it’s a comparative experiment—you want to find out what the difference is between this control sample and this disease sample. But you don’t just want to look at two samples; you want to look at hundreds to eliminate biological variation. The technology is now at the point where you can quantify thousands of proteins in hundreds of samples to really look for the new biomarkers of disease that are going to be the future of precision medicine, precision diagnostics, and potentially companion diagnostics.

**Q:** How long will it be before well care becomes a reality?

**A:** This is not happening tomorrow, but it’s coming like a freight train. China is putting $9 billion in the next 10 years into something called Healthy China 2030, into precision medicine or wellness testing. I think there is a shift now to disruption in health care, just as we’ve seen other industries get disrupted.

*Erica Tennenhouse, PhD, is the managing editor of Clinical Lab Manager.*
**BIO-RAD DDPCR MICROSATellite INSTABILITY ASSAY**

Bio-Rad’s Droplet Digital PCR (ddPCR) Microsatellite Instability (MSI) research use only assay is available for early access customers.

The ddPCR MSI assay can be completed in one day on a ddPCR-based platform to quantify the level of MSI present in colorectal tumors. Using either a blood or FFPE sample, the assay quantitatively identifies mutations in five loci that lead to identification of MSI status. Colorectal tumors that test positive for MSI-high are candidates for treatment with immune-checkpoint inhibitors. Bio-Rad’s assay is simple, highly sensitive, and provides a standardized output that does not require a pathologist’s interpretation. The test can use patient blood samples in the absence of tumor tissue and does not require matched normal tissue or normal blood samples.

**VERAVAS PRODUCT PORTFOLIO TO MITIGATE BIOTIN INTERFERENCE**

Veravas has launched a portfolio of products that can improve the accuracy of current diagnostic test results by helping laboratory professionals detect and manage biotin interference in patient samples. The new VeraBind Biotin will support diagnostic manufacturers in redeveloping lab assays to be biotin-interference free. VeraTest Biotin and VeraPrep Biotin offer immediate solutions to address biotin interference in existing diagnostic tests. VeraTest Biotin is a digital qualitative test that screens for biotin interference in less than five minutes. VeraPrep Biotin can determine if biotin levels are clinically significant and, using targeted nano magnetic beads, capture and remove biotin from a sample. Proof-of-concept studies have demonstrated the ability of these products to rule in or out biotin interference, determine clinically significant levels, and successfully reduce interfering biotin in patient samples. These products are for research use only.

**THERMO SCIENTIFIC GENERAL PURPOSE PRO CENTRIFUGE SERIES**

The Thermo Scientific General Purpose Pro Centrifuge Series has been developed to deliver a safe and regulatory-compliant benchtop separation solution to meet an array of application needs, from clinical protocols and cell culture procedures to microplate processing. The General Purpose Pro Centrifuge Series provides scientists with: A unique glass touchscreen that facilitates a simpler user interface for immediate, effortless workflow and operation monitoring, and easy cleaning; an ergonomically enhanced industrial design that enables the quick and safe change of any of its 19 rotor types in just three seconds through its auto-lock rotor exchange function; superior sample capacity, performance, and biocontainment through its Fiberlite carbon fiber rotors and ClickSeal biocontainment lids; and a compact separation solution featuring connectivity-ready technology, while optimizing benchtop space. The General Purpose Pro Centrifuge Series meets global compliance standards.

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**solutions FOR THE CLINICAL LAB**

From assays to analyzers, these are some of the latest and greatest products for use in clinical research and diagnostic labs.
**SYSMEX PS-10™ SAMPLE PREPARATION SYSTEM**
Sysmex America has announced the availability of its PS-10™ Sample Preparation System for use in flow cytometry. The highly automated and flexible PS-10, designed for complex laboratory tests and routine flow applications, provides clinical labs a new level of workflow efficiency and confidence in results. One of the most important but labor-intensive activities of clinical flow laboratories is sample preparation. The PS-10 automates sample preparation, alleviating primary operational bottlenecks in busy clinical flow laboratories, as well as eliminating variability between different operators. The PS-10 also offers programmable sample preparation for antibody cocktails and reduces the amount of manual transfer of samples performed by laboratory staff.

**HELMER SCIENTIFIC GX SOLUTION REFRIGERATOR**
Helmer Scientific has announced the expansion of their GX Solution Refrigerator line to include models from 13 to 56 cu ft. GX Solutions are professional medical-grade refrigerators with OptiCool cooling technology. Helmer Scientific’s introduction of GX Solutions takes cold storage to new levels by focusing on optimizing temperature, noise, and energy management. The expansion of GX Solutions to include all refrigerator models positions the line to meet future energy standards. GX Solutions excel in three key temperature management areas: uniformity, recovery, and stability. Achieving temperature uniformity throughout the unit, keeping temperatures within +/-1°C, guarantees customers that contents are stored at the right temperature regardless of where in the unit they are placed. In addition, GX Solutions recover faster than conventional technologies after prolonged door openings. These units are also able to maintain temperature stability, creating fewer deviations to avoid significant changes in temperature. These temperature management solutions ensure the protection of sensitive clinical and scientific products such as blood therapies, medications and vaccines, and patient samples.

**PERKINELMER VANADIS® NIPT SYSTEM**
PerkinElmer has announced that its Vanadis® NIPT system has obtained CE-IVD mark. This non-invasive test provides screening results for trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome), and trisomy 13 (Patau syndrome). The Vanadis NIPT system has been validated in an external clinical study conducted in France. The blinded study analyzed 80 samples from pregnancies affected by trisomy 21 and 670 samples from unaffected pregnancies, classifying all cases correctly, with only one sample failing to generate a result. Unlike existing NIPT technologies, which require more complex platforms such as sequencing or microarrays, the Vanadis NIPT platform is the first of its kind designed to simplify screening for trisomies 21, 18, and 13. The Y chromosome can be measured as an optional marker. This cost-effective, high-throughput, scalable platform measures fetal chromosomal trisomies in maternal plasma by targeted fluorescent labeling and counting specific cfDNA fragments, removing the costly and data-intensive steps required for gene sequencing or microarray solutions.
MEDTEST DX CLINITOX SOLUTION
MedTest Dx has introduced an improved line of Clinitox calibrators and controls for confirmation testing. The new product line provides laboratories performing confirmation testing a comprehensive, reliable, easy-to-use, and customizable calibration and controls solution designed for accuracy and efficiency, with extended shelf life and simplified documentation. Clinitox calibrators and controls are ready-to-use, liquid formats that simplify calibration and quality control procedures. They can be fully customized to meet the unique needs of individual laboratories, taking into consideration specific testing requirements, LC-MS instrumentation, and sample matrices. Custom profiles are easily edited or updated as needs change. Clinitox calibrators and controls come as ready-to-use single use ampoules with batch and lot certifications, ensuring they deliver the quality laboratories require.

INSTRUMENTATION LABORATORY GEM® PREMIER CHEMSTAT IVD ANALYZER
Instrumentation Laboratory (IL) has announced the unveiling of their latest innovation, the GEM Premier ChemSTAT in vitro diagnostic (IVD) analyzer with intelligent quality management. A new and complementary member of the GEM® Premier™ family, the GEM Premier ChemSTAT system is a whole-blood analyzer designed for rapid basic metabolic panel testing at the point of care, primarily in hospital emergency departments and clinical laboratories. The system provides laboratory-quality results on-demand, in less than 70 seconds, from venous or arterial whole blood samples, with no preparation required. Ultimately, this aids in diagnosis for timely triage of life-threatening conditions and enables rapid risk stratification, prioritization, and treatment of high-risk, acutely ill patients. Recently, IL initiated commercial release of the GEM Premier ChemSTAT system in select hospitals.

THE NATIVE ANTIGEN COMPANY RUBELLA VIRUS-LIKE PARTICLES
The Native Antigen Company has announced the release of its rubella virus-like particles (VLPs). The rubella VLPs are a unique product in the company’s new range of Rubella virus reagents, adding to the company’s extensive selection of recombinant VLPs that offer researchers a reliable source of high-quality reagents for immunoassay development and manufacturing. The first-to-market rubella VLPs are expressed as recombinant proteins in the company’s proprietary mammalian cell expression system. Recombinant expression of the rubella structural polyprotein in HEK293 cells enables reliable and cost-effective production of high-quality VLPs, helping to ensure researchers achieve consistent and accurate results throughout immunoassay development and scale-up manufacturing. The Native Antigen Company also offers rubella antigens, monoclonal antibodies, and ELISAs for use in a wide range of research applications.
Diagnostic laboratories are continually pressured to improve the accuracy of their tests. This pressure is heightened by regulated clinical quality metrics and increased quality assurance monitoring and documentation requirements. Meanwhile, these labs are also tasked with processing more tests in less time while managing the challenges of operating with fewer staff members and tightened budgets. Fortunately, advanced tools and powerful software systems are available that provide greater insight into—and control over—quality management while also improving lab efficiency.

The following are several quality management tools that can also help create a more efficient laboratory:

- Automated instrument calibration and calibration verification programs help laboratories maintain quality and reduce compliance risk while eliminating nonproductive analyzer time.
- Usable and actionable reports put valuable quality assurance metrics into the hands of the laboratorian, while business intelligence reporting brings greater visibility to clinical performance and productivity to enable informed decision support.
- Performing laborious manual reviews of quality statistics is time-consuming and, when using antiquated quality control rules, can be confusing and inconsistent to the end user. Powered by innovative big data analytics, web-based quality assurance and management tools help labs simplify the process of running controls and verifying result acceptability, reducing the margin of human error and increasing the quality monitoring of results. Furthermore, applying six-sigma principles to quality control programs can result in lower false-rejection rates and less time spent needlessly repeating quality control analysis.
- Features such as real-time performance feedback, color-coded instrument status alerts, and interactive troubleshooting guidance can help detect and resolve failures before they can impact patient results and workflow efficiency.

Laboratory operations have the greatest chance of improving when all members of the lab staff are properly trained on hardware and software quality management solutions.

As staff shortages, increasing workload, and decreasing reimbursement continue to influence lab policies and procedures, so will the demand for products and services that bolster laboratory accuracy. By leveraging quality assurance programs and innovative technology tools, labs can expedite workflow, improve safety, and optimize their use of diagnostic laboratory solutions. This will give laboratory professionals more time to focus on the scientific expertise they bring to the patient care continuum.

Danette Godfrey, MS, MT(ASCP), is director of IVD product marketing at Sysmex America, Inc. In this role, she is responsible for product, service, and integrated technology solutions marketing for the company’s innovative hematology, urinalysis, and flow cytometry testing technology. Danette’s 25 years of health care experience includes both medical laboratory technical and marketing positions.
The Key to Speed and Certainty in Drug Screening

Automation solves many of the challenges associated with screening today’s drugs of abuse
by Christian Scherling, PhD

As the numbers of addicts and drug-related deaths continue to soar in the US and Europe, forensic and diagnostic labs are looking for efficient methods to discriminate drugs of abuse that provide an easy workflow and are sufficiently sensitive to detect extremely low quantities of highly potent synthetic opioids in the urine of victims.

The need to screen for drugs of abuse is growing.

The monitoring of drugs of abuse in clinical laboratories has had to broaden from the usual suspects—cannabis and illegal opioids such as heroin—to address the burgeoning abuse of such prescription opioid painkillers as OxyContin (oxycodone) and synthetic opioids like fentanyl and its analogues. In 2017, drug-related deaths in the US hit a record of 72,000.

Synthetic opioids like fentanyl are approximately 290 times more potent than morphine as measured in the rat tail-withdrawal assay, and carfentanil has more than 9,000 times the potency of morphine. Carfentanil is one of two agents that are certified for use for tranquilizing large animals, such as elephants and rhinoceroses. It is available illegally on the dark web and is more profitable for dealers than heroin.

Drug screening is crucial not only for stemming the abuse of prescription opioids but also for evidence in criminal investigations. The potency of synthetic opioids means that many abusers are unconscious, comatose, or dead on arrival at the emergency room. One of the most important pieces of evidence is the confirmed presence of the drug itself in the tissues of the victim. This direct evidence is vital in a criminal investigation to link the victim to the cause of death and the source of the drug. However, the sensitivity of the usual methods of tissue analysis—GC, HPLC, and ELISA—are inadequate to detect the low but significant concentrations of fentanyl and its more powerful analogues. Consequently, a more sensitive and discriminating detection technology is called for.

Mass spectrometry (MS) has sufficient analytical power for drug detection, but there are still a few obstacles to overcome to implement MS as a routine analysis tool of clinical and forensic samples. MS is expensive (instruments cost upward of US$100,000), it is conventionally not an automated technology, and the sample matrix, urine, is complex and may contain unexpected contaminants that make the spectrograms inconclusive.

The sheer volume of samples and the lack of automated sample prep methods have prompted many labs to “dilute-and-shoot” the urine sample directly into the mass spectrometer. This leads to long and expensive instrument downtime, which labs often compensate for by buying more mass spectrometers, thus making the whole approach less viable.

The number of samples that demand analysis is steadily increasing, and the burden on a lab’s drug screening operation is already heavy. This is unlikely to change anytime soon. Data from the CDC indicate that drug overdose deaths were around 10 percent higher in 2017 than in 2016.

Automating the MS analysis workflow is now a key to success, especially when it comes to sample preparation prior to MS. An automated MS workflow is both flexible and efficient. Workflows can be easily created to address both targeted opioid analyses as well as more exploratory studies, such as quantification of metabolites of the drug in response to therapy or when there may be multiple unidentified illicit and medicinal drugs. A multiple extraction workflow can take less than three hours for 96 samples.

For drug screening, the value of the information lies squarely in the speed and certainty of the delivered answer. Automation is key to both.

Christian Scherling, PhD, studied metabolomic and proteomic studies for his doctorate and has held postdoc positions in core facilities in metabolomics and systems biology. He has extensive experience in automated workflows, consulting with labs around Europe. At Tecan, he focuses on automated sample preparation for mass spectrometry applications for pharma, clinical diagnostics, omics (metabolomics, proteomics, lipidomics), and forensics and toxicology.
Lab results giving you a headache?

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