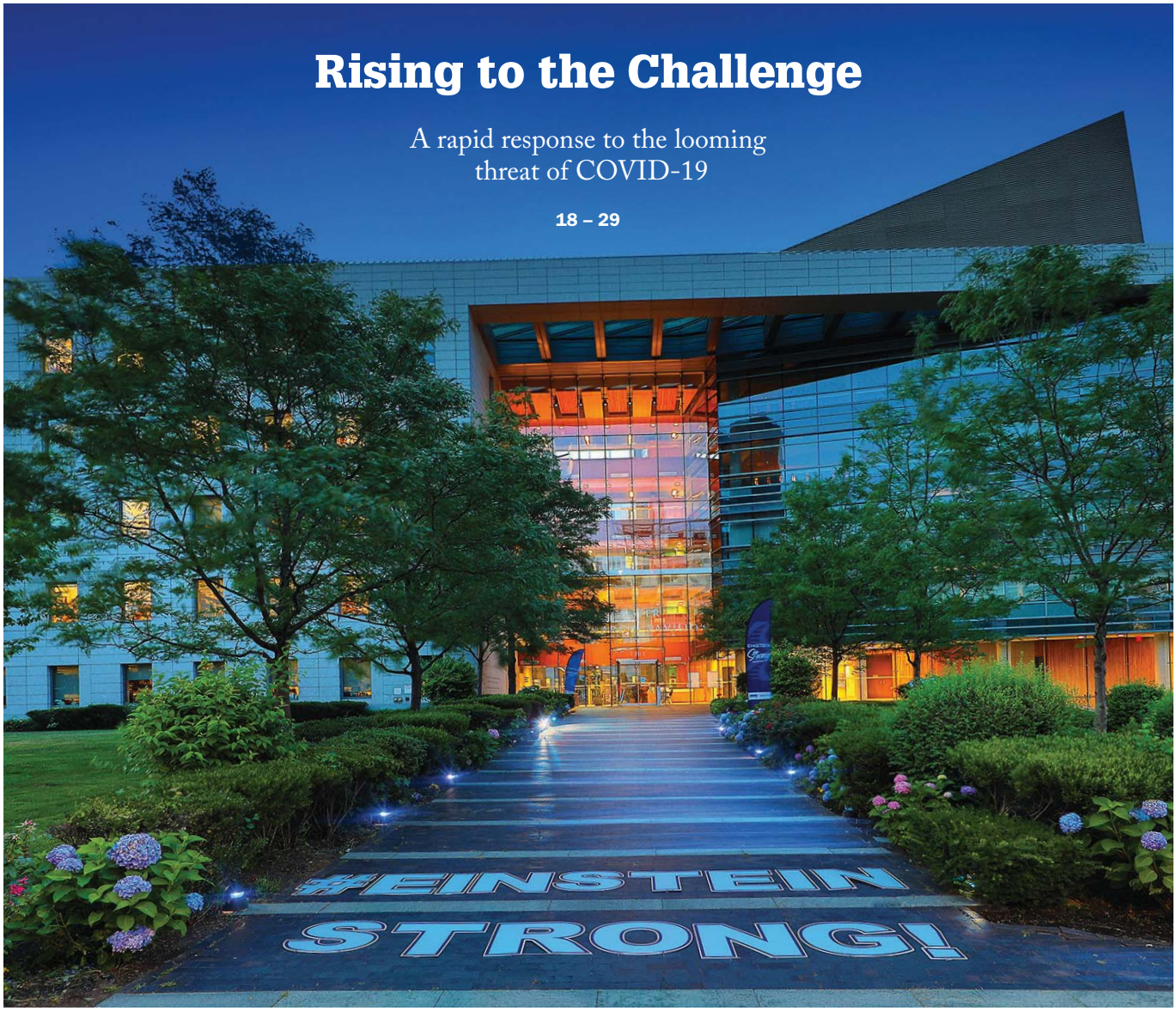
DECEMBER 2021 # 81

# the Pathologist®

*Official society partner of The Pathologist*

SPECIAL TAKEOVER!
*Montefiore Medical Center and Albert Einstein College of Medicine*






## Rising to the Challenge

A rapid response to the looming threat of COVID-19

Agilent
Dako

# A More Complete Picture with Ki-67 IHC MIB-1 pharmDx (Dako Omnis)

- 20% of patients with HR+, HER2− Early Breast Cancer (EBC) are at risk for disease progression[1].
- Identifying patients at high risk can facilitate treatment decisions to potentially improve outcomes.

## Ki-67 IHC MIB-1 pharmDx (Dako Omnis) sets a new standard for clinically relevant Ki-67 interpretation and scoring[2]:

- Now available in the U.S. as an aid in identifying patients with EBC at high risk of disease recurrence for whom adjuvant treatment with Verzenio® (abemaciclib) in combination with endocrine therapy is being considered[2].
- Now an important component of comprehensive EBC risk assessment

For more information contact: pathology.solutions@agilent.com

Scan here to learn more:

References: 1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Aromatase inhibitors versus tamoxifen in early breast cancer: patient-level meta-analysis of the randomised trials. Lancet. 2015, 386, 1341–1352. 2. Ki-67 IHC MIB-1 pharmDx (Dako Omnis) [Instructions for Use]. Santa Clara, CA: Agilent Technologies, Inc.

For countries outside the United States, see the local Verzenio product label for approved prescription information to guide therapy.

This information is subject to change without notice.


D69501/2021DEC02

Agilent
Trusted Answers

# Access for All

*One institution's mission to provide education and medical care to its underserved community*



My travels to international scientific meetings and inspections of clinical laboratories from India to Guantanamo Bay over the years have shown me a diversity of healthcare systems. These experiences have opened my eyes to the social and economic challenges faced by underserved communities across the globe. As chair of the pathology department at an academic medical center in one of the poorest counties in the United States, I find that we are quite fortunate to deliver the highest quality of pathology services to the people living in the Bronx.

Montefiore Medical Center was founded in 1884 by Jewish philanthropists to help chronically ill people who were denied care by other hospitals. In addition to advances in medicine, Montefiore made community care a priority. Because our Bronx community is one of the most economically challenged urban counties in the US, Montefiore created the nation's first hospital-based Department of Social Medicine in 1950 to better serve its patient population.

Albert Einstein College of Medicine opened its doors in 1955. The new medical school welcomed Jews, African Americans, and women in a time when most other centers of medical education imposed strict "quotas." In 1963, Montefiore became the teaching hospital for Einstein – and, today, attracts trainees from all over the world who dream of a career in medicine with a strong commitment to social justice.

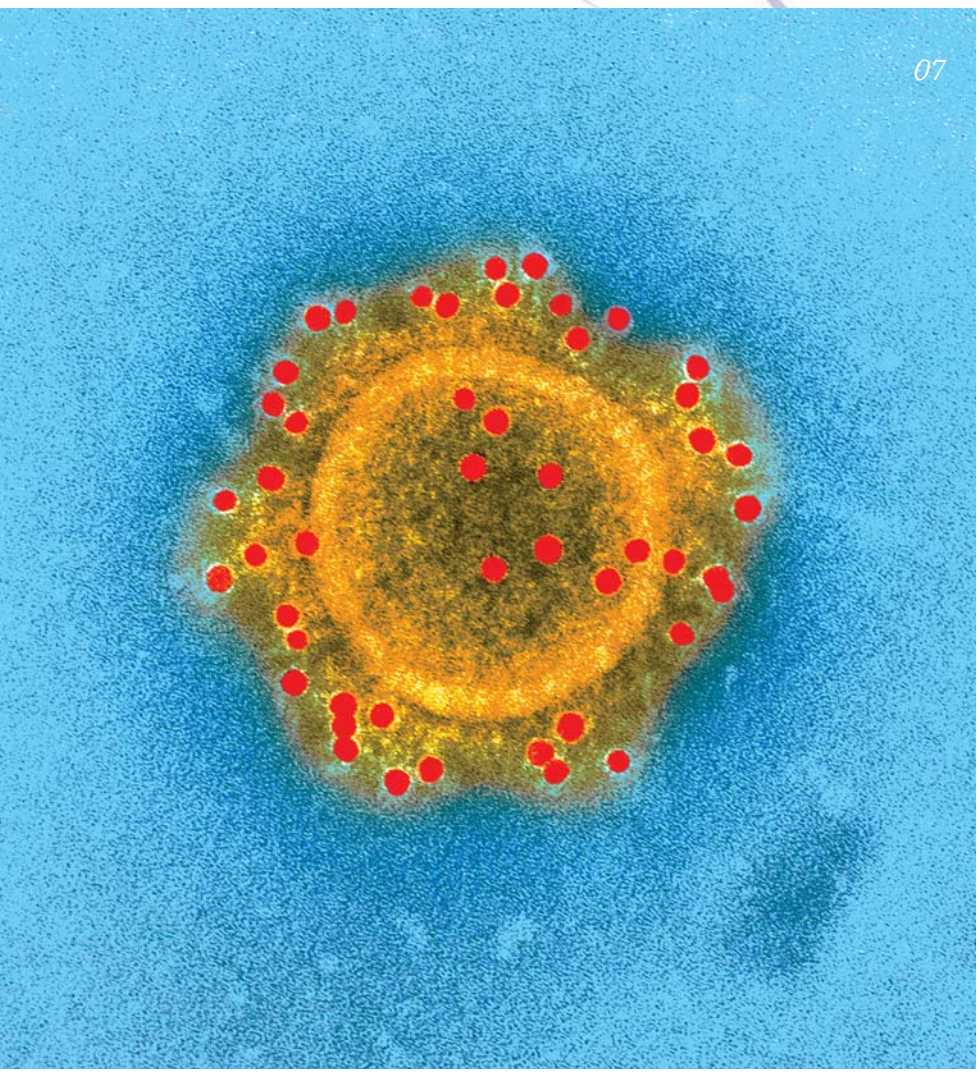
Integral to Montefiore's history is the history of our department. Some of our past chairs include Leopold G. Koss, a founder of cytology; David Marine, nominated three times for a Nobel Prize for his pioneering work on thyroid physiology and pathology and the prevention of simple goiter by iodide; and Harry M. Zimmerman, considered the godfather of neuropathology. In light of this proud lineage, pathologists at Montefiore are integral members of the healthcare team – and, as such, our residency program prepares trainees to practice in healthcare teams immediately upon completing their training.

The COVID-19 pandemic has made the unique expertise of laboratory professionals and the vital role we play in clinical care visible for all the world to see and acknowledge. My colleagues and I are honored to collaborate with Michael Schubert and his team on this takeover issue and, in sharing some of our stories with you, we hope you will find inspiration for both thought and action in these profoundly interesting times.

**Michael B. Prystowsky**

*Michael B. Prystowsky is Professor and University Chair, Montefiore Einstein Department of Pathology, Montefiore Health System, Bronx, New York, USA.*

# Contents

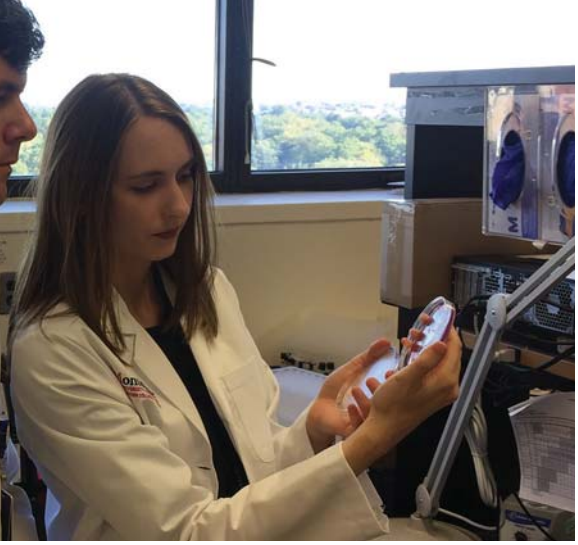


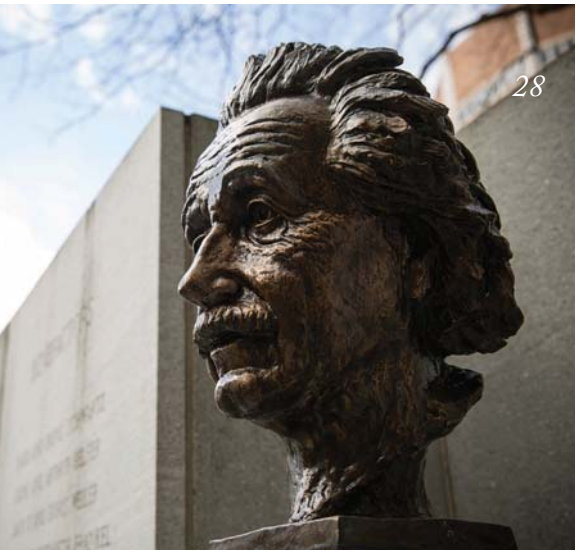





## On The Cover

*Albert Einstein College of Medicine.*




## Feature



## In Practice



## NextGen



## Profession



## Reports



## Sitting Down With




the Pathologist

ISSUE 81 - DECEMBER 2021

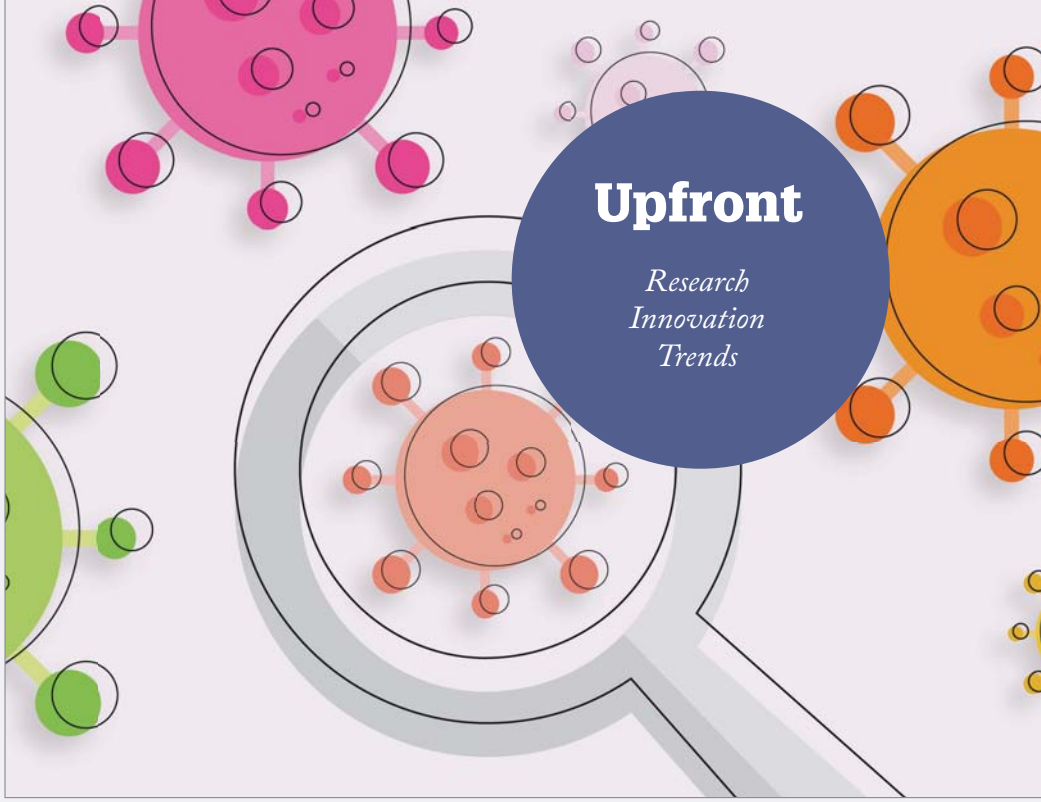




Change of address info@thepathologist.com
Hayley Atiz, The Pathologist, Texere Publishing Limited, Booths Park 1, Chelford Road, Knutsford, Cheshire, WA16 8GS, UK

General enquiries
www.texerepublishing.com | info@thepathologist.com
+44 (0) 1565 745 200 | sales@texerepublishing.com

Distribution: The Pathologist (ISSN 2055-8228), is published monthly by Texere Publishing Limited, Booths Park 1, Chelford Road, Knutsford, Cheshire, WA16 8GS, UK. Single copy sales $15 (plus postage, cost available on request info@thepathologist.com). Non-qualified annual subscription cost is available on request.




# Discrepancy Distress?

**Not all COVID-19 tests yield the same result – and, in some cases, this can mean the difference between positive and negative**

When COVID-19 first hit, Montefiore-Einstein's pandemic response team took on the task of implementing diagnostic COVID-19 testing. To that end, they developed and evaluated an ELISA that measured IgG and IgA antibodies to the SARS-CoV-2 spike protein (1). This assay, the subject of a laboratory-developed test (LDT) application, was transferred to the clinical laboratory and also used in a study of convalescent plasma as a therapeutic agent for COVID-19.

"The most common issue in SARS-CoV-2 testing and interpretation is understanding the antigen used for the test and how it relates to vaccination response," says response team member Louis M. Weiss, who was part of a team that investigated the accuracy, reliability, and discordance in SARS-CoV-2 testing platforms (2). He explains, "It is critical to understand the parameters of testing and what a test means in a clinical setting to provide useful information to our clinical colleagues. Given the urgency to develop these tests and lack of standardized material during the early stages of the pandemic, most SARS-CoV-2 IgG antibody tests were developed and approved as qualitative assays with a positive or negative result reported based on a cutoff value." In response, the Montefiore-Einstein pandemic response team investigated tests in a real-world testing scenario in which patients are only tested once – and found a lower sensitivity with the current cutoff compared with published sensitivities on several of these commercial tests (3). "The assays evaluated performed well based on the sensitivity and specificity studies," explains Weiss. "Their main shortcoming was their qualitative reporting. Discrepancy analysis demonstrated that patients who had grey zone results (i.e., just below the cutoff) on some assays had positive results on others. It should be appreciated, however, that all of the assays tested in this study performed well in identifying patients with past COVID-19 infection, which is the major role for these tests in the clinical setting."

*See references online at: tp.txp.to/dis-distress*

INFOGRAPHIC

# Where Are the Pathologists?

**A summary of pathology matches for 2021 US residencies**

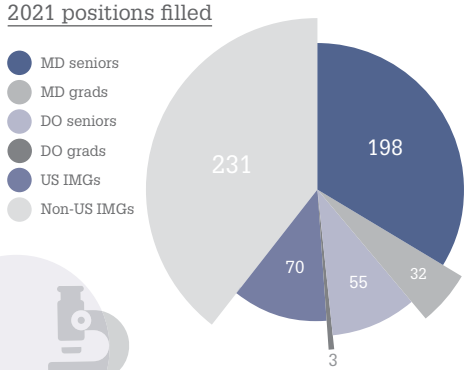
the Pathologist

Positions offered and filled

611 positions offered

589 positions filled

2021 positions filled



QUICK HITS

## The latest breakthroughs in pathology and laboratory medicine

Credit: Louis Reed/Unsplash.com

*Left Behind*

The Association for Molecular Pathology has highlighted major barriers to achieving truly interoperable genomic data in electronic health records (1). The report identifies challenges such as lack of sufficient information, limitations in interoperability standards, lack of consensus guidelines on best practice, and variability between labs in the structure and content of genomic reports.

*Collaboration is Key*

The European Platform for Neurodegenerative Diseases (EPND) has announced that it will be developing a collaborative platform to promote efficient sample and data sharing within European research networks (2). The platform hopes to accelerate biomarker, diagnostic, and treatment discoveries for people with neurodegenerative diseases.

*Express Test*

Researchers have developed an electrochemical assay to identify antibiotic resistance in less than 90 minutes – a marked improvement on the one- to two-day wait for conventional tests (3). The technique uses mediated extracellular electron transfer to directly measure cellular respiration and classify strains as antibiotic-resistant or -susceptible.

*Tailored Treatments*

Therapeutic monitoring of isoniazid and rifampicin serum concentrations in adolescents and children may enable fixing of dosages and more tailored tuberculosis treatment (4). The researchers found that low plasma concentration levels of either drug led to poorer treatment outcomes and onset of drug-resistant strains.

*Laying Foundations*

RareCan – a company aiming to accelerate rare cancer research development – has been granted approval from the NHS Research Ethics Committee to set up its BioResource at Newcastle University (5). In doing so, the company hopes to reduce the time it takes to provide rare cancer researchers with samples from months to weeks.

*See references online at: tp.txp.to/qh-3*

Credit: Rawpixel.com

# Accessible Assays

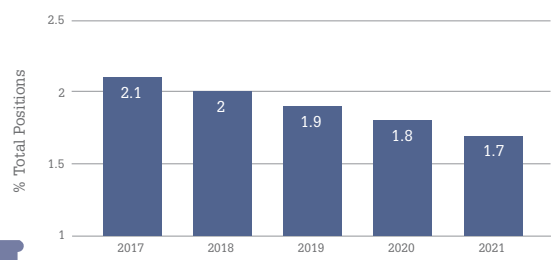
## New approaches to COVID-19 testing offer more accurate diagnostics for resource-limited settings

A common approach to COVID-19 containment is the use of point-of-need testing, which allows communities to scale up testing when infection rates are high or new variants are detected. For many areas, however, this is easier said than done – especially those with fewer resources. To address this gap, a new study examined two recombinase-based isothermal techniques with low resource requirements for SARS-CoV-2 detection (1).

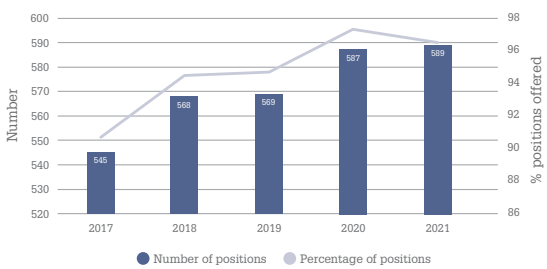
The two assays, reverse transcription recombinase polymerase amplification (RT-RPA) and reverse transcription recombinase-aided amplification (RT-RAA) evidenced similar diagnostic accuracy levels, with sensitivities of about 76 percent against target genes RdRP and ORF1ab and specificities of 94 to 98 percent. Combining N and RdRP targets in RT-RPA increased the assay's sensitivity to about 85 percent – a promising start for more widely accessible COVID-19 testing.

*See references online at: tp.txp.to/access-ass*

Pathology match share over time




Pathology positions filled over time




*Reference*

1. *National Resident Matching Program (2021). Available at: https://bit.ly/31AXUQP.*

# Getting Ahead of Infectious Disease

## Are new technologies replacing culture-based assays in infectious disease diagnosis?

Culture-based assays are often considered the mainstay of clinical microbiology – but, increasingly, new technologies are offering alternatives that can boost the speed or accuracy of diagnosis. Wendy Szymczak, Director of the Clinical Microbiology Laboratory and Associate Professor of Pathology at Montefiore-Einstein, is exploring these alternatives to bring infectious disease patients faster, more accurate diagnoses and treatment options.

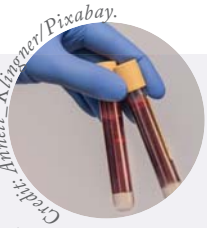
"My colleagues and I began working on a next-generation sequencing (NGS)-based assay to predict antimicrobial resistance to *H. pylori* because the organism is very difficult to culture and, even when cultured, grows so slowly that routine phenotypic susceptibility results can take weeks," says Szymczak. "We were able to show that NGS can accurately predict resistance to clarithromycin and levofloxacin, two antibiotics often used to treat infections."

But NGS carries challenges of its own – costs, lack of FDA-approved infectious disease assays, the need for bioinformatics expertise, and more. And although Szymczak believes these are surmountable challenges, she and her colleagues are exploring other options.

"We began using MALDI-TOF to identify pathogens directly from blood culture bottles at the end of 2013," she says. "By using MALDI-TOF as part of the diagnostic workup for two elderly patients with nonspecific clinical presentations, we were able to rapidly identify *Listeria monocytogenes* from positive blood cultures, which allowed the prompt initiation of pathogen-directed treatment (1)." More recently, the team have adopted multiplex nucleic acid amplification tests (NAAT) to detect pathogens in cerebrospinal fluid (CSF) specimens. "Last month, we had two patients with meningitis caused by *L. monocytogenes*. The organisms were detected using this NAAT, which provides results in a little over an hour," says Szymczak. "This is important because blood cultures can take 24 hours or longer before becoming positive, so a NAAT that can be performed directly on CSF can provide a timelier diagnosis."

To stay at the cutting edge of rapid diagnostics, Szymczak recommends journal clubs, webinars, workshops, and conferences (even virtually). "As these new technologies continue to emerge, we all have a lot to learn, but that's why I think laboratory medicine is such an exciting field!"

*See references online at: tp.txp.to/ahead-of-dis*



Credit: Annett_Klingner/Pixabay.

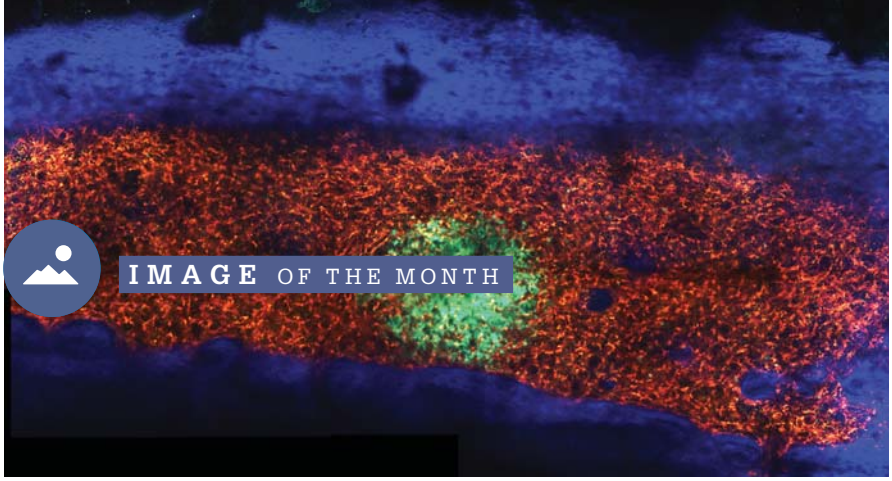
# Hidden in Plain Sight

## Accurately assessing population exposure to viruses

Throughout the COVID-19 pandemic, we've heard about rising numbers of cases. But assessing a population's exposure to a virus is difficult because existing methods may not account for multiple circulating strains, rates of vaccination, and levels of natural immunity. Recognizing this, researchers in Vietnam tested 24,402 serum samples collected between 2009 and 2015 for antibodies against 11 human influenza A strains (1). After obtaining a composite antibody measurement, they found that 26 percent of the Vietnamese population is exposed to H3N2 influenza every year and 16 percent is exposed to H1N1 – higher than expected in temperate countries.

"Our study population had almost zero influenza vaccination, so we were able to use our antibody measurements as true indicators of past influenza infection," said co-lead author Maciej F. Boni (2). "But we still need a better understanding of how to distinguish infected individuals from vaccinated individuals, and how to include the effects of antibody waning into an analysis like this."

*See references online at: tp.txp.to/finding-virus*




*Plasma Cell Secrets*

The Fooksman laboratory at Montefiore Einstein researches normal and malignant plasma cell physiology. These antibody-generating immune cells can survive for decades in the body. Because plasma cells are the architects of long-term immune response, it's crucial to understand their life cycle and function. A better understanding of these cells can also support improved diagnosis and treatment of plasma cell malignancies such as multiple myeloma. In support of this research, David Fooksman and colleagues use in vivo imaging for cell visualization.

The image above depicts a large, tiled area of bone marrow in a live mouse showing a cluster of GFP+ multiple myeloma cells (green) developing in the tibial bone marrow, with CXCL12-producing cells in red, and compact bone shown in blue.

To see more images from the Fooksman lab, visit: *tp.txp.to/plasma-cell*

*Credit: David Fooksman.*

Do you have a photo suitable for Image of the Month?
Send it to edit@thepathologist.com

## QUOTE of the month

*"Specific to the clinical microbiology laboratory, we have seen major technologic advancements happen over the past decade. We've seen MALDI-TOF become routinely used for pathogen identification, increased use of multiplexed nucleic acid amplification tests, the emergence of rapid susceptibility platforms including a method that can be performed directly from positive blood culture bottles, and a system that uses magnetic resonance to identify bacteria and yeast directly from blood specimens. Most recently, we are beginning to see clinical laboratories adopt next generation sequencing (NGS) for pathogen detection, antimicrobial resistance prediction, and strain typing. These new technologies have allowed us to provide results in a more rapid and accurate manner allowing for optimal patient management and treatment as quickly as possible."*

Wendy Szymczak, Learn more about Szymczak's work at: *tp.txp.to/rise/anysci*

# Changing the Narrative

### Making multiplex tissue imaging more accessible with digital pathology platforms

Though multiplex tissue imaging can help to diagnose and understand complex diseases, it heavily depends on the user's experience in reviewing, annotating, and describing tissue features. Could readily available software ease the process by supporting knowledge and result sharing? In a new paper, researchers describe the landscape of software available for analyzing tissue images and highlight the need for interactive online guides that can help histopathologists to make complex images more accessible for non-specialists (1).

They demonstrate this concept via a software interface called Minerva – an open-source platform that allows users to explore large multiplex images via web browsers. Minerva combines multi-omic and tissue atlas features to allow pathologists to move across images and tries to mimic specialized histology expertise. What did the authors conclude? It comes as no surprise, but they state that "such interactive narrative guides can effectively disseminate digital histology data and aid their interpretation (1)."

*See references online at: tp.txp.to/multi-iss-img*

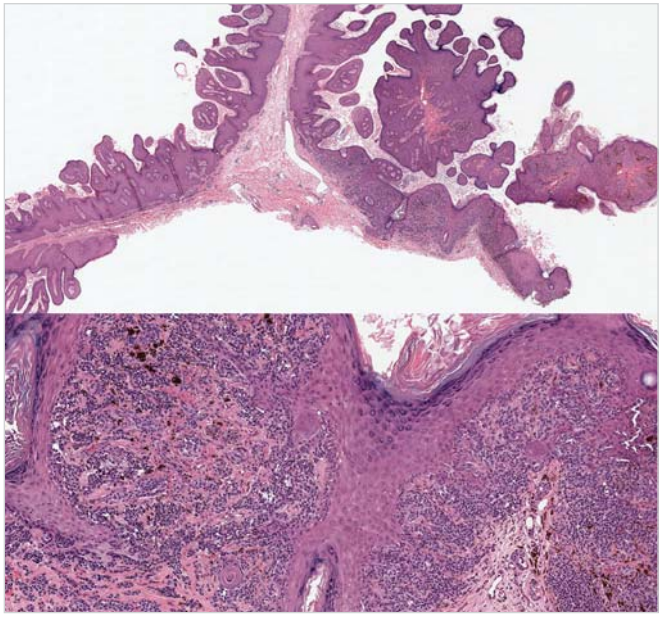
## CASE OF THE MONTH

A 73-year-old Caucasian male with a history of multiple non-melanoma skin cancers presented to dermatology for evaluation of a growth on the left scalp. He reported that the lesion had been present for over three years and was slowly becoming larger and more exophytic over time. More recently, the lesion had bled spontaneously and was intermittently painful to the touch. The patient was otherwise in good health and had no known history of immunosuppression.

A pink-brown verrucous plaque with filiform projections and focal hemorrhagic crust involving the left parietal scalp was observed on physical examination. The lesion measured 5.2 x 3.8 cm. Saucerization biopsy of the most inferior, exophytic portion of the lesion was performed for histopathologic analysis.

What is the diagnosis?

*a) Unna's (papillomatous) nevus*
*b) Inflammatory linear verrucous epidermal nevus (ILVEN)*
*c) Verrucous pseudonevoid melanoma*
*d) Verrucous carcinoma*



---

Answer to last issue's Case of the Month…
*a) Branchial cleft cyst*

Branchial cleft cysts usually present as neck masses. Mediastinal mass is a rare presentation; to our knowledge, only six cases have been reported to date. The official diagnosis is defined as a cyst derived from the remnants of the branchial apparatus, a precursor to many head and neck structures. This arch overgrows the second, third, and fourth branchial clefts forming the cervical sinus, which is usually lined with respiratory epithelium. A focal area of lymphoid aggregate is present in the cyst wall with adjacent pigment-laden macrophages, findings suggestive of cystic rupture. However, the additional classic finding of keratinaceous luminal debris is absent.

Cysts are usually unilocular and lined by various types of epithelium, including stratified squamous and respiratory types. Fibrosis is frequently visible, but without the thick, heavy capsule seen in metastatic cystic squamous cell carcinoma. Absence of dysplasia, pleomorphism, and increased mitoses rules out malignancy. The lack of dermal, musculoskeletal, or neuroendocrine components suggests against a diagnosis of mature cystic teratoma. Thymoma is ruled out due to the absence of thymic tissue.

*Submitted by Erina McKinney, University of Kansas School of Medicine, Kansas City, Kansas, and Huiwen Bill Xie, Assistant Professor, Duke Department of Pathology, Raleigh, North Carolina, USA.*

**To register your guess, please go to http://tp.txp.to/1221/case-of-the-month**
**We will reveal the answer in next month's issue!**

*Case of the Month is curated by Anamarija M. Perry, University of Michigan, USA.*

the
# Pathologist®

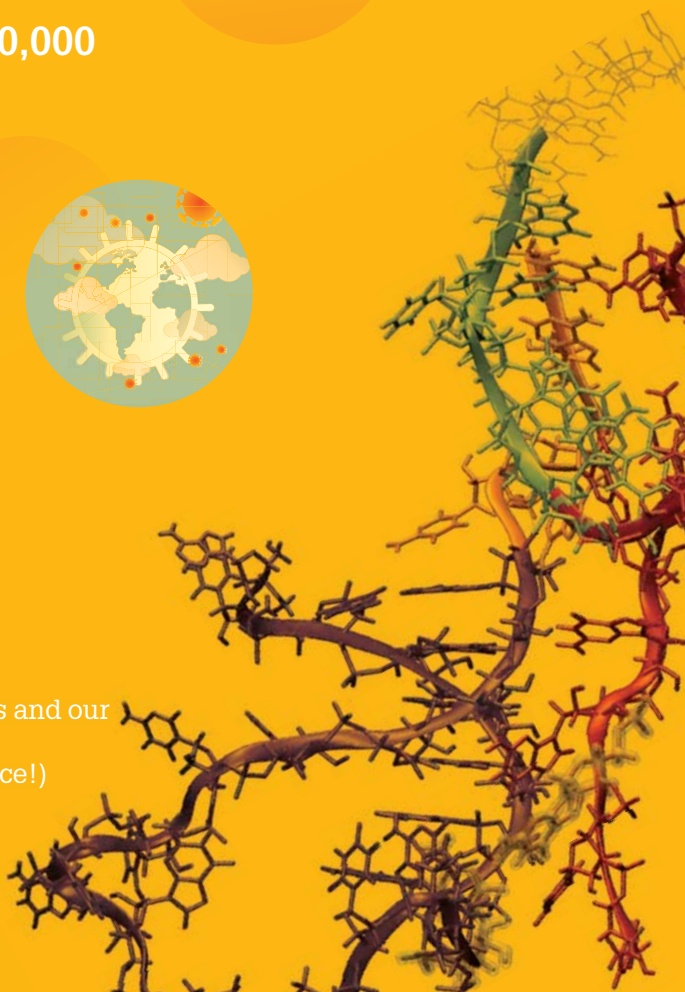
## Empowering Laboratory Professionals to Shape the Future of the Field

The Pathologist brings people together. We give a voice to everyone in the laboratory. We tell stories. We provide a platform for connections and exchange. And we actively listen to our readers, contributors, and community members.

**Join our global community of over 200,000 pathologists today!**



**Or visit thepathologist.com/register**



**Registration is always free and includes:**

- access to all of our articles, including online exclusives and our issue archive
- a regular print or digital magazine (or both – your choice!)
- a weekly newsletter rounding up the latest in science and medicine

**In My View**

*Experts from across the world share a single strongly held opinion or key idea.*

# Collaborating in Crisis

## How working with pathologists helped us curb COVID-19 – and keeps us ready for the next challenge

*By Kartik Chandran, Professor of Microbiology and Immunology and Harold and Muriel Block Faculty Scholar in Virology, Albert Einstein College of Medicine, Montefiore Health System, Bronx, New York, USA*

Nothing brings people together like a crisis. For those of us in the scientific community, all it takes is a global pandemic.

As a virologist, basic scientist, and translational researcher, I am interested in emerging viruses. My laboratory studies pathogens that predominantly affect people in countries with few resources and weak or nonexistent public health systems. Our goal is to develop vaccines and therapeutics that will help underserved populations suffering from these emerging infections.

Many viruses are constantly emerging that do not manifest as pandemics, but are endemic to specific regions. My lab works on viral agents that are household names – such as Ebola, Marburg, and West Nile – as well as those less familiar to the public. We're part of an international consortium focused on developing antibody-based therapies against these and other life-threatening diseases.

Here in the Bronx, we see a diverse population from all over the world. Many are underserved individuals with more complex genetic backgrounds to their immune systems than are generally observed in less diverse communities. They are often people at higher risk for lifestyle diseases such as diabetes, which have their own complications and affect people's ability to respond to infectious diseases. It's also a mobile population; for example, many folks travel back and forth between the Bronx and the Caribbean to visit family. During their travels, they may become carriers of viruses or mosquito-borne infections not yet common in the US. This can present a public health problem, but also provides us with opportunities to develop therapeutics by isolating naturally occurring human antibodies that people in the Bronx have generated in response to infection.

Until COVID-19, my laboratory had never really worked with pathologists; we sourced clinical samples from outside clinicians. Then, in January 2020, SARS-CoV-2 shook the world.

*"The Bronx became the 'epicenter of the epicenter.'"*

An American traveler returning from Europe brought it to our shores, making the New York metropolitan area the early US epicenter. The Bronx became the "epicenter of the epicenter" – and a partnership was born at Montefiore Einstein.

I knew some of our pathology faculty in passing, but others I had never met

before. During the first COVID-19 surge, we came together and worked closely for more than a year. In all of those interactions I was – and continue to be – impressed with their professionalism, entrepreneurial spirit, and willingness to roll up their sleeves and get things done. In short, they are great partners and collaborators.

In the early days of the pandemic, my lab collaborated with faculty and trainees in pathology to develop antibody tests not yet available commercially. Pathology had focused their initial efforts on developing a qPCR test, but didn't have an antibody assay, so we joined forces to make one from scratch. We ran patient samples that came to us from pathology, had weekly meetings, and worked hand in hand in the laboratory and over Zoom. A pathologist colleague provided us with longitudinal samples of individuals who had been hospitalized with severe COVID-19 and recovered; these informed the development of our tests by allowing us to do a thorough and detailed examination of the antibody response and other parameters of these individuals' sera and correlate them with clinical outcomes.

To be successful in science, and in life, it's important to be a good communicator. In working with our colleagues in pathology, I have been impressed with the high level and quality of communication. They are straight shooters, willing to listen and consider all levels of stakeholders. They're not so invested in their own point of view that they can't entertain those of others. These are very important traits in collaborators.

I have also noticed the way our senior pathology faculty treat trainees – not just their own, but ours as well. They are all great mentors to junior faculty and trainees – nurturing them, helping them develop professionally, and giving them independence and authority. They clearly understand that this is the next generation of scientists and we need to do everything we can do to support them. I think of them less as "pathologists" and more as "scientists" – and as people who really care about those who work for them. This is the litmus test as far as I am concerned.

COVID-19 bonded us. Acutely aware of the urgency of the crisis at hand and the needs of the moment, we united. Like soldiers in the same army unit, we went through battle together – and we want to keep that camaraderie going. We established a standing meeting to keep us talking and to make sure we're ready to mobilize when the next challenge arises.

*"We want to keep that camaraderie going."*

When we work collaboratively, both sides bring complementary skillsets to the table. The pathologist's indispensable contribution allows us to not only diagnose conditions, but also improve their outcomes through research. The power of working with pathologists lies in leveraging their knowledge, not just their ability to obtain patient samples. They inform how we think about – and treat – diseases.

It's incredibly valuable to collaborate with people whose day-to-day work is different from ours. It's an opportunity to hear another point of view, see our belief systems for what they are, and come up with something new. We must push ourselves to remain open – and keeping our relationship with pathologists going keeps us all from retreating into our silos.

# The Social Justice System

## Medicine is a team sport – and the goal is better healthcare for all

*By Andrew D. Racine, System Senior Vice President and Chief Medical Officer, Montefiore Health System, and Executive Director, Montefiore Medical Group, Bronx, New York, USA*

My journey to Montefiore began almost 30 years ago. In 1992, I was recruited to be the Associate Director of Pediatrics at Jacobi Hospital, an affiliate of Montefiore Medical Center and a teaching hospital for the Albert Einstein College of Medicine. In 1998, inspired by the legacy of its commitment to the use of health care as an instrument of social justice, I moved over to Montefiore to serve as Chief of the Division General Pediatrics.

Montefiore serves a largely poor, underserved, and diverse population of people from across the globe. In that regard, our pathologists see many unique cases and diagnose diseases that pathologists in other areas of the United States may never see. The demands on our department, due to both the

volume of illness we see and the breadth of conditions presenting in our patients, make this a department unlike any other in the country. We see both first-world diseases and those that originate in developing countries – and being alert to all possibilities distinguishes the work our pathologists do every day.

But these are not the main things that set the pathology department at Montefiore apart from its peers. What makes our pathology department unique is its people. Like those of us in other areas of clinical medicine, the pathologists who come to this institution do so out of a drive to support an underserved community. This manifests itself in a commitment to delivering the highest quality of laboratory and pathology services to the greatest number of our patients in the most reliable and efficient manner possible.

The Montefiore Einstein pathology department is committed to bringing the most cutting-edge technology to bear on clinical challenges so that the poorest patients in the country benefit from some of the most advanced systems available. Tackling the disparities that are prevalent elsewhere through the application of these systems is a key contribution our pathology department makes to the delivery of care in New York City, in our region, and beyond.

Medicine is a team sport. Within that team, each of us has a distinct role to play – and because we depend on one another for the team to function at its best, we revel in one another's excellence. Being able to rely on the precision, timeliness, and accuracy of the findings emerging from the Department of Pathology makes our clinicians better and ensures that our patients benefit from the concerted application of medical science at its finest. That said, our colleagues in pathology demonstrate not just a willingness, but a distinct appetite for involving themselves in every aspect of the delivery of care at Montefiore, up to and including our devotion to population health. This makes them – and you – much more than just "the folks behind the machines in the lab."

Pathologists are, first and foremost, physicians. Like all physicians the qualities that distinguish good pathologists are devotion to their craft (which means a commitment to both the science and the art), devotion to their patients, devotion to their colleagues, and an awareness of the part they play in the delivery of care. Our pathology faculty and trainees exemplify all these qualities and strengthen the institution far beyond what happens within the confines of the laboratory.

The dedication and expertise of our pathology faculty and trainees were critical in our ability to respond to the challenges of the initial wave of COVID-19 in spring 2020. The scarcity of PCR test equipment and reagents placed extraordinary strains on the institution's ability to triage patients and determine where and how to treat the waves of sickness arriving at our doorstep. Our pathologists' resourcefulness in setting up testing equipment overnight, seeking new physical spaces to conduct tests, sourcing adequate reagent supplies, and rapidly turning around test results made it possible for Montefiore to position itself at the forefront of testing, and therefore of treating, the enormous volumes of patients who fell ill at the outset of the pandemic. Without their contributions, our response would have been crippled and our ability to handle the vast amount of illness irretrievably constrained.

The pathology department's contributions to Montefiore's COVID-19 response is just one example of its vital role in the functioning of this complex institution. Another is augmenting the reach of our nationally recognized school health program.

The Montefiore School Health Program was founded in the 1980s by David Appel, a physician in the Departments of Pediatrics and of Family and Social Medicine. It now serves tens of thousands of students in over 100 schools throughout the Bronx. The Department of Pathology was instrumental in securing COVID-19 point-of-care testing (POCT) in many of these school health practices, bringing sophisticated testing platforms directly to the venues where they could do the most good.

The positioning of POCT in schools, as well as in our emergency departments, enables us to rapidly diagnose COVID-19 infections and apply contact tracing and isolation effectively to limit the spread of the disease. It also decreases the amount of time COVID-19 patients spend in our emergency departments (EDs) by allowing rapid decision-making regarding bed assignments. In addition, by carefully tracking POCT trends in our EDs, we gain a window into the trends of disease prevalence in the population coming to us for care and can therefore predict the course of the pandemic at our institution more accurately.

Finally, the Department of Pathology helps us address the pressing issue of healthcare disparities. Race-based testing for certain categories of illness has, over time, exacerbated healthcare disparities, particularly with respect to African Americans. Our pathology department has worked in coordination with others – for example, our division of nephrology, with whom they revised the eGFR measurements we use to eliminate the race-based aspect of this laboratory metric. In addition, by providing POCT via our School Health Program, the department has lessened disparities in access to cutting-edge diagnostic technologies. Now, schoolchildren in the Bronx have equal – or perhaps superior – access to diagnostic testing compared with other populations.

For these reasons and many more, I am delighted to have been given this opportunity to express my pride – and our pride as an institution – in the skilled and dedicated practitioners of laboratory medicine with whom we are fortunate to work, day by day, side by side, to improve health outcomes and quality of life for a diverse and underserved patient population. I hope that other institutions will see Montefiore Einstein as an inspiration to follow – and, of course, we're happy to answer questions and offer advice at any time!

# Coming Together to Lead

## The laboratory's central role in community health care

*By E. Blair Holladay*

These past two years have truly shown us the value of community. When the pandemic first hit, pathologists and medical laboratory scientists around the world came together to fight the outbreak of the virus. They discussed best practices for getting people tested, shared resources and equipment with those in desperate need, collaborated on public policy strategies, and led the charge to get the public vaccinated for the health and safety of people everywhere.

At the same time, healthcare systems were battling healthcare inequities put under a harsh spotlight by the virus. Non-white populations have been disproportionately affected by the pandemic, experiencing higher rates of severe disease and death. COVID-19 exposed a deep need to correct these disparities – and a need for our laboratory community to step forward and be the conduit that levels the playing field so that patients, no matter who they are or where they live, have equal access to high-quality care.

If you think that the laboratory can't be the bridge between healthcare and patients, or isn't in the ideal position to lead such change – why not? What is stopping us? Our community of pathologists and medical laboratory scientists is vast. We are the caregivers walking with patients from the beginning to the end of their care journey. We are the first to know their diagnoses and to understand the journey that lies ahead for them. We are the ones who can heal these communities – and that healing must start with the laboratory and flow through the rest of the healthcare continuum. If not us, then who? It is imperative that pathologists and medical laboratory scientists guide the corrections needed to reverse these inequities for all patients.

In April 2021, I had the pleasure of sitting down with Jasmine Marcelin, Assistant Professor in the Department of Internal Medicine and Associate Medical Director for the Antimicrobial Stewardship Program at the University of Nebraska Medical Center. She was part of our docuseries, "The Scientists Who Saved the World: The Fight Against COVID-19," and shared insight into the chasms of inequities underrepresented populations are experiencing, as well as what must happen to change course. To start, we must ensure that we are connecting with the communities we serve and meeting them where they are. Marcelin noted that mobile testing and vaccine units certainly play a role – but that the key to strategizing care lies in understanding how a community leverages its resources.

"Healthcare in general has not done a great job of truly engaging with the community to ascertain what resources are already there and how we can leverage those," Marcelin said in the interview. Community centers, for example, are already participating in various activities – could they also become local testing center triage when needed? Churches and other local health clinics could also act as resources. There is no blueprint, Marcelin said, and it doesn't need to be done in the same way in every city; things can be adapted to the communities being served.

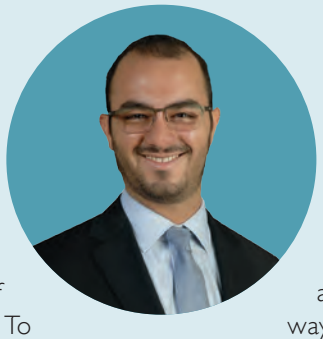
Because the laboratory is the epicenter of testing, it makes sense that we lead community outreach programs to provide underrepresented groups with the care they need. Collaboration is foundational to the laboratory and we know from experience – both recent and past – that when we act together, we are StrongerTogether. Now is the time to use our combined knowledge and expertise to help reach those who have not historically had access to the care they need.

# Torrent of Praise

**It has been almost two years since the Ion Torrent™ Genexus™ Integrated Sequencer was introduced to the world. We are proud of its reception by the laboratory community and of the role it has played in enabling laboratories around the world to provide fast genomic profiling services – even in times of crisis. In this article, selected users from around the world share their experiences with Ion Torrent™ Genexus™.**

## Speed and Accuracy with Restricted Headcount

*Leomar Ballester, Assistant Professor, Molecular Pathology and Neuropathology, and Co-director, Molecular Diagnostics Laboratory, Department of Pathology and Laboratory Medicine, University of Texas Health Science Centre, Houston, Texas, USA*



Today's laboratories must provide accurate results as quickly as possible – often with strictly limited personnel numbers. How robust is the Genexus™ Sequencer in the face of these goals and constraints? To address this question, Leomar Ballester assigned a small team (three individuals) to screen FFPE tissue samples using the Genexus™ Sequencer in combination with the Oncomine Precision Assay. In brief, the team assayed SNVs, CNVs, and fusions with reference to standard commercial controls. The results were excellent; at 5 percent minimal allelic frequency (MAF), the Genexus™-Oncomine system detected 100 percent of variants. Detection sensitivities were particularly encouraging in SNV screens, with 75 percent of SNVs detected at a MAF of 2.5 percent (see Figure 1).

But Genexus™ has other favorable attributes too. Leomar emphasizes the platform's advantages over competing technologies such as fluorescence in situ hybridization (FISH) or immunohistochemistry (IHC). In particular, he notes the ability of Genexus™ to detect a broad range of genomic variants, including both mutations and amplifications – and, by way of illustration, cites the example of *ERBB2* mutations in colon adenocarcinoma. Clinical studies in colorectal carcinoma suggest that over 30 percent of *ERBB2* mutations comprise short variant alterations – and these may be detected by Genexus™, but not by IHC or FISH. This is a critical distinction because tumors driven by these short variant alterations may be responsive to targeted therapy; it is therefore vital to patients that we use screening technology that can identify these points of therapeutic intervention. For these reasons, Leomar values the key advantages of Genexus™: speed, accuracy, and a high degree of sophisticated automation. Together, these minimize man-hours while reducing turnaround times to as little as two days.

| Gene ID | COSMIC ID | Identifier | HGVS nomenclature | Amino acid | 10% AF targeted | 5% AF targeted rep 1 | 5% AF targeted rep 2 | 2.5% AF targeted |
|---|---|---|---|---|---|---|---|---|
| *AKT1* | COSM33765 | Substitution | c.49G>A | p.E17K | 18.0% | 10.1% | 9.0% | 4.7% |
| *BRAF* | COSM476 | Substitution | c.1799T>A | p.V600E | 18.7% | 7.4% | 9.3% | 3.4% |
| *EGFR* | COSM12378 | Insertion | c.2310_2311insGGT | p.D770_N771insG | 9.8% | 4.4% | 2.9% | 2.2% |
| *EGFR* | COSM6225 | Deletion | c.2236_2250del15 | p.E746_ A750delELREA | 11.2% | 6.1% | 5.5% | 2.8% |
| *EGFR* | COSM12979 | Substitution | c.2573T>G | p.L858R | 7.8% | 5.7% | 5.8% | Not detected |
| *EGFR* | COSM6240 | Substitution | c.2369C>T | p.T790M | 7.4% | 3.7% | 4.8% | Not detected |
| *FLT3* | COSM783 | Substitution | c.2503G>T | p.D835Y | 16.9% | 7.6% | 8.8% | 3.2% |
| *IDH1* | COSM28747 | Substitution | c.394C>T | p.R132C | 15.9% | 6.5% | 5.9% | Not detected |
| *KIT* | COSM1314 | Substitution | c.2447A>T | p.D816V | 7.8% | 2.9% | 8.3% | 2.8% |
| *KRAS* | COSM521 | Substitution | c.35G>A | p.G12D | 14.1% | 7.7% | 8.8% | Not detected |
| *PIK3CA* | COSM760 | Substitution | c.1624G>A | p.E542K | 9.6% | 4.9% | 7.2% | 2.7% |
| *PIK3CA* | COSM763 | Substitution | c.1633G>A | p.E545K | 14.5% | 5.9% | 7.0% | 4.0% |
| *PIK3CA* | COSM775 | Substitution | c.3140A>G | p.H1047R | 13.6% | 5.9% | 9.5% | 2.8% |

Figure 1. Reliable detection of SNV at a minimal allelic frequency of 5 percent or higher.

## Streamlined Workflow for Solid Tumor FFPE Analysis

*David Seidman, Scientific Director for Molecular Diagnostics and Serology Laboratories, Sentara Healthcare Laboratory Services, Newport News, Virginia, USA*

David Seidman's laboratory has compared the performance of the Genexus™ technology with that of competing systems and recently presented a head-to-head assessment of the Genexus™ automated workflow technology (Genexus™ Purification System and Genexus™ Integrated Sequencer) and their existing semi-automated workflow system (based on the Ion Chef™ and Ion GeneStudio™ S5 sequencing and semi-automated extraction platforms). Their findings were clear: the Genexus™ technology, by virtue of its unprecedented automation and workflow streamlining, shortens turnaround time from the four days typical of the Ion Chef™/ Ion GeneStudio™ platform, to only two or three days – a time savings of up to 50 percent.

David's team also undertook a detailed comparison of the Genexus™ Purification System with a competing extraction system, the Promega Maxwell RSC™ 48. Each platform requires some sample pre-processing and has a similar footprint; a key difference, however, is that the Genexus™ platform quantifies both DNA and RNA. Although the Promega technology can process 48 samples in parallel, it can only extract either DNA or RNA. The Genexus™ platform processes 12 samples in parallel, but extracts both DNA and RNA simultaneously, resulting in 24 quantified samples (12 RNA and 12 DNA) per run. Furthermore, the Genexus™ software has built-in flexibility that allows each laboratory to set specific quality control criteria per sample so that successful analysis can be determined with reference to the most appropriate measures for each piece of research. Many laboratories will appreciate this feature. Finally, David notes that the high degree of automation in Genexus™ limits the opportunity for human error; this reduces not only variability in results, but also turnaround time – an important attribute in applications such as cancer diagnosis, where speed is of the essence.

---

## Oncology Biomarker Testing and SARS-CoV-2 Surveillance – a Crisis Combination

*Paul Hoffman, Head, Laboratory of Clinical and Experimental Pathology, Louis Pasteur Hospital, Nice, France*

The pandemic has placed unique demands on the laboratory community – primarily with regard to the need for widespread, rapid SARS-CoV-2 testing at high volume. To provide the capacity this unprecedented situation requires, many molecular diagnostics laboratories, including those not traditionally involved in virus surveillance, have diverted resources to either PCR- or sequencing-based SARS-CoV-2 tests. For example, Paul Hoffman's team – already familiar with the Oncomine Precision Assay for cancer biomarker screening – recently evaluated the Ion AmpliSeqTM SARS-CoV-2 Insight Research Panel, used in conjunction with the Genexus™ Integrated Sequencer and Pangolin analysis software. The aim was to determine the platform's suitability for prospective SARS-CoV-2 surveillance. Can Genexus help us address the pandemic's unique challenges? Paul's opinion is unambiguous; he states that the high level of automation in Genexus™ means that fewer personnel are required to maintain workflow, which enables efficient operation without sacrificing social distancing. The automation features also contribute to the ease-of-use of Genexus™ and enable a very rapid turnaround time (~24 hours).

Furthermore, Paul notes that the Genexus Integrated Sequencer allows his lab to process up to 112 samples per week at high quality. The high sensitivity of variant detection makes the Ion AmpliSeq SARS-CoV-2 Research Panel an excellent resource for viral surveillance. In summary, Paul notes the general benefits of NGS advances such as Genexus™ – an approach that permits smaller laboratories to provide genomic profiling services across different fields, thereby enabling them to contribute to the diagnostic challenges raised by the pandemic. In other words, laboratories can divert their expertise to SARS-CoV-2 surveillance without precluding use of the Oncomine Precision Assay for tumor biomarker testing in tissues from patients with a broad range of solid tumors, including lung cancers

*Find out more at www.oncomine.com/genexus-oncology*


Montefiore
The University Hospital for Albert Einstein College of Medicine
111
East 210th Street
Montefiore
Henry and Lucy Moses Campus
Montefiore
Montefiore

*Credit: Courtesy of Montefiore Health System.*

# RISING TO THE BIGGEST CHALLENGE

MONTEFIORE-EINSTEIN'S PATHOLOGY DEPARTMENT WAS READY AND MORE THAN WILLING TO TACKLE THE COVID-19 CRISIS HEAD ON – BUT ALSO ABLE TO ADAPT AND COLLABORATE AROUND UNPREDICTABLE PROBLEMS TO SERVE THE INCREASINGLY DESPERATE HEALTHCARE NEEDS OF THE BRONX

*Credit: Courtesy of Montefiore Health System.*

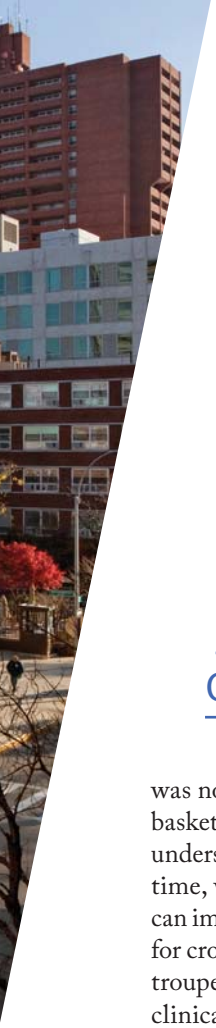
When New York confirmed its first COVID-19 patient, no one could have anticipated the tidal wave that would later crash into low-income neighborhoods like the Bronx. Here, five pathologists from Montefiore-Einstein share their accounts of the pandemic – and how the pathology department was able to rise so quickly to the challenge of bringing service and care to the surrounding communities.

Amy Fox, Vice Chair, Clinical Research; Division Chief, Point of Care Testing & Outreach Laboratories; Advisor, Molecular Infectious Diseases Diagnostics; and Professor, Montefiore Einstein Department of Pathology, Bronx, New York, USA

I was, at the time, director of our Virology Laboratories. By the time we got a call from the New York State Department of Health, announcing that they were allowing our laboratory to perform COVID-19 in-house testing, we already had patients suspected of having COVID-19 in the hospital. However, no one could have anticipated the full scale of what was to come, and it wasn't until the significant increase in the numbers of possibly infected patients coming through our doors that we began to understand the severity of what was happening.

We quickly realized that we would outgrow our in-house capacity for laboratory testing using the initial platform we had started with (under an Emergency Use Authorization). That's when I started reaching out for assistance from everyone who I thought might be working on COVID-19 testing. At the same time, we reached out to colleagues and industry partners, asking them to put us on their list for platforms and reagents as they were being developed. Shortly after that, I learned that the prioritization and distribution of supplies was being controlled at the level of the White House – a shocking, distinct difference between this pandemic and any public health emergency we had been through previously. In fact, I can't recall a time in my 30-year career when we were getting information filtered through industry leaders who had been in communication with the White House. It was surprising – and totally unprecedented.

The Montefiore leadership immediately accepted what we needed to do and we had ongoing, weekly meetings with C-suite leaders – constantly sharing information in a bi-directional fashion. The pandemic is the only time I've been given carte blanche – a blank cheque – to get the job done. That empowerment, though initially scary, allowed us to build in redundancy and reach out to all of our industry partners; there



"THE RELATIONSHIPS FORGED DURING THOSE DAYS OF THE ACUTE CRISIS ARE THE SILVER LINING IN THIS AWFUL CLOUD."

Amy S. Fox. Courtesy of Montefiore Health System.

was no way we were going to put all our eggs in one industry basket. Our partners reciprocated with nothing but kindness – understanding our need to build in redundancy; within a short time, we were up and running on six different platforms. You can imagine the impact this had on laboratory staff and the need for cross-training, but our team functioned like a master ballet troupe. My own energies were split between oversight on the clinical lab side of testing on multiple platforms and working with the research team on developing COVID-19 antibody testing. Everyone stepped up and brought their A-game, which resulted in a strong partnership among Einstein researchers, infectious disease colleagues, and clinical laboratorians.

## A SENSE OF CAMARADERIE

Over time, the intense energy and enthusiasm of the moment has waned, but the camaraderie remains. Though SARS-CoV-2 is no longer the focus of every project, there is still something special about having gone through that unique experience with our scientists, clinicians, and clinical colleagues. We entered into and emerged from the trenches together and, though I would never want to do it again – and we can't forget that we're still living through the pandemic – the relationships forged during those days of the acute crisis are the silver lining in this awful cloud.

At the same time, the pandemic has highlighted some real challenges ahead. For example, medical technologists are in seriously short supply in the US and, in particular, in New York. What's the solution? The answer is complicated and costly. Laboratory medicine needs a bigger seat at the table. While the role of "the lab" has gained a degree of recognition on the national and global stage as a result of COVID-19, I'm not so sure that we, as laboratory medicine professionals, have done a good job of capitalizing on the increased visibility.

## LOOKING BACK, LOOKING AHEAD

We need to reflect and ask what we could have done differently when COVID-19 first took over the Bronx; however, I believe we should also be asking this same question of our organizations and professional societies. There was a lot of misdirection early on in the US and, by the time laboratory professionals were finally allowed to voice an opinion, the situation was beginning to resolve. But how much time was lost? What if the CDC had sought guidance earlier from laboratory directors at major university hospitals who have been doing this type of work for a long time? Instead, CDC officials waited until the last days of February 2020 to announce that testing was being opened up to our laboratories – a decision that came down without warning. Although we can't go back and change the past, the input of experienced laboratory professionals would have been valuable early on and would have avoided significant delays in diagnostic test implementation.

At Montefiore, we've always taken care of those who have no one else to care for them. Here in the Bronx, where we work with one of the poorest patient populations in the US, there was not a single healthcare professional in our Montefiore Einstein community who did not go above and beyond. The pandemic has shown us that when an unanticipated, horrific situation arises, the humanity of every individual has the potential to surface. When you're in the midst of a crisis, seeing the best of humanity all around you is what keeps you moving forward.

Everyone who enters the trenches emerges differently; the question is, what happens the next day? Many of my colleagues are reevaluating whether they want to stay in healthcare. For others, the pandemic has given a sense of clarity about what's important. I just hope it's sustainable, that those of us who have been granted this clarity can hold onto it, and that it guides us through whatever comes next.

Lucia "Lucy" Wolgast, Director, Clinical Pathology Laboratories, and Associate Professor, Montefiore Einstein Department of Pathology, Bronx, New York, USA

We were preparing for COVID-19 even before admitting our first patient; working with New York State to test persons of interest, trying to screen people who were coming into our emergency department, and developing in-house testing. The day we admitted our first patient, I met with the laboratory staff to reassure them that we had the right safety protocols in place while encouraging them to get on board with our important mission. Initially, there were a few people who were nervous – but who wouldn't be? Nevertheless, throughout the pandemic everyone stepped up, asking what needed to be done, rather than what they had to do.

The Bronx was one of the worst-hit counties in the US. Usually, it's a very active place but, on the day we shut down, all was quiet; looking back, that was probably one of the saddest moments – seeing the vibrancy of the city and neighborhood suddenly stripped away. The Bronx was suddenly a ghost town – until you stepped through the doors of the hospital into complete chaos. Our mission was clear: to fight the pandemic and take care of our patients. But I also needed to make sure the staff were okay – and that they could physically and mentally handle what was happening. I not only oversee the lab staff with testing but also the phlebotomy staff – and they really had it rough. They were going to the COVID-19 floors and drawing blood from patients, witnessing firsthand the scale of the illness. I tried to be as supportive as possible and constantly checked up on them. They were risking their lives to take care of patients and do their jobs, and I was just their cheerleader as we all tried to get through our days together.


*Credit: Barry Winiker/Getty Images.*

> "IT WAS LIKE A TIDAL WAVE OF SWABS HITTING THE LAB. THEY WERE COMING IN FROM EVERYWHERE."

## THE COVID-19 COMMAND CENTER

The week we started testing, it was like a tidal wave of swabs hitting the lab. They were coming in from everywhere – the pneumatic tube systems, people dropping off at the STAT window, and, eventually, deliveries and courier services from our collection tents. I couldn't believe how quickly the volume increased – we had "the test" and everybody wanted it. We realized that we simply couldn't do it all in one place – we also had other testing to do – so we decided that all the swabs and processing should be in a dedicated space with a whole new processing team. And that was the start of Montefiore's COVID-19 Command Center. However, the day we started construction, I suddenly felt so exhausted that I had to go home. I woke up the next morning to many phone calls about the center, but I had a fever so I couldn't go into work. The next day, I found out I had COVID-19. Wendy Szymczak and Sean Campbell were assigned as the new heads of the center.

## NEW WORKFLOWS

When I came back to work two weeks later, other staff were out with COVID-19 and I mobilized the surgical pathologists – who no longer had surgical cases to sign out – to cover crucial laboratory areas that needed oversight. A few covered one of the Emergency Department's rapid response laboratories that was expanding its COVID-19 PCR testing. A few helped support the phlebotomy team on the morning rounds, which were very busy with patient draws. At that point, all the inpatient floors had COVID-19 patients and the clinical teams were ordering numerous tests. The phlebotomy staffing levels were not keeping up with the volume of orders and patient draws and, many times, the

Lucia "Lucy" Wolgast. Courtesy of Montefiore Health System.

phlebotomists were returning to the same patients several times a day. Concerned about their safety and burnout, I knew we needed to standardize test ordering for the inpatient COVID-19 patients. To help with this, we created order sets in collaboration with the IT and clinical teams that included all the tests we felt were important for COVID-19 monitoring. This led to less-frequent blood draws because all relevant tests could be drawn at a single time by the phlebotomist, on a schedule with limited contact between the phlebotomists and COVID-19-positive patients.

Some operational challenges were mitigated when we created the new COVID-19 inpatient order sets, updated our COVID-19 PCR ordering into expedited and routine orders, and expanded our courier services. Over time, we no longer needed the command center; we dismantled it after a couple of months, but we are keeping the new ordering systems in place and even applying them to our day-to-day, non-COVID-19 work. The pandemic was a lesson in the need to be fully prepared; it's almost irrelevant what the next challenge is, as long as you have the right foundation in place. For me, that meant to have a ready and willing laboratory team, to communicate with them effectively, and to gain their trust – all while listening to their feedback and making adjustments along the way. Collaboration has been at the heart of our pandemic fight – not only within our teams, but across departments with our Albert Einstein College of Medicine colleagues in the development of antibody testing for COVID-19. I can only hope this collaborative spirit endures post-pandemic.

Sean Campbell, Associate Director, Clinical Chemistry and immunology Laboratories, and Assistant Professor, Montefiore Einstein Department of Pathology, Bronx, New York, USA

At the end of February 2020, I was in Spain. As soon as I got back to the Bronx, everything exploded and I was appointed second-in-command of our new, under-development COVID-19 Command Center (Lucia Wolgast had tested positive for COVID-19, as she mentioned above). Everything happened so rapidly that sometimes it felt like we were just trying to keep our heads above water. Within the first week of Montefiore's first confirmed patient, we had set up the command center as a triage center for specimens, with multiple reference labs that we could send to – we received all the samples for COVID-19 testing, made sure the testing was accurate, checked in on the patient's condition, and directed samples to the most appropriate lab. At first, we were sending all samples to reference labs, but as testing was increasingly brought in-house, we had decisions to make. Next, rapid testing appeared; it only took 45 minutes but was highly restricted in terms of volume, so we had to decide between rapid testing versus traditional testing.

While we were dealing with everything changing almost minute to minute, there was a very real and understandable fear amongst our clinicians. We came close to running out of reagents for tests; because patients were being tested multiple times per day, it was hard to keep stock. To help staff the command center, medical students joined the fray – and they were absolutely incredible, doing incredible work right in the thick of it. They ensured that everything got to each lab; if something went missing, they tracked it down. They also made protocols and flowcharts, and ensured processes were consistent across shifts. Alongside the shifting requirements of COVID-19 testing, they also dealt with the other volumes of the lab – and because they were willing to take that pressure off the main lab, it meant the command center was able to do an incredible job.

On top of that, Montefiore rapidly expanded its ability to take in patients. We had about 800 beds but, at our peak, we had around 1,200 concurrent COVID-19 patients. Even now, you can see the remnants of our setup; for example, we have an auditorium that has false walls and hookups for oxygen. We rapidly converted every available space – even our children's hospital essentially shut down and was turned into an adult hospital and ICU.


A typical street scene in the Bronx. *Credit: Jason Torres/Montefiore Health System.*

Even in the early stages of the pandemic, ensuring the technologists had the right supplies was not straightforward – everyone got hit with surprise needs, particularly for tests that we only occasionally needed prior to the pandemic. Sure, we could do the tests – but we weren't expecting the sheer volume. PCR reagents were running out everywhere… And we even had people with 3D printers explore the potential of making swabs! At the time, I was associate director of our Hematology and Coagulation Laboratories and worked closely with Clinical Chemistry. We were lucky that very few of our technologists got sick, which meant we were able to keep the lab on track; without technologists, the lab comes to a standstill.

As far as current challenges go, we still encounter supply issues and shortages, but they tend to change from week to week. Our biggest challenge now is burnout. We've been dealing with the pandemic for over 18 months now and our technologists have been working extremely hard the whole time. There's no quick fix for this, considering the pandemic is still ongoing, but we try to support everyone the best we can so we don't have issues with people retiring early or leaving because they can no longer handle the constant stress.

The pandemic has at least had a lasting impact on the visibility of laboratory medicine. Locally, it has been helpful in prompting collaborations and relationships with departments we wouldn't have usually connected with. Personally, prior to the pandemic I had not had opportunities to forge relationships with the infectious disease or emergency department teams. The pandemic brought us together and I have formed meaningful, professional relationships with my colleagues across the institution that I will take with me as we go forward.

Sean Campbell. Courtesy of Montefiore Health System.


Wendy Szymczak, Director, Clinical Microbiology Laboratory, and Associate Professor, Montefiore Einstein Department of Pathology, Bronx, New York, USA

I actually don't remember our first confirmed patient, but I remember when we started getting patients who were at least suspected of having COVID-19. We knew something was coming and we started to have regular meetings about what we were going to do and how we couldn't do testing because, at that time, the health department was the only place that was able to offer testing. We knew we would have to come up with a workflow to coordinate testing with them – but how? How were we going to get the specimens? How were we going to keep track of everything? What safety protocols did we need to change and implement? There were many unknowns.

Luckily, some of our faculty members and lab directors had been through previous, smaller pandemics like swine flu in 2009 or the first SARS pandemic, so there was at least some collective knowledge that we could draw upon. From that, we developed a preliminary plan for simple things, like how to deliver specimens, so when our infectious disease colleagues sent an email letting everyone know we had our first suspected patient and that they met the health department's testing criteria, we were prepared to send the specimens out for testing. That day we had one specimen, the next day we had three or four; the day after 20, and then 100 – there was an exponential growth and we had to rapidly come up with new processes to handle the large influx. I admit, I did make some slightly naive assumptions that the health department would be able to do a lot of the testing, that there wouldn't be such a need for us to bring it in-house, and that we wouldn't receive such a large volume of specimens so quickly. Fortunately, there were others in our department who knew we needed to start thinking about having the capabilities to do testing on site and guided us to start developing it early on.

There was a lot of adrenaline – I think I was on autopilot a lot of the time, but it felt good to have a job where I could come to work and feel like I was doing something to contribute. Not knowing what was going on or what was going to happen was a really out-of-control feeling. And it was hard coming to work in the Bronx; I live in the city and take the train to work every day, and at the start of the pandemic I had to walk past a truck with bodies on it to get to Montefiore – the truck was from a neighboring hospital, but I knew we had them too.

Credit: Courtesy of Montefiore Health System.

> "WE DECIDED TO TEST THE HIGH-ACUITY PATIENTS THAT NEEDED FASTER TURNAROUND TIMES IN OUR IN-HOUSE PLATFORM, BUT WE STILL HAD TO MAKE THE DECISION OF WHO GETS WHAT."

It was an awful thing to walk by and see every day. But once I got into work, it was a unique experience – I had never known everyone working together so efficiently. Nothing was siloed; we were working within our department and also collaborating with our colleagues in such a well-organized and efficient manner. Everyone was so involved and wanted to do whatever they could to help.

## TIME TO CENTRALIZE

We realized early on that we had to change our workflows because we didn't have the infrastructure in place for the large volume of SARS-CoV-2 specimens we were receiving. The command center was set up as a centralized location in which we could have dedicated staff to triage specimens for SARS-CoV-2 testing, while clinical teams could communicate with us and we could provide guidance and answer any questions they had.

Within a few days of conceptualizing the center, we came up with how many staff we would need for 24/7 coverage, identified physical locations for the room, and secured computers, phones, and a network for it. Unfortunately, two days later, the lab director came down with COVID-19, so Sean Campbell and I were put in charge and we worked together to direct the command center, teach the medical students and dental associates (who we used to staff the center) to come up with protocols, and oversee the overall operation. Eventually, our pathology residents and some of our colleagues from anatomic pathology also helped out. It was a real collaborative effort to keep the center functioning.

Once we brought in our first SARS-CoV-2 PCR-based test, we only had a certain number of reagents per day, so we had to decide the amount of specimens that were going to either go to the health department or to reference labs once they started offering tests. We decided to test the high-acuity patients that needed faster turnaround times in our in-house platform, but we still had to make the decision of who gets what – we needed staff who could actually make a clinical decision based on how the patient was doing. And that's why it was helpful to have medical students in the command center – they had basic knowledge to be able to handle those tasks and helped us develop protocols as we brought in more and more testing platforms and then transitioned to all in-house testing.

## COLLABORATIVE EFFORT

The pandemic was one of the first times that our clinical labs worked with basic science researchers at the medical school to rapidly develop a clinical assay. Some of the concepts for our antibody testing were actually developed by our colleagues before manufacturers were releasing similar. The command center staff retrieved remnant serum specimens from patients with and without COVID-19 so that these specimens could be used to develop and validate serology tests. My colleagues within clinical pathology worked alongside the basic research teams to compare test performance for several serologic assays and to ask new research questions. The project really built a bridge between us and our basic research scientist colleagues.

In the future, what I've learned from this experience is that you have to start building testing capabilities much earlier than you initially think. And I think there needs to be more pandemic preparedness across the board. In short, I hope that COVID-19 – and the realization that the lab is here behind the scenes to help – will be used to prepare for future outbreaks.

Wendy Szymczak. Courtesy of Montefiore Health System.

*Credit: Courtesy of Montefiore Health System.*

## FIVE KEY LESSONS LEARNED

*Amy Fox*: "Under the right set of circumstances, everyone is and should be your partner because everyone has a role in improving the situation."

*Lucy Wolgast:* "Mobilize your team early, communicate effectively with them, and get the buy-in of your staff. We can't prevent pandemics from happening but, for any kind of emergency, your team is your greatest asset. If I take anything positive from the pandemic it's that, as a team, we are much closer and stronger because of it."

*Sean Campbell:* "We need to stay in our lanes a little less – or at least make sure to reach out to our colleagues more. What we achieved at Montefiore was only possible because of the complex relationships we formed between departments that allowed us to get things moving very quickly – and get us to a place where, even though we had 1,200 patients, we were able to handle it. We can't stop people from getting sick, but we can always do our best."

*Wendy Szymczak:* "You have to spend time and money preparing for emergency situations because there is so much involved. When there are competing priorities, preparing for a potential outbreak in the distant future can be hard to justify. But COVID-19 is just the tip of the iceberg – we will see more outbreaks in future, and the worst thing we can do is be complacent in our healthcare needs."

*Yitz Goldstein:* "You have to do what's right and what's good. But it's important to know that sometimes, even when you have conviction, you may be wrong. At Montefiore, we pivoted left and right as the situation progressed. Learning to admit when you're wrong is essential in a situation where you have to make decisions on the fly. It's okay to be wrong as long as you don't continue to dig yourself into that hole. It's like a lightning bolt searching for a path to the ground – when it finds one that won't work it moves onto the next until it finds one that does."

D. Yitzchak "Yitz" Goldstein, Director, Virology Laboratories, and Assistant Professor, Montefiore Einstein Department of Pathology, Bronx, New York, USA

On March 1, 2020, New York City had its first confirmed case of COVID-19. By then, our pathology department was working with the various city and state health departments on testing of suspected cases and had also begun validation of our own SARS-CoV-2 assay to rapidly test our most seriously ill patients (though it was still tentatively called 2019-nCoV at the time). Although FDA guidance was often found to be lacking in those early days, we quickly completed and submitted our Emergency Use Authorization paperwork to the FDA for clinical testing and performed our first clinical test on March 9. The days and timing are clear in my mind because, within a few short days, our hospital was hit – and hard.

Quickly realizing the demands were outstripping our laboratory capacity, we began plans to implement many different testing platforms to meet the needs of our patients. In such a densely populated area like the Bronx, it was hard to know where COVID-19 was and where it wasn't. In the beginning, patients were told to stay at home if they were stable; we couldn't do any better without ensuring increased testing availability. It was a frightening time. Running through the reports of patients each week, one single word became far too prevalent: Deceased. It was shocking to see the number of patients being lost to an overwhelmed system.

## THREE-PHASE COLLABORATION

Everything we could possibly do, we tried and, eventually, we built three components to the lab that coincided with the three phases of testing: the pre-analytic phase, analytic phase, and post-analytic phase. In the pre-analytic phase, we needed to triage COVID-19 patients – the Command Center was the solution for that and it was the central part of this phase of testing.

The analytic phase of testing was next. At each stage of the pandemic, we incorporated new technologies to ensure sufficient throughput, ultimately operating seven or eight different testing platforms. This was necessary to overcome the massive international supply chain disruptions that we began to experience. Having this much redundancy ensures that if one manufacturer was short on supplies we could pivot seamlessly to another who could provide them.

In the post-analytic phase, the information flow had to get back to the clinicians in a reasonable amount of time. It was pandemonium in the beginning and, because we didn't have efficient IT solutions in place for something as simple as a clinician order, we still needed ways to get specimens to the laboratory. Clearly, the flow of information is essential to the three phases of clinical laboratory testing, and it needs

D. Yitzchak "Yitz" Goldstein. Courtesy of Montefiore Health System.

to be near instantaneous, so we worked with our IT partners and very quickly became a well-oiled machine to achieve the ideal workflow.

The work was happening from the bottom up, and the fact that we were constantly communicating throughout the hospital – with managers and directors at the bench – was a powerful approach. However, the work could not have been possible without our technologists. These men and women are the gasoline on which our internal-combustion engine continues to run, and they are owed more thanks and appreciation than can be showered on them in a lifetime. They worked harder than I had ever seen, voluntarily changing their schedules to expand laboratory operations and simply ensure that as many samples as possible could be completed by our lab. From all directions, we joined forces in the middle to effectuate change at a rapid pace – something that may have been unique to Montefiore because of the mutual respect and trust we have for each other. The technologists who performed the hundreds of 1000s of tests at Montefiore really deserve the highest commendation for their efforts – without question.

There is an entire world of medical laboratory technology that is completely hidden – not only from patients, but often from our clinician colleagues, as well. While a sample may be dropped off at the lab and clinicians magically get a result in the lab system, there is too little taught about what we actually do in the lab. COVID-19 has exposed the value of the laboratory sciences to a broader population that have taken an interest in it and will continue to ask questions. The fact that more people than ever now understand what a PCR test is versus an antibody test is a remarkable feat for the lab. However, we need to capitalize on this and ensure that every doctor and patient realizes that the services we provide are essential to patient care. It's truly a testament to our performance that, prior to the pandemic, many didn't even know we existed, let alone our diverse, value-added functions to the hospital and its patients.

## PROUD OF THE PEOPLE

As much as we are proud of the systems we put in place – the command center, testing, and IT systems – none of it would have been possible without the people. Throughout the pandemic, everyone was running at 250 percent by choice. By being upfront with our teams about what was coming and maintaining a constant, immediate flow of information with our technologists, our staff understood the gravity of what we were doing and knew what needed to be done to get through it. No one ever questioned it – they were here, ready and willing to serve, and they were going to do it at the highest levels because the communities in the Bronx needed them.

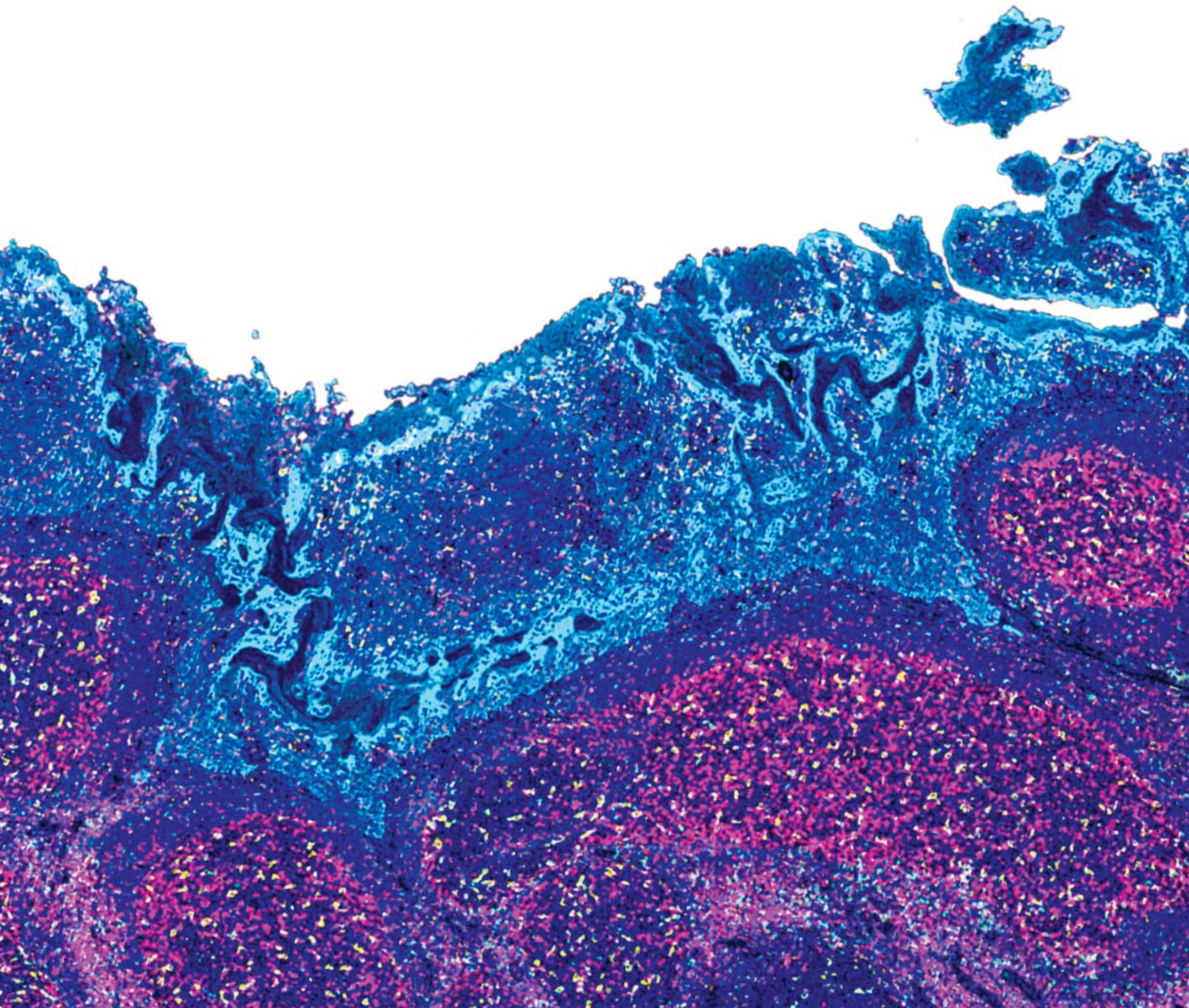
Perhaps the silver lining of the pandemic is the realization that we can achieve more together than we can individually. We are more than the sum of our parts – the hospital and the medical school. We have been coming closer and closer together and we hope that the relationships fostered throughout the pandemic will continue and further mature. There really is a tremendous opportunity to take what we've learned through this trial by fire and produce something great – but we may still have to break down some walls to get there.

The pandemic has shown us that, where there's a will, there is absolutely a way – and likely a willing partner to help when you need it.

ULTIVUE

# FlexVUE

8-plex panel | 13 variable markers | Lots of possibilities



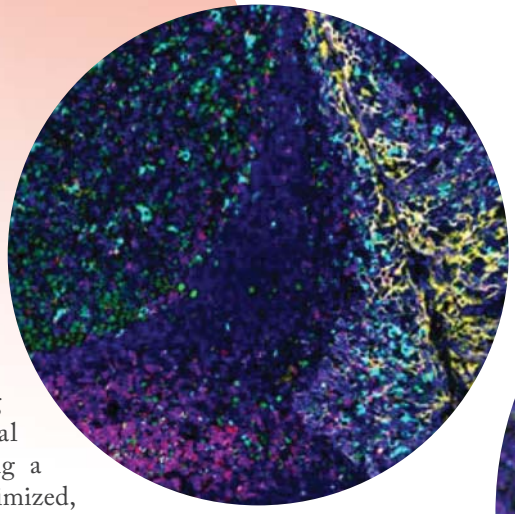
the Pathologist

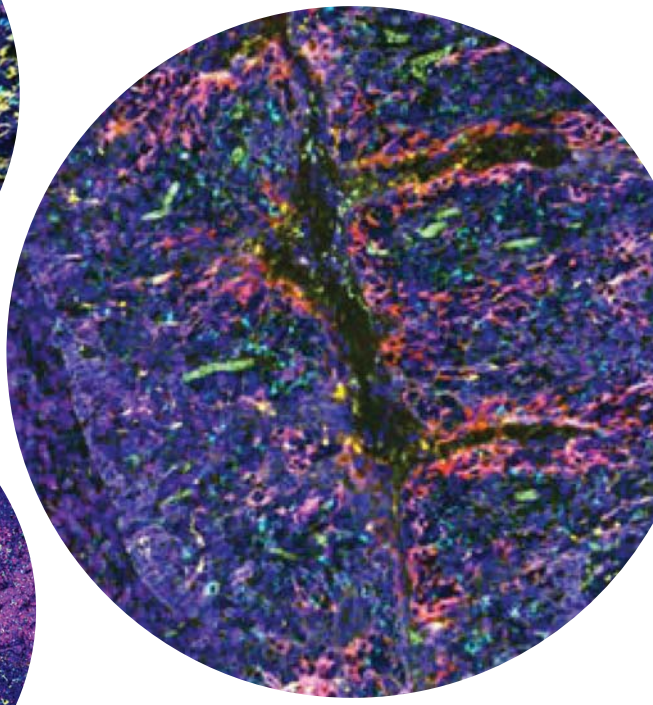
# THE INNOVATORS

SHOWCASING THE PRODUCTS AND COMPANIES MAKING A DIFFERENCE IN 2021

# FLEXIBLE SOLUTIONS WITH FLEXVUE

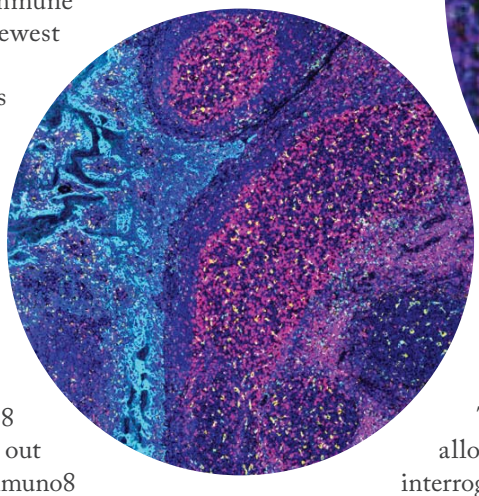
*Quickly customize your immune panels with Ultivue's new innovation*





Ultivue is setting a new standard for multiplexed immunofluorescence solutions by characterizing immune biology to reveal spatial insights – offering a flexible option with pre-optimized, verified, application-focused immune panels. This is evident in its newest product offering: FlexVUE™.

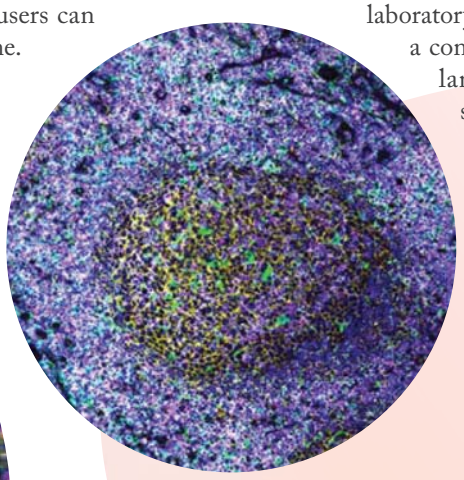
When Ultivue's customers expressed their feedback, they said they liked the immune-focused content and dedicated panels for whole slide imaging, but might want to exchange one or two biomarkers for others. The goal of FlexVUE is to provide customers with the ability to customize Ultivue's current eight-marker Immuno8 FixVUE™ panel by swapping out one to two markers from the Immuno8 backbone that includes CD3, CD4, CD8, CD68, FoxP3, PD-1, PD-L1, and CK/Sox10.

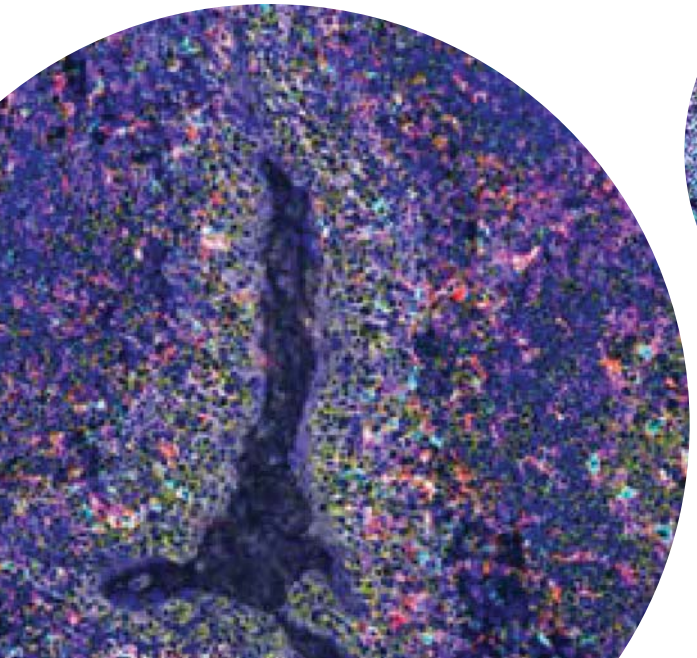


Users can exchange up to any two markers with those in the Immuno8 FixVUE panel. The additional markers that can be swapped in include Ki67, GRzB, CD45RO, CD56, CD20, CD11C, CD163, CD206, CD14, CD15, CD11b, MHCII, and HLA-DR. In addition, these pre-optimized markers, plus the robust InSituPlex® technology, means that users can customize their panels without losing valuable time.

The importance of FlexVUE is clear: it is flexible, allowing users to quickly customize panels and interrogate mechanism of action, and easy to use, with pre-optimized, flexible staining that can be used across any tumor indication. FlexVUE also has rapid turnaround times – users can quickly establish assays for early-phase clinical IO studies and robust transfer to contract research organizations for deployment, demonstrating a straightforward validation process when adding new markers.

FlexVUE offers custom options that allow laboratory medicine professionals to gather a comprehensive view of the immune landscape – or delve deeper into specific cell types and areas of the tissue microenvironment. Ultivue's out-of-the-box thinking brings pathologists and translational scientists the most innovative solutions – and, with no need to optimize and validate, all the work is done for you!





# PROSCIA CONCENTRIQ®: INTEGRATING AI APPLICATIONS INTO PATHOLOGY WORKFLOWS

*The digital pathology platform guiding laboratories into the next era of data-driven medicine*

The era of artificial intelligence (AI)-enabled pathology is here, empowering laboratories with new ways to help improve patient outcomes and accelerate breakthroughs. To realize its full potential, organizations must adopt a portfolio of AI applications for specific diseases and use cases – likely consisting of applications developed by a number of different organizations. From workflow solutions that help pathologists work more efficiently to image analysis applications that unlock new insights, AI will help organizations cope with the surge in demand for diagnostic services. However, to optimize the value of this AI, it must be tightly connected to routine research and diagnostic workflows.

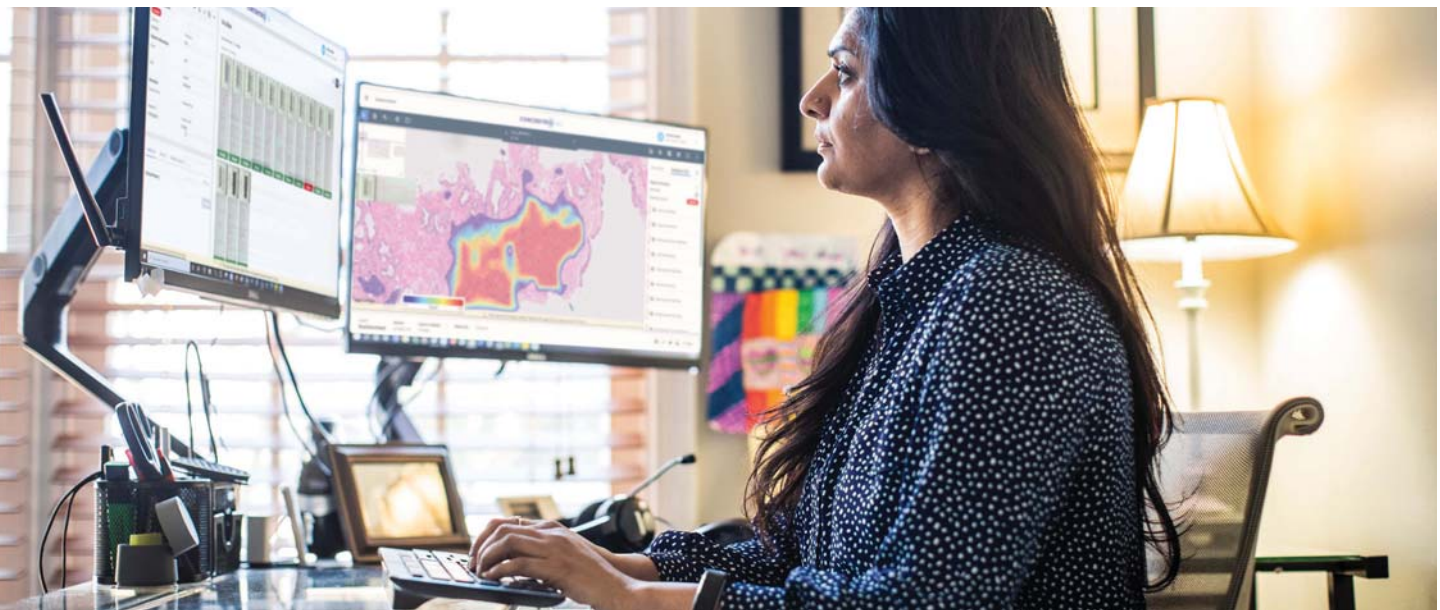
Proscia Concentriq* is an open platform that sits at the intersection of digital and computational pathology. Concentriq seamlessly integrates a variety of computational solutions built by Proscia, Proscia's customers, and validated partners directly into the workflow. It offers the robust functionality needed to carry out day-to-day tasks alongside powerful AI applications, helping leading laboratories (including 10 of the top 20 pharmaceutical companies) to transform their pathology operations.

Through its API, Concentriq provides a clear path forward for digital pathology adoption by presenting computational applications natively within the routine workflow, making a broad suite of solutions available to pathologists without them ever having to leave the platform. This differentiated approach enables pathologists to view AI results alongside images and other important data. Full integration empowers them to make more informed decisions by providing a holistic view of integrated pathology data, and eliminates time wasted toggling between different applications. The Concentriq API also provides the flexibility required to quickly incorporate valuable solutions as laboratory operations scale and new technologies emerge.

This future-proofing extends beyond AI. Concentriq offers best-of-breed interoperability that supports leading scanners and laboratory information systems, centralizing data across even the largest distributed organizations. The platform is also helping pathologists to make a seamless transition to digital with an experience designed to feel natural to the pathologist, including a responsive viewer, keyboard shortcuts, and intuitive presentation of critical information. Additionally, Proscia offers digital transformation consulting services and other professional services to help laboratories navigate all stages of their journey.

The promise of AI-enabled pathology is unprecedented – from optimizing operations to unlocking new insights that shape the way we understand disease. With Proscia Concentriq, laboratories are realizing quality and efficiency gains today while positioning themselves for long-term success in the new era of diagnostic medicine.

**For Research Use Only in the United States: requires FDA clearance.*



# THE HIVE™: THE BEES' KNEES OF SINGLE-CELL TECHNOLOGY

*The portable, handheld device delivering innovation to the single-cell genomics space*

Honeycomb Biotechnologies began as a PerkinElmer Accelerator project in 2018, based on technology developed and licensed from the Massachusetts Institute of Technology. Although extremely promising, our first customer training was a disaster and we quickly realized that the "academic" version of our product was not suited for widespread commercial adoption. So we went back to the drawing board and designed an entirely new, user-friendly format – the HIVE. As with many things in life, it took us longer to develop than planned, but it resulted in something different and stronger than before.

The HIVE™ is a portable, handheld, single-use device developed by Honeycomb Biotechnologies for the capture, storage, and genomic profiling of single-cell biological samples. The capture protocol is simple; cell suspensions are loaded into HIVEs with a pipette, followed by a cell preservative that locks in the cell's expression profile. HIVEs can then be stored and shipped to a central processing location for library preparation and sequencing.

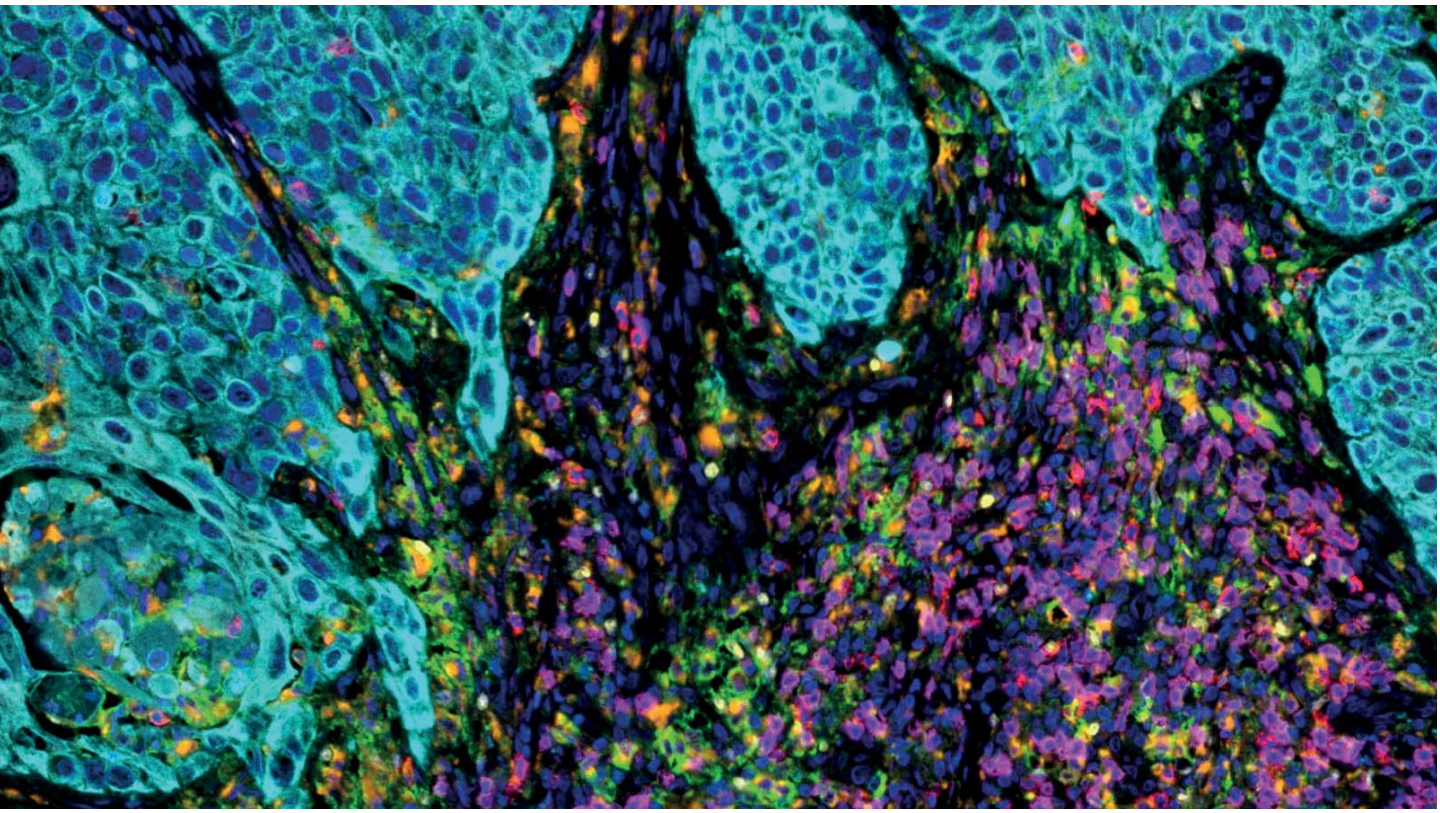
At Honeycomb, we strongly believe that single-cell genomics will follow the trajectory of genomics and next-generation sequencing – initial basic research followed by new diagnostic and therapeutic applications. Based on our strengths in distributed sample capture and storage, we believe we are ideally suited to accelerate single-cell opportunities in the clinical domain.

RNA and protein expression changes rapidly for cells once they are removed from a host; therefore, true expression profiles require sample processing as soon as possible after acquisition. The concept of instrument-free sample capture with storage greatly expands the opportunities for single-cell profiling, especially for customers pursuing distributed research.

How is Honeycomb defining this research? The HIVE delivers three areas of innovation to the single-cell space: i) gentle loading of cells into nano-wells, enabling the capture of almost any type of cell; ii) an instrument-free capture approach that allows for sample collection almost anywhere; and iii) storage capability that facilitates sample processing at almost any time. We believe that our ability to operate in entirely new settings (both distributed and clinical) will accelerate the overall growth and opportunities of the single-cell universe.

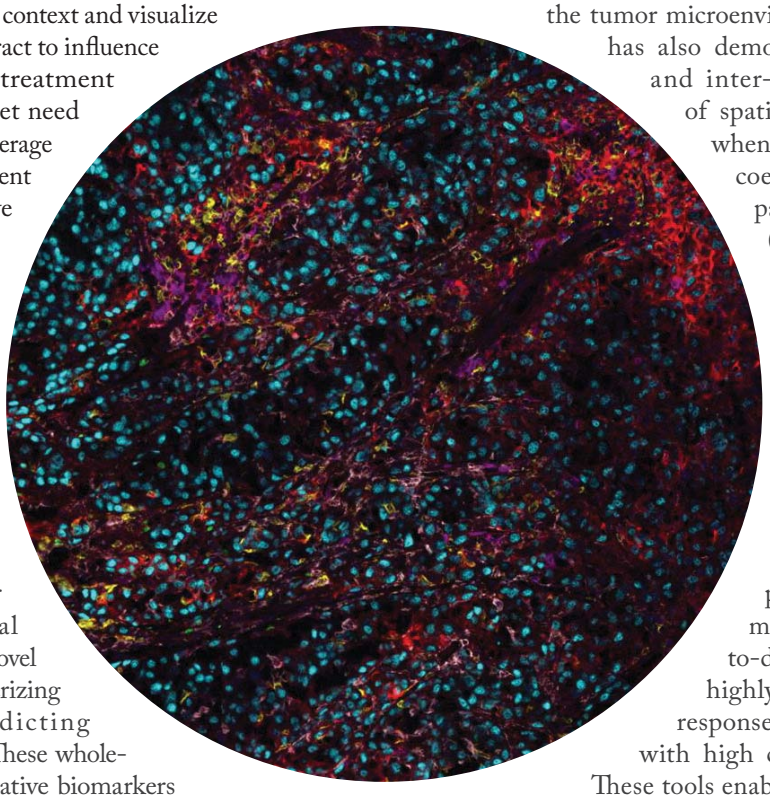
# CONTEXT MATTERS IN CANCER BIOLOGY

*Akoya is leading the way with spatial phenotypic signatures – a novel class of biomarkers for predicting response to immunotherapy*



*Images provided by Akoya Biosciences.*

In the world of cancer biology, context matters. As The Spatial Biology Company®, Akoya Biosciences' mission is to bring context to the world of biology and human health through the power of spatial phenotyping. The company offers comprehensive single-cell imaging solutions that allow researchers to phenotype cells with spatial context and visualize how they organize and interact to influence disease progression and treatment response. There is an unmet need in immuno-oncology; the average response rate of 20–30 percent is a clear indication that we need better biomarkers to predict which individuals will respond to treatment and, in turn, improve patient care.



That's why Akoya Biosciences is leading the charge – offering whole-slide imaging solutions that empower pathologists to discover novel signatures in the tumor microenvironment. Spatial phenotypic signatures are a novel biomarker class for characterizing solid tumors and predicting immunotherapy response. These whole-slide, image-based, quantitative biomarkers measure the interactions and cell densities of tumor and immune cells in the tumor microenvironment – helping laboratory medicine professionals identify the best treatments for their patients.

Unraveling the complexity and dynamics of the tumor microenvironment requires assessing a variety of tumor and immunological biomarkers. By leveraging Akoya Biosciences' Vectra®Polaris™ system for multispectral imaging, researchers can undertake rapid and accurate spatial phenotyping. Furthermore, using Akoya's novel biomarkers for multiplex immunofluorescence (mIF)-based spatial phenotyping can reveal the relationship between immune cells and tumor cells, leading to the discovery of unique spatial phenotypic signatures while preserving the architectural features of the tumor microenvironment. Recent research has also demonstrated the high intra- and inter-laboratory concordance of spatial phenotypic signatures when measuring the densities, coexpression, and proximity parameters of immune cells (1) – and, with Polaris powered by proprietary multispectral imaging technology for mIF as the fastest quantitative digital pathology imaging platform, pathologists can rapidly and accurately spatial phenotype at scale.

The importance of spatial phenotypic signatures and mIF in the pathologist's day-to-day work is clear: they are highly predictive of a patient's response rate to immunotherapy with high concordance across labs. These tools enable pathologists to identify appropriate patients and offer them the right treatment – and Akoya Biosciences will help you get there.

*To learn more about spatial signatures, visit: www.akoyabio.com/clinical-applications/*

*Reference*

1. *JM Taube et al., J Immunother Cancer, 8, e000155 (2020). PMID: 32414858.*

# R-TRACKER: A TRUE MILESTONE IN SPECIMEN TRACEABILITY

*Milestone is committed to enhancing patient safety with a new disruptive technology*

**Traceability is of paramount importance for patient safety** – this is not a choice, but an ethical obligation. However, while most agree that chain of custody is pivotal in pathology labs to ensure patient safety, several steps in the anatomic pathology (AP) analysis process – from accessioning to specimen processing – are not fully tracked or are done manually. Manual scanning is a tedious, time-consuming, and error-prone task in which operators are required to scan hundreds of cassettes one by one. This bears the risk of tracking errors and – ultimately – misdiagnoses.

Milestone is committed to providing new tools to trace specimens across the laboratory. **Milestone's latest innovation, the R-Tracker**, is an automatic rack scanner that replaces the laborious task of manually scanning each cassette by detecting both the cassette's presence and the accuracy of its corresponding barcode. **Through an innovative, patented double sensor technology, automatic scanning is completed within a few seconds** – ensuring accurate cassette documentation and traceability and, therefore, contributing to patient safety. What's more, the R-Tracker can save laboratories a dramatic amount of time by freeing up valuable operator time – up to **95 percent over manual scanning.**

The R-Tracker is the first of a new kind of tracking devices designed to enhance specimen traceability and workflow optimization. It provides an **all-in-one solution for scanning, checking, and tracking**. Accurate documentation of scanned cassettes and codes is immediately available to the laboratory information system. The R-Tracker is also designed to go hand-in-hand with other current and upcoming tracking solutions from Milestone, such as the MileWATCH monitor and tracking system – enabling real-time data sharing and biospecimen traceability for OR and AP instruments.

The R-Tracker is a game changer for both lab workflow and operator efficiency. Most crucially, it represents a giant step forward for patient safety, thereby fully embracing Milestone's mission of helping patients.

*For more information, please visit: tp.txp.to/milestone*

# REDEFINING DIAGNOSTIC REFERENCE STANDARDS

*Find out what Horizon Discovery's diagnostic reference standards can do for your workflow*

Horizon Discovery offers diagnostic reference standards in a variety of formats and genetic variants to allow researchers and clinicians to find the best process control for their diagnostic application. Reference standards can help pinpoint the fault in a workflow or serve as an assay control. Horizon's reference standards offer a reliable, reproducible, and affordable option for increasing confidence in your diagnostic assay.

Regardless of format, Horizon's reference standards have variants at varying allelic frequencies that mimic the complexity of biological samples seen in clinic. Typically, an allele can be found at 50 percent or 100 percent allelic frequency, depending on whether it is heterozygous or homozygous in a cell line. Blending a variant cell line with additional cell lines that harbor different mutations generates reference standards with different allelic frequencies – mimicking the heterogeneity seen in diagnostic samples. These variants have been constructed both from existing cell lines harboring the variant of interest and by inserting mutations into cell lines using genetic engineering techniques such as rAAV and CRISPR.

Horizon's unique strategy of cell line-derived products allows the mutation to be present in the context of the whole genome at the correct genetic loci and surrounding genetic environment. Customers have identified this as an important factor when performing subsequent bioinformatic analysis and next-generation sequencing (NGS) workflow optimization using Horizon standards.

Furthermore, Horizon's reference standards can support validation across the entire workflow – whole process control, monitoring sample DNA quality and yield, optimizing assay conditions with known variants, and fine-tuning your data reporting accuracy. They are also appropriate for most analysis techniques, including NGS, large-panel NGS, Sanger sequencing, and qPCR.

Horizon's business is underpinned by its portfolio of cell engineering tools and services, featuring gene editing technologies such as CRISPR, base editing, and gene modulation technologies such as RNAi. Horizon supports and enables critical elements of the drug development and therapeutic value chain, particularly in precision medicine. This rich heritage of gene editing has led the way in the development of its cell line-derived reference material.

*Horizon's products are available to purchase online at: tp.txp.to/hor-disc*

# INTRODUCING EASY NGS FOR YOUR LAB

*Overcoming challenges of the typical NGS workflow with the Ion Torrent™ Genexus™ System*

Next-generation sequencing (NGS) is becoming an increasingly significant part of genomics testing, but the technological footprint and expertise involved make it difficult to implement in many labs. Thus, the sheer power of NGS becomes its weakness – it can interrogate thousands of genes at a time, but the time, resources, and knowledge required all make the technique the province of specialized labs that accept outsourced work. Ordinary labs, for whom the size and complexity of NGS equipment means it may not even physically fit in their space-constrained laboratories, have had few other options but to accept the difficulties and delays of this workflow. However, thanks to the Ion Torrent™ Genexus™ System, the days of outsourcing NGS research are numbered.

Consisting of two connected devices – the Ion Torrent Genexus Purification System and the Genexus Integrated Sequencer – the Genexus system provides an almost completely automated workflow with as little as 20 minutes of hands-on time and results ready for analysis within one day – a far cry from the multi-day process of many other NGS workflows. This level of automation helps increase reproducibility and efficiency and reduce personnel costs. The Genexus system also avoids the challenges of cobbling together a working solution from different manufacturers; the software follows samples from beginning to end, making error detection and method control simple and intuitive.

For applications as diverse as oncology biomarker profiling, SARS-CoV-2 research assays, and inherited disease research, the Genexus system offers an easy solution. Up to four distinct assays can be combined into a single run (even with as little as one sample in the run), enabling the Genexus system to scale up or down as needed. Its GX5 gene chip can even be partially used and then finished at a later time with other samples due to its high stability.

Thermo Fisher Scientific provides ample and easily accessible support for the Genexus System, including hands-on orientation with its SmartStart program, training centers around the world, smart remote support, and field service engineers available on short notice to diagnose and repair problems. The company's consulting and qualification services also improve the chances for performing installation and qualification testing – ensuring that instruments are functioning correctly and ready to go. Similarly, Thermo's analytical validation services can accelerate the researcher's launch timetable and reduce costs by providing project management services and managing the analytical validation workflow – helping researchers to make sure their assays perform at the expected level and instruments operate within desired parameters. With all this in mind, it's clear that the Genexus System supports molecular labs in working to their fullest potential.

*Learn more at: www.oncomine.com/genexus*

**In Practice**

*Technologies and techniques*
*Quality and compliance*
*Workflow*

# Beyond the Laboratory

## How healthcare outreach is making a difference in underserved communities

*Michael Schubert interviews Mark Suhrland, Amy S. Fox, and Michele St. Louis*

An activity from the School Health Program curriculum: students learn to prepare a healthy snack with their teacher. Photo courtesy of Montefiore Health System ©Matthew Septimus Photography.

A School Health Program nurse shows students an approach to asthma self-management. Photo courtesy of Montefiore Health System ©Jason Torres Photography.

Montefiore Medical Center is located in the Bronx, which boasts 1.4 million residents – approximately one-third of whom are immigrants and nearly two-thirds of whom speak a language other than English at home. Most of this population relies on social programs such as Medicare or Medicaid to provide healthcare – and many are entirely uninsured. With such a diverse and underserved population, the providers at Montefiore and at Albert Einstein College of Medicine take it upon themselves to become a part of their community – and to give back in every possible way.

How does Montefiore reach out to underserved communities in the Bronx?

*Mark Suhrland:* When I arrived at Montefiore in 1985, they had already established an extensive network of ambulatory care practices throughout the Bronx and lower Westchester County. Now, we also have a School Health Program that offers diagnostic and preventative care to the school-age population and the free Einstein Community Health Outreach (ECHO) clinic, where Einstein medical students provide care to uninsured patients. We have sidewalk services – literally outside the hospital doors next to the bus stop – where companies offer home health care and provide information on Medicare, Medicaid, and child health plans. And, of course, we have health fairs such as See, Test, and Treat. The purpose of these offerings is to engage the public and help them discover the options and services available to them.

We are often guilty of the assumption that everybody knows about preventative health care and health maintenance – but that's not always the case, especially with a large population that may not have had access to health education.

Tell us about Montefiore's outreach programs…

*MS:* See, Test, & Treat was created by a pathologist, Gene Herbek, who examined Native American homelands throughout the United States and found little or no access to healthcare. He identified two common women's health issues that would benefit from screening – cervical lesions and breast cancer – and developed mobile units that traveled to these homelands to provide mammograms and Pap tests. Now, the program has spread to all kinds of communities with poor access to healthcare – including inner-city populations like ours.

Montefiore implemented its See, Test, & Treat program eight years ago with a great deal of support from the Department of Pathology, our chairman, and partners in obstetrics and gynecology and radiology. Our key focus was on providing not just testing, but also health education to help people understand the importance of prevention and help them gain regular access to healthcare. We offer mammograms and Pap tests. A key component in patient engagement are the pathology residents


and cytology fellows, who show patients what abnormal cervical cells look like under a microscope and discuss the role of the human papillomavirus (HPV) in cervical disease – which leads to a wider conversation about the value of HPV vaccination for patients' families, especially their children.

We never had any difficulty finding providers – everyone was eager to lend a hand. Our biggest challenges lay in finding a space large enough to run the program as it grew and in encouraging patients to stay and wait for their results. Everyone is busy and some want to leave right after undergoing the test – so it can be a challenge to engage them and make healthcare screening and prevention "real" enough to motivate them to remain, learn a little more, and receive their results.

*Michele St. Louis:* David Appel created the Montefiore School Health Program to provide comprehensive healthcare – that is, medical, dental, mental health, and now even vision – to as many students in the Bronx as we could. Over the years, our reputation has grown to the point where people reach out to ask us, "Can you open a health center in our school?" Now, the program – led by Rosy Chhabra – is the largest of its kind in the nation, with 32 sites throughout the Bronx and Yonkers serving all age groups.

*Amy Fox:* When times get tough financially, it's typically these kinds of programs that are cut first – but I would say that the School Health Program at Montefiore is untouchable due to its vital mission. The Department of Pathology is privileged and honored to partner with the program and provide on-site laboratory services for the students. For us, it's all about the children. These are children whose parents can't take time off from work to take them for vaccinations or eye appointments – and who often don't even know how to navigate our complex healthcare system. Imagine how much those children benefit from having it all right there at school!

There's something important about knowing that, at the end of the day, you've made a difference in a child's life. That's why we fight to get the services that Michele needs – and that's why my extraordinary team is there and dedicated to helping. That's why, even when the pandemic closed schools, Montefiore leadership kept as many of our centers as possible open to continue providing care (and COVID-19 testing).

How do you publicize your programs?

*MS:* We have a Facebook page and a Twitter account where we advertise See, Test, & Treat events – but we also try to get out into the community in person. We talk to store owners, put up posters, and advertise in local newspapers and television channels, because we know that not everyone is on social media. We promote the event at the ECHO clinic, reach out to their family and friends, and invite other health and outreach organizations to help us spread the word as well.

We also connect with religious organizations in the community. One of the major lessons we've learned since launching the program is that it's important to be diverse and creative in our outreach. Think about the community infrastructure that already exists – for instance, churches. If we talk to a few


See, Test, & Treat, a community outreach program spearheaded annually by the Montefiore Einstein Department of Pathology in the Bronx, New York, offers free breast and cervical cancer screenings, same-day results, and follow-up care to women with limited or no health insurance. At the double-headed microscope, pathology trainees invite attendees awaiting test results to join them in viewing Pap specimens. Trainees practice their communication skills with real patients, explaining the science behind the screenings as well as the pathologist's role in patient care. Attendees can also pick up patient education pamphlets about the HPV vaccine produced by Mark Suhrland, Cytopathology Division Chief, with a grant from the College of American Pathologists Foundation.

people at a church and put a poster up in the foyer, we gain an automatic level of trust within that church community – and people talk to each other and support each other in attending. Another great example is local politicians; we reach out to them and provide posters and, as soon as they promote the event to their constituents, it gains another layer of trust – and we gain another opportunity to provide preventative care where it's most needed.

Why do you think it's important to reach out to underserved communities?

*MS:* Many people in those communities don't fully understand the importance of screening and prevention – but, if we can detect potential issues before they become major problems, we can save both costs and lives. Hospitals, clinics, insurance – all of this can be quite daunting to people who aren't well-versed in how the system works. Often, people give up before they even start. We try to simplify things so that patients can just walk in, be entered into the system, and be given a healthcare provider who stays in touch with them to support their health education and maintenance. We model this during our See, Test, & Treat events; each participant has a volunteer "health navigator" who takes them from one station to the next and explains each one to demystify the process. The more comfortable patients become with the system, the more likely they are to

Pathology department volunteers Frances Mendez, Fellowship Administrator (left), and Dolis Ruiz, Quality Management Systems Supervisor (right), checking patients in at the reception desk. Both volunteers are bilingual in English and Spanish.

continue receiving preventative care.

At the most recent See, Test, & Treat event, we had a 50-year-old patient come in for her first-ever mammogram and Pap test. We discovered both breast cancer (ductal carcinoma in situ) and a squamous cervical lesion – allowing us to offer treatment, monitoring, and follow-up care. To some, the number of patients we see at these events may seem modest – but, if we identify even one patient who needs our help, the event has done its job. In fact, at our 2021 event, 29 percent of patients had abnormal Pap smears – a significant proportion.

Unfortunately, the pandemic forced us to suspend the event in 2020. Although See, Test, & Treat did return in 2021, patients were reluctant to attend due to anxiety over COVID-19 – even though we had strict safety guidelines (masks, temperature screening, social distancing) and an infectious disease specialist on site to ensure that we were operating as safely as possible. Our attendance level was much lower than in previous years. That's a challenge we currently face across the healthcare system; patients are reluctant to seek medical care because they fear exposure to COVID-19. In fact, four patients who registered for the 2021 event didn't show up – so we weren't able to offer them the care they may need.

*MSL:* The people in these underserved communities are struggling; they depend on us. We felt an obligation to use the

School Health Program to help them understand and navigate the pandemic. We created a new set of questions for telehealth visits: How are you managing during COVID-19? How are you feeling? Have you had any losses? Do you need any concrete services? Have you lost your job? Do you have a place to live?

They might seem like odd or extreme questions, but these were the problems our community members were facing – and we had to be there for them. Thankfully, we also offer mental health services! We're very excited to have our students back in school, though, because now we can catch up on needs that we would normally have spotted earlier, but didn't, because we weren't seeing the kids every day during lockdown.

### What happens in communities that don't have this kind of outreach?

*MSL:* For many people, we were their only health care option – their neighborhood health centers were either closed or inaccessible to them for socioeconomic reasons. In communities without services like ours, people's medical needs are often neglected. That can end up costing them their jobs, their families, or even their lives.

*AF:* There's also a level of comfort involved in going to a familiar place for care. Children have to feel comfortable talking to their physician and it can take a long time to build that level of trust. If you overlay an unfamiliar healthcare provider onto the existing fear and instability of a pandemic, the stress can become unbearable – especially in an emergency – and people may go without medical care entirely.

### What challenges do you face in administering community outreach programs?

*AF:* Funding is the biggest challenge. An initiative like this requires a lot of staff and supplies – and, although we do bill patients who have insurance for services, we never deny care to patients who can't pay. That means we have to make up the shortfall somewhere. We have some private and some public funding but, even so, it's a challenge to keep the service staffed and running.

People are always surprised when they come into the school because they're expecting to find a school nurse. Instead, they find receptionists, licensed practical nurses who prep patients, providers who take care of them, mental health providers, dentists, optometrists, and community health organizers to help us ensure that we're meeting the needs of the entire school community. Keeping that large team in place is a challenge, but it's vital to doing the work our community needs.

### How can other institutions follow in your footsteps?

*MS:* Build a presence in the community. Reach out in different ways to give yourself the best chance of being heard by your target populations. Communicate in different languages; partner with community organizations; and, most importantly, be proactive.

The See, Test, & Treat program is fantastic and I strongly recommend it to anyone who is considering community outreach. The College of American Pathologists oversees the program and offers tremendous resources and support; for example, they hold regular conferences and Zoom calls where people share information about what has and hasn't worked for them. Different strategies work in different locations and populations – and, once you join a program like See, Test, & Treat, you not only gain access to all the information that has been gathered so far, but also get help with customizing it to your particular setting.

*MSL:* Make partnerships. You need a champion who knows how important these services are and will push to get the services, funding, and support you need. And it does require fighting for until you're established and the positive change you're making becomes obvious. That's when things flip – suddenly, people are coming to you to grow the program.

*AF:* Open your eyes and look around you to see where help is needed. And remember that no one person does this themselves. I wouldn't put the burden of this solely on a healthcare institution that happens to be in an underserved community. It's a three-way partnership; you need buy-in from your leadership, relevant NGOs, and industry. (Sometimes it's a four-way partnership that involves government as well.) Don't leave anyone behind when you implement a culture change.

*MSL:* The most important thing is to be curious about your community. What do they need and how can you provide it? Montefiore's situation is not unique – even affluent communities have pockets of extreme need. I guarantee that, if you look for ways to offer help and bring about change, you will find them!

*Mark Suhrland is Professor of Pathology at Albert Einstein College of Medicine and Chief of the Cytology Section, Montefiore Einstein Department of Pathology, Montefiore Health System, Bronx, New York, USA.*

*Michele St. Louis is Clinical Assistant Professor of Family Medicine at Albert Einstein College of Medicine, Medical Director of the Montefiore School Health Program, Montefiore Medical Group, Montefiore Health System, Bronx, New York, USA.*

*Amy Fox is Professor of Pathology and of Pediatrics at Albert Einstein College of Medicine; Chief of Point of Care Testing and Outreach Laboratories and Vice Chair for Clinical Research and Faculty Development at Montefiore Einstein Department of Pathology, Montefiore Health System, Bronx, New York, USA.*

NextGen

*Research advances*
*New technologies*
*Future practice*

# Future Forward

## How Montefiore's ground-breaking Pathology Residency Program is setting up residents for success in the 21st century healthcare team

*By Tiffany Hébert, Adam Cole, and Bryan Harmon*

As an institution, Montefiore Einstein dates back over 125 years ago, when it was established to care for patients with debilitating and chronic illnesses. Montefiore has always greatly valued medical education and has trained many generations of physicians across all specialties. And that vision became even stronger when the Albert Einstein College of Medicine became a part of the Montefiore Health System.

Given the constant focus on medical education, we were inspired to revamp the curriculum of our Pathology Residents Program as part of our strategic planning. We had been aware for some time of the looming retirement cliff and, therefore, a potential pathology labor shortage – a problem that may have been accelerated by the pandemic. Despite those pressures, pathology training has lengthened over the years, starting paradoxically with the shift from a 5-year to a 4-year residency training program. Since that shift, we have noticed increasing numbers of residents feel the need to complete one or two fellowships to be marketable in the employment arena. Such delays affect people's futures – their ability to save for retirement, start a family, and establish themselves professionally. When redesigning our residency program, we were keen to see if there was a way to tailor training in such a way that people would feel more comfortable and confident seeking a job afterwards.

We also knew we needed a program that would address the ever-evolving professional role of the pathologist. Teamwork has always been paramount; however, the teams have diversified to include many allied health professionals and advanced practice providers. Moreover, there is a renewed focus on quality over quantity of care. We wanted to make sure our residents had the requisite adaptability to work within emerging health systems, with an eye toward patient safety and quality management. Finally, we wanted the Pathology Residency Program to reflect Montefiore's core values: humanity, innovation, teamwork, diversity, and equity.

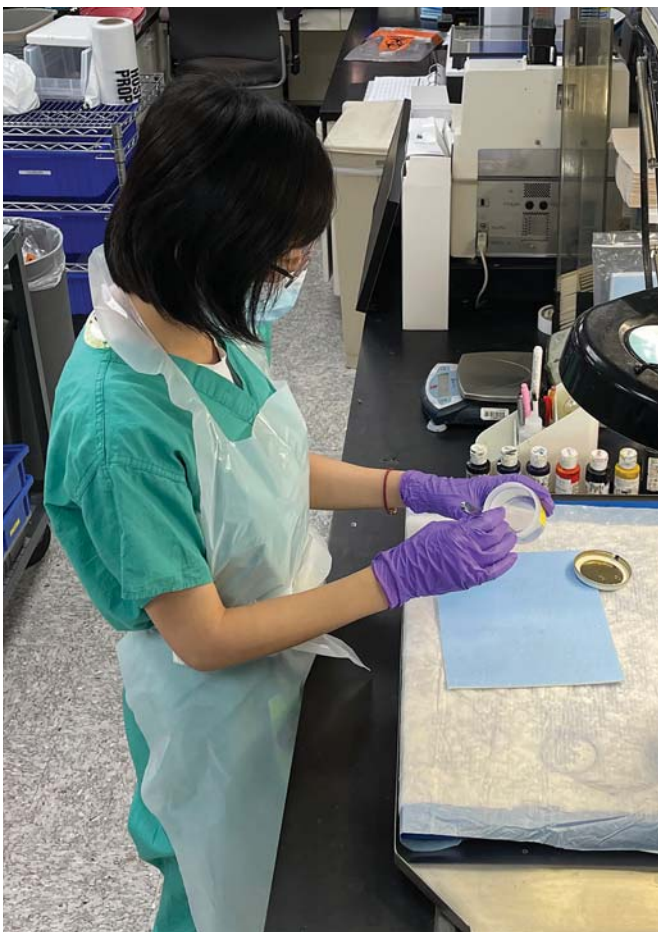
### The program in a nutshell

The redesigned program is divided into three main phases. There is a two-year foundation phase, during which residents cover core anatomic and clinical pathology rotations, and are exposed to (and involved in) lab management and clinical consultative experience. Rather than simply teaching our trainees how to recognize patterns, we instill process-oriented learning – the process in working up a case that leads to a diagnosis. This foundation prepares residents to excel in the academic environment, community hospital setting, or commercial laboratory. Over the course of the program, a wide variety of regularly scheduled teaching conferences are conducted in various subspecialties of pathology and other relevant clinical departments. And trainees also participate in dedicated daily didactic time.

The two foundation years are followed by the one-year integrative (or hybrid) phase, where residents return to some clinical pathology rotations while embedded within the clinical team in a consultative role. The hybrid rotations encompass endocrine pathology, infectious disease pathology, transplant pathology, and hematology clinical consultation – spending time in both laboratory and clinical settings that are complementary to one another. Modern medicine is (or should be) a very collaborative process, and though pathologists are, of course, diagnosticians, we feel they should be equally good communicators. And so, through this hybrid phase, our residents not only gain a deeper insight into how

Philip Gialanella, Manager of the Clinical Microbiology Laboratory, mentoring two pathology residents.

Wendy Szymczak, Director of Clinical Microbiology, shows resident Raquel Yokoda a COVID-19-positive PCR test curve read by the Cepheid machine during their validation study of the test in stool.



Jiani Chai, Pathology Resident PGY-2, in the cutting room.

## Diverse opportunities

On top of the unique structure of the curriculum, the racially, ethnically, and culturally diverse patient population sets Montefiore's Pathology Residency Program apart from others. The Bronx is home to over 1.4 million individuals – and when you walk around the hospital or down the surrounding streets, you pass people who come from all over the world and from all sorts of different backgrounds. With such a large and diverse population, residents training at Montefiore get to learn firsthand about a staggeringly wide variety of diseases. Pathogens – such as malaria – that may be quite uncommon in other US training programs are all but guaranteed to be seen by our residents throughout their training at Montefiore.

The Bronx is also one of the most underserved counties in the country; many of our patients come to us without a history of regular and easy access to appropriate medical care. As a result, many present with advanced and complicated pathologies that provide a unique challenge and educational opportunity for our trainees. One example of how our residents – and the whole department – are committed to the Bronx community is the "See, Test, and Treat" program (see page 42) which is a community outreach event that offers uninsured and underinsured women in the Bronx free breast and cervical cancer screenings, rapid results, and free follow-up care, if needed.

laboratory science impacts patient care, but also foster essential communication skills to support genuine collaboration with their clinical colleagues. Residents will round on patients with the clinical teams, serve as a liaison to the clinical laboratories, help guide test selection and present results back to the teams, follow the cases where they lead, and explore additional subspecialties.

Finally, to address the fact that so many residents feel the need to complete numerous fellowships before moving into an attending role, we recalibrated our rotation schedule to allow for a longer-term focused fourth-year elective. The elective is used as a period of prolonged and intensive immersion in an area where the resident is likely to pursue a career – mastering skills and functioning at a higher level with graduated responsibility and scholarly activity. As a kind of "mini-fellowship" built into the residency, it helps prepare our residents to make a successful transition to becoming an attending physician.

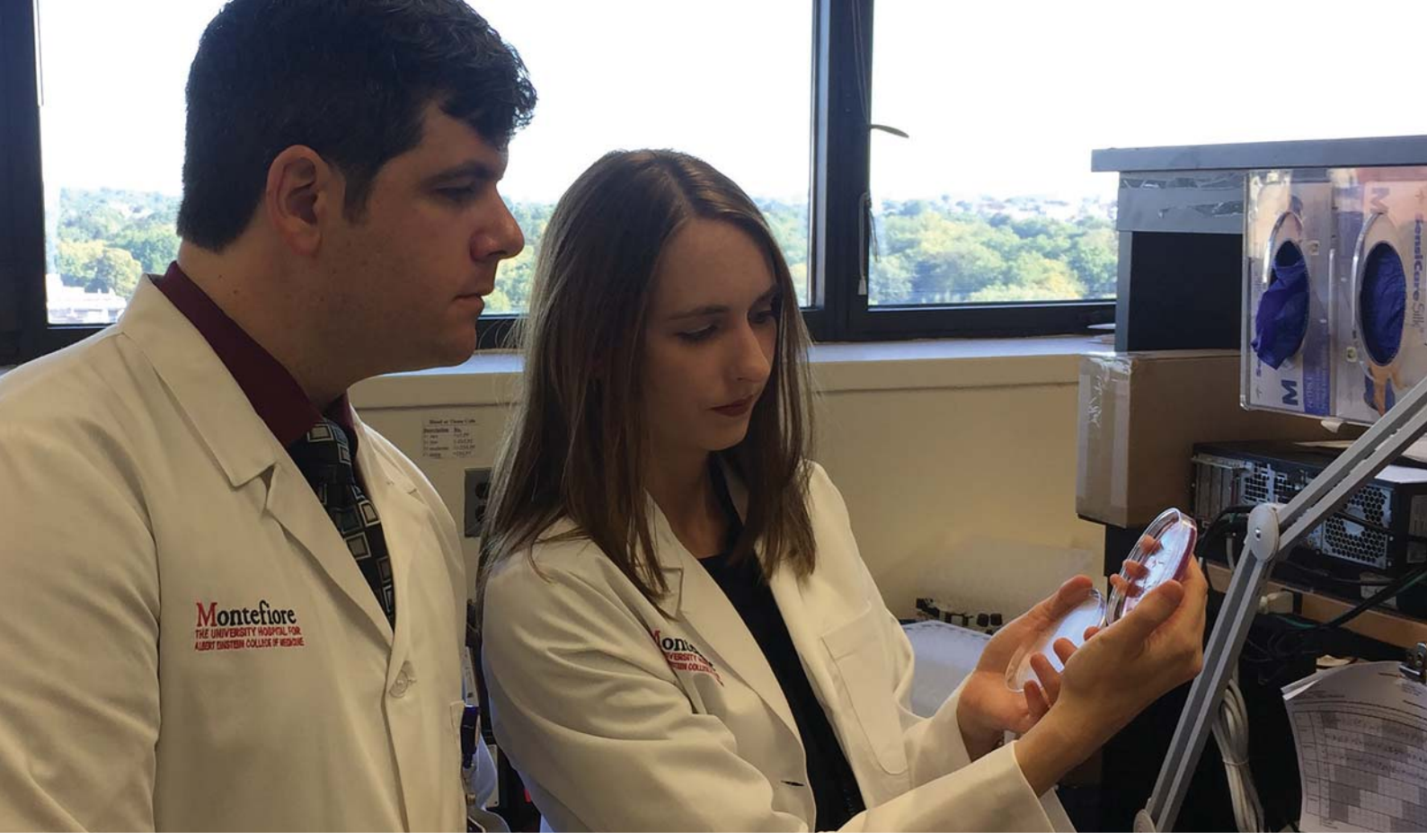
### Making the transition

Whenever significant change is required (or simply attempted), the most difficult task is usually generating buy-in from all stakeholders; fortunately, we were blessed with strong support from our chair and other administrators. When we identified the changes we wanted to make, we reached out to rotation heads and residents to seek their feedback and expertise to vet the project – this collaborative approach was key to later success. We also needed a complete shift in mindset – away from time spent on a rotation and toward looking at what constitutes acquisition of competency for a given rotation. In particular, we had to consider what experiences needed to be available for residents to attain those skills; for example, can they serve in a consultative capacity to endocrinology on the most appropriate tests to use in the workup of a patient?

### No wrong turns on the path to pathology

There is no one "right" path to pathology – we have seen people in our residency program take many roads to get here, illustrating that anyone can find their way to the field. Some have even had full-blown careers in other sectors before even turning to medicine. One particularly interesting example from the past few years is Angela Baldwin, who was a navy flight surgeon prior to joining our residency program! During her time in our program, she also did some journalistic work in television as a contributor to the ABC News Medical Unit, and is now completing her forensic pathology training at the New York City Office of Chief Medical Examiner.

Once in medicine, we have had people come over from other specialties and prior clinical careers before realizing their true calling was pathology, particularly international medical graduates who face significant hurdles to complete graduate medical education in the US. Having observed candidates take many different routes, we can confidently say you are never too old to do what you really want to do! Varied experiences color what a person brings to pathology, making the field all the more exciting.




In the clinical microbiology lab: Wendy Szymczak with pathology resident Greg Dickinson.

Why Montefiore? Beyond the unique program in a diverse setting, Montefiore cultivates a very nurturing environment; indeed, it is our great strength. As well as being supportive, our culture is very collegial, kind, and generous – and we look for candidates who reflect our own values.

Fortunately, we receive hundreds of impressive applications to our residency program each year so we can afford to be picky! Those individuals who are offered an interview are guaranteed to be bright and accomplished; beyond that, we are looking for team players, empathic individuals, and motivated candidates who are committed to their professional development and to serving our diverse community. On top of that, we also value curiosity. Pathology is a broad field, and so those candidates who have an open mind and a thirst to learn new things find their way to the top of the list.

Certainly, we're looking for the best candidates, but it's a two-way street – and so we know we must offer the best in return! Our program delivers a wonderful overall training experience and the opportunity to serve a community that desperately needs our services, while maintaining a collegial work environment and family-friendly atmosphere. There are many fine training programs out there and, although candidates need to figure out which programs will put them in the best position to reach their professional goals, they should strongly consider which program feels like the "best fit" for them on a personal level.

If you are looking for a program that values interdisciplinary patient care, a focus on providing opportunities for residents to pursue their interests, and a culture of compassion and support, then Montefiore is the right place for you. Our advice for getting a place? Take an elective in pathology – the field is vast and what you learn in your typical, basic sciences pathology courses often does not reflect the reality of life as a practicing pathologist devoted to patient care. Once we look beyond the numerical metrics of a candidate, the single most important criterion is the person's passion for and understanding of what it means to be a pathologist. This may well be your career for the rest of your life, and we want it to be something that you feel will bring you happiness. So, explore your scientific curiosity, get involved in research projects that interest you, and continue to contribute and be of service to your community.

*Tiffany Hébert is a pathologist and Director of the Pathology Residency Program at Montefiore Medical Center, and Associate Professor of Pathology at Albert Einstein College of Medicine, Bronx, New York, USA.*

*Adam Cole is a pathologist and Associate Director for Clinical Pathology of the Pathology Residency Program at Montefiore Medical Center, Bronx, New York, USA.*

*Bryan Harmon is a pathologist and Associate Director for Anatomic Pathology of the Pathology Residency Program at Montefiore Medical Center, Bronx, New York, USA.*

*See references online at: tp.txp.to/prep-pf*

**Profession**

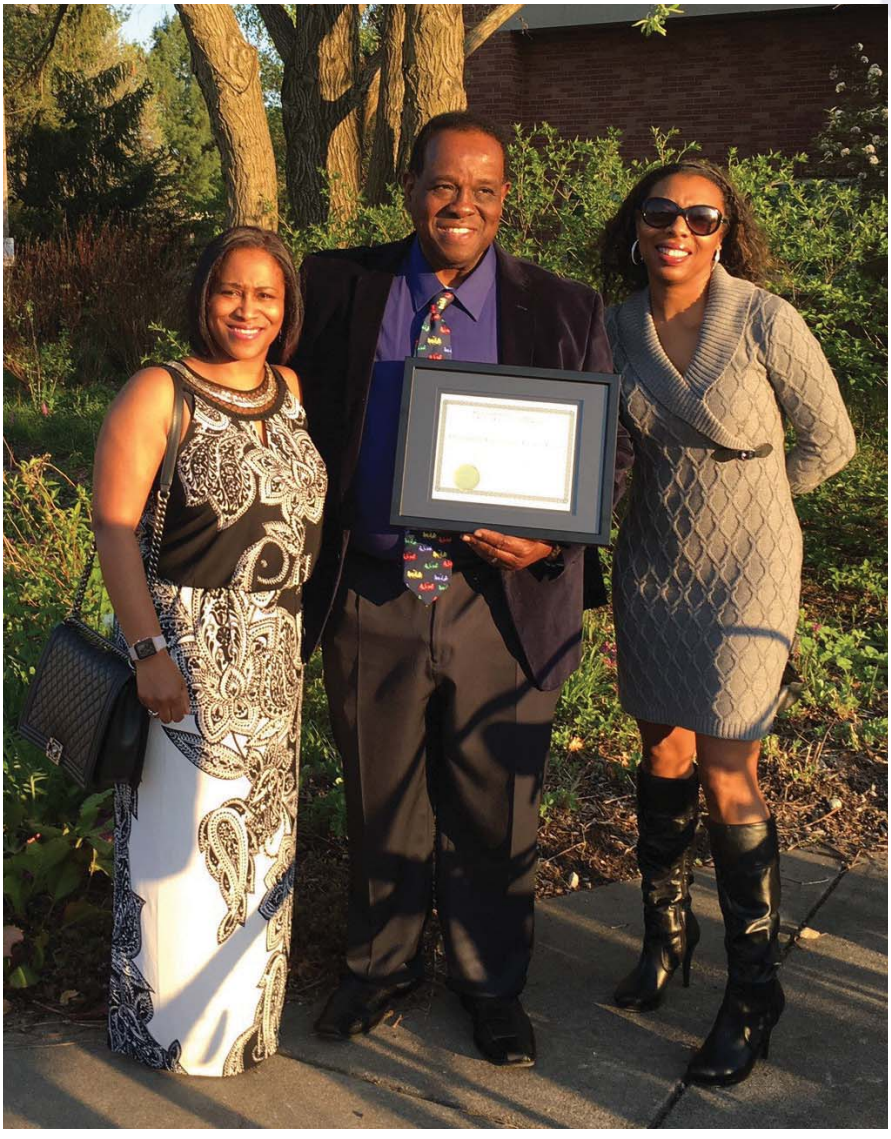
*Your career*
*Your business*
*Your life*

# Like Father, Like Daughter

## Two generations of physicians discuss their work, careers, and lessons learned

*Tiffany Hébert and John Hébert, III, in conversation*

Medicine is often a family affair – and that's certainly true in the Hébert family, where John Hébert, recently retired from an over-30-year career in obstetrics and gynecology, passed his scientific and medical instincts down to daughter Tiffany Hébert, now a pathologist, pathology residency program director, and an associate professor of pathology at Montefiore-Einstein. To find out more about how a dedication to patient care runs in the family, these two expert physicians interviewed one another about their lives and the lessons learned over their careers in medicine.



John Hébert, recipient of the Michigan State University College of Human Medicine's Outstanding Community Faculty Award, with daughters Tiffany Hébert (left) and Nicole Graham.

*Tiffany Hébert*: What made you want to become a physician?

*John Hébert:* I grew up in Albuquerque, New Mexico, and didn't have a lot of role models. But I do recall two interactions with physicians. When I was in the ninth grade, my mother had some complications with her last pregnancy and ended up having a cesarean section. The doctor who performed it was the first African American physician I had ever seen – and I never forgot that he successfully took care of my mother and delivered my youngest brother. We also had a family practitioner who encouraged me to pursue a career in medicine. In fact, when I went to medical school, my first elective

encounter was back in Albuquerque with that same practitioner. I think those are the things that cemented my desire to become a physician and an obstetrician in particular.

*JH*: Tiffany, what inspired you to become a pathologist?

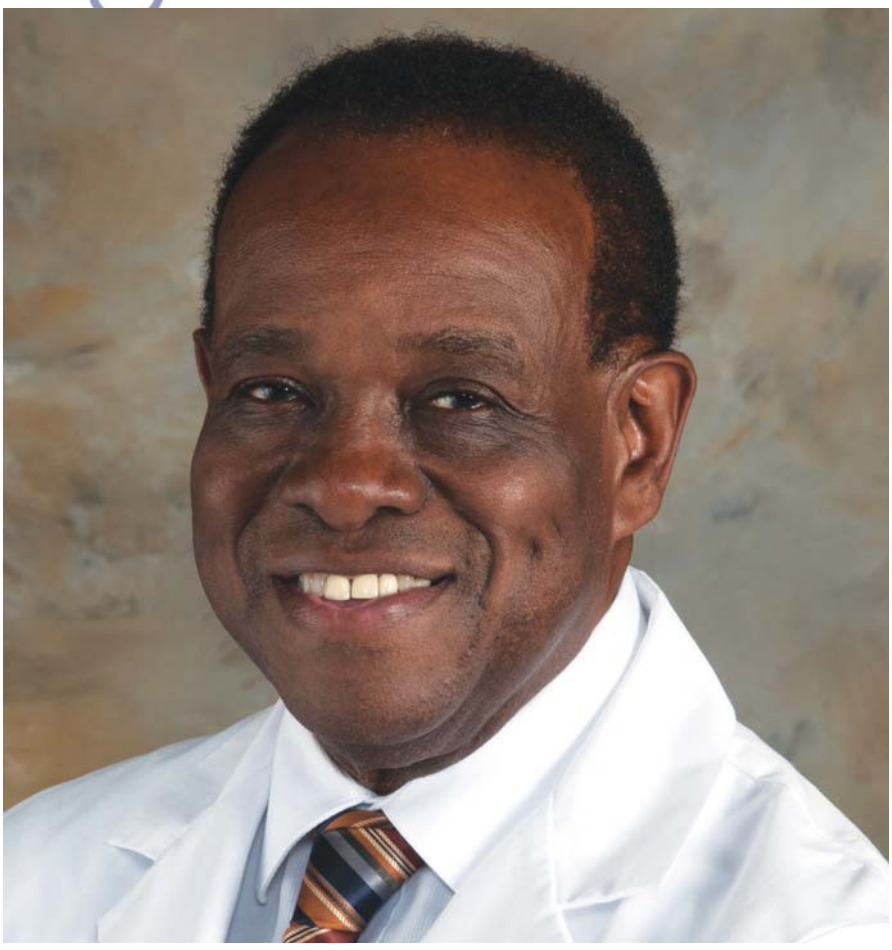
*TH:* My decision to pursue pathology came a lot later than your decision to become a physician. I went into medical school thinking I was going to be an OB/GYN just like you. I enjoyed my OB/GYN rotation, but I enjoyed learning about pathology and histology even more. From the first-year histology course, I remember looking at the tissues under the slide and thinking, "I can actually recognize these things really quickly and easily. I could be good at this."

I remember you let me borrow a microscope from your office so that I could look at slides on my own. I was really attracted to having the final answer – the knowledge that would guide the patient's treatment. I was more interested in seeing a tumor than in removing it.

*TH*: What inspired you to dedicate your career to serving the underserved?

*JH*: I came from a large family – 10 children in total. Growing up, we were not well off and we took advantage of assistance programs in our community, which really helped us succeed. I'm proud to note that all 10 of us are college graduates – but that wouldn't have happened without community involvement and other people taking an interest in us. So when I had an opportunity to pay it forward, it came naturally to me.

As a medical student, I started volunteering in areas where students could assist – evaluating children, physical examinations, and so on. Eventually, it moved beyond medicine into community outreach and other areas such as the Urban League and the Rotary Club. It gave me a good feeling to know that I was in a position to make life better for other people who were less advantaged.



John Hébert, III. Photo by Doug Pike. Reprinted with permission from Hurley Medical Center, Flint, Michigan.

*JH*: Although you're a pathologist and I'm an OB/GYN, what lessons did you learn from my career?

*TH*: You left some pretty enormous shoes to fill! I think the most important thing I learned from you is work ethic and the importance of sacrifice. I grew up watching you prepare lectures, put together content for your students, and host informal get-togethers – so I saw the camaraderie between you and your residents. I try to model things like that because I've learned from you that you can't halfway do medicine. It's not so much a career as it is a calling – so it's not enough to just go to work and do your job. You have to ask yourself, "How am I contributing to my community and the rest of the world?"

*JH:* As director of Montefiore's pathology residency program and a graduate of the program yourself, how important was it to you that the program worked with underserved communities?

*TH:* Many of the things that excite me about being here remind me of things I saw with you when I was growing up. I remember going with you to volunteer at the Adolescent Health Center at the high school next door to mine. That made a big impression on me.

A lot of people think of pathology

Tiffany Hébert. Photo courtesy of Montefiore Einstein.

as a basic sciences or as "just looking at slides" – but our department is very involved in the Bronx community. We have point-of-care testing in schools, which reminds me of your work in providing off-site community care. We run a See, Test, & Treat program to screen underserved populations for breast and cervical cancer – along with basic health education provided by our residents. That's important because in pathology, you sometimes feel divorced from that patient context – but we all went into medicine because we wanted to help people, so I see this as a great opportunity for us all to have direct contact with the people who need us most and to be a real part of our Bronx community.

*TH:* When you first started, did you set yourself any goals? And, looking back, how many did you achieve?

*JH:* When I first started to do community outreach, my goal was simple – to make a difference in people's lives. You mentioned the the Adolescent Health Center; my goal there was twofold: to provide optimal prenatal care in teen pregnancies and to try and make sure that that adolescents had access to appropriate contraception in the future. We know that, once a teenager has a baby, they're far less likely to continue their education. And, in many cases, the teens we saw at the Adolescent Health Center had become pregnant before they had access to contraception. So, after ensuring that both mom and baby were healthy, we tried to make it possible for the mom to complete her education.

My goal was always to have an impact. I never joined an organization just to pad my résumé. I found that the best way to have an impact was to assume a leadership position so that I was actively involved in policy and effecting change. My wife – your mom – would often tease me by saying that, every organization that I joined, I had to become president. That's not because I wanted the title, but because I thought I could – and still can – have the most impact by taking a leadership role.

*JH:* What brings you the most pleasure in your work?

*TH:* Two things. The first is that I love biology. I enjoy the patient care aspect of my job, the intellectual stimulation of

challenging cases, and the knowledge that the right answer will guide my patient's care. The second is the teaching. I love interacting with young people who are fresh and full of potential. It's wonderful to share knowledge with them, see the lights go on in their heads, and learn from them. And, of course, I love seeing amazing things under my microscope every day.

*TH:* What do you consider to be your greatest achievement to date?

*JH:* I think my greatest achievement is the success of my graduates. I was a residency program director (as you are now) for 25 years. My graduates practice all over the country; some have gone on to subspecialty fellowships, whereas others now teach at major universities. In 17 of the past 20 years, we had a 100 percent pass rate for board examinations. That's what I consider my greatest achievement.

I think it's important to teach the next generation of physicians without compromising clinical care for the patients you serve. Many physicians are excellent clinicians, but have little interest in teaching, or vice versa. I think you have to balance quality education with optimal patient care.

*JH:* What lessons have you learned from your own career – and are they different to what you learned by observing my career?

*TH:* I learned a lot about teaching. Nothing in medical education teaches you how to teach! Watching you teach made it seem easy because you're a natural teacher. It wasn't so easy for me when I started, because I didn't have a very good skill base; my classes were one long PowerPoint slide after another. I like to think I've improved on that!

I also think medicine has changed over the years. It has become more family-friendly and welcoming to women than it was when you first started. We understand that sacrifices are necessary, but we also understand the value of balance and of maintaining our own wellbeing. I've learned a lot from my residents, because they're from a different generation. At first, there's that knee-jerk reaction, because it's not what you're used to – but then you think to yourself, "Maybe they're right and the way we did things was wrong." And look how much happier they are! So I've tried to keep an open mind and learn as much from them as I have from you.

*TH:* What are the most important lessons you've learned over your career – and what legacy would you like to leave behind?

*JH:* The most important lesson I have learned is that it's essential for physicians to take an active role in training the next generation. We all started on day one with a baseline of zero medical knowledge. To become proficient in your specialty of choice, you have to be educated – and that entails more than just reading a textbook. The clinician who is most well-rounded is the one who recognizes the importance of combining quality teaching with quality clinical care. Admittedly, it takes a little longer; at three o'clock in the morning, when I'm closing an abdomen with a second-year resident, I could get home a lot faster if I did it myself – but that resident would lose a valuable learning opportunity.

As far as my legacy is concerned, I think my graduates speak for themselves. I'm also proud of the fact that the institution from which I just retired recognized my contributions to student and resident education by naming a unit in the hospital after me. There's no greater legacy than that!

*JH:* What advice would you give to incoming pathology residents who want to follow in your footsteps?

*TH:* Remember that you are part of a healthcare team – and that you must interact with that team to have a positive impact on your patient. How? One way is to get involved in tumor boards and become a consultant to the clinicians you work with. Another is to attend conferences together. Remember when you and I went to the American Society of Colposcopy and Cervical Pathology meeting together? I think it's really important to go to the clinical counterparts of our pathology meetings, so that we know what's happening on the other side of the coin. When I was very young, I'd sign something out and not think twice about it. Then I went to a tumor board and they decided what was going to happen based on the pathology report. I was stunned. I had never been fully aware of what my work meant to the patients until that moment.

Take advantage of opportunities to get involved with medical education on a national level. One of the most important activities I've participated in is the Association of Pathology Chairs' National Program Directors' Committee. Getting involved with peers, hearing the wonderful things they're doing, participating in faculty development… all of those things will make you a better teacher.

Keep an open mind. Listen to and accept constructive feedback – because you'll always learn from it. Even if you don't completely agree with it, you may find a kernel of truth in it.

*JH*: I agree with that. I always told my residents, "You can always learn from any attending you work with – even if it's what not to do." Never stop learning.

*John Hébert, III, is an obstetrician/gynecologist and Residency Program Director, Obstetrics and Gynecology, Hurley Medical Center, Flint, Michigan, and Associate Professor of Obstetrics and Gynecology, Michigan State University College of Human Medicine, East Lansing, Michigan, USA.*

*Tiffany Hébert is a pathologist and Residency Program Director, Anatomic and Clinical Pathology, at Montefiore Medical Center and Associate Professor of Pathology at Albert Einstein College of Medicine, Bronx, New York, USA.*

MEMBERSHIP 2022

# UNITED COMMUNITY MAKING AN IMPACT

It all starts with you. You perform the crucial tests and analyses needed to inform patient care and treatment, directly impacting the lives of countless people every day.

**This impact is amplified when we all come together**— To share our experiences and knowledge so we continue to advance together; to recognize the important work of our colleagues; and to make our voices heard as one to drive positive change for our profession and for the patients we serve.

Together we create the education needed to keep you at the top of your game. Together, we work to address disparities in healthcare and drive public policy. Together, we connect with each other to encourage personal and professional growth. **We can't do it without you.** The entirety of the lab community needs to come together to improve patient care.

Renew your membership today to continue to share your voice to this powerful community!

**www.ascp.org/renew**

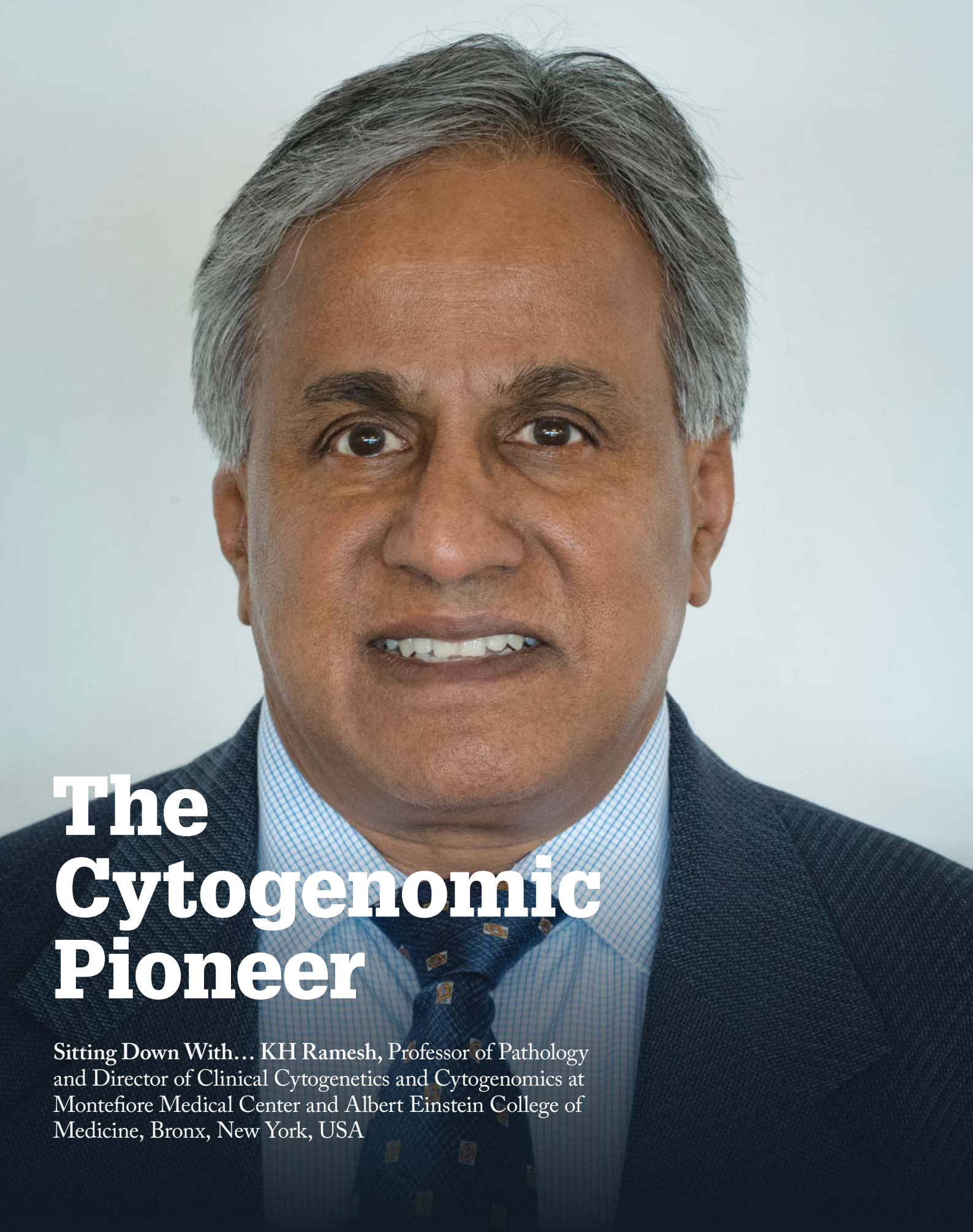
ASCP **STRONGER**TOGETHER

# *Spotlight on...* Technology

## LX500ec prints on-demand full-color or monochrome medical labels

LX500ec is a compact color label printer designed for use in labs and other medical environments. It produces specimen labels, name badges, wristbands, and other narrow-format outputs, including many waterproof substrates. With a high print resolution, it prints razor-sharp text, graphics, photos, color alerts, and logos along with 2D barcodes.

*pt.dtm-medical.eu*



# The Cytogenomic Pioneer

**Sitting Down With… KH Ramesh,** Professor of Pathology and Director of Clinical Cytogenetics and Cytogenomics at Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, New York, USA

Tell us about your roundabout journey to pathology…

When I was young, my passion was to be a physician – but I did not have the grades to get into a government-run medical college in India. Unsure that my parents could afford to send me to a private medical school, I thought I might try to get into one through a sports scholarship – but there were so few spots available in that category and so many candidates who had achieved a lot more in sports than I had that this approach unfortunately did not succeed.

So I made a different, but still related choice: to study a subject that would put me in the medical field. Via the sports scholarship route, I got into a master's program in biology, majoring in genetics, then landed a research assistant job in the Department of Pathology at a prestigious academic hospital and cancer institute in Bangalore. After two years in that job, I moved heaven and earth to convince Krishna Bhargava, the chair of pathology and also the director of the cancer center, to allow me to register for a doctoral degree in genetics at Bangalore University without giving up my job.

How did your interest in cancer cytogenetics and cytogenomics begin?

My interest began during my PhD, which focused on the effects of ionizing radiation on human chromosomes in cancer patients receiving radiation therapy. Krishna Bhargava (now my advisor) worked late and so did I, because he had warned me not to do any research during my normal working hours. Some evenings, he called me to transcribe his pathology reports as he looked at the most difficult cases under the microscope. I had no knowledge of pathology but, every now and then, he showed me interesting histological patterns and pointed out abnormal cells that confirmed his diagnosis. I often remember the time he showed me Reed-Sternberg cells (owl's-eye appearance) characteristic of Hodgkin lymphoma and, just to make sure, asked me to draw what I had seen under the microscope! I started to put things together and dug deeper to understand the changes that occurred at the cellular and gene level to turn normal tissue into cancer.

You've worked across countries – sometimes even at the same time. What are the key similarities and differences between pathology in India and in the United States?

I can only speak to what I remember from when I left India some 35 years ago. I think the key difference is the lack of resources in India compared to where I am now (although it might not be so bad at present; I believe India is catching up). The key similarity I see is the people – the same intelligence and enthusiasm exists in both countries. By sharing knowledge and breaking down international barriers, we have greatly advanced the development of new and innovative tests in India, which has ultimately led to better patient care than when I left. I think the future looks bright in both places.

What was the proudest moment of your career?

Defending my PhD thesis successfully in Bangalore. I moved to the US while writing my thesis – against the advice of my mentor, who repeatedly warned me that it would be best to finish before going abroad. I insisted and fought for his, and the state government's, permission. I have always been a risk-taker and did not want to miss the opportunity to work under the late Avery Sandberg, a world-renowned geneticist. I did not realize how daunting it would be to adjust, work on the project, and write the thesis all at once. A few months became a year and a half – but I ultimately succeeded! Looking back, having a doctoral degree opened many doors for me and made many achievements possible.

You are often in close contact with clinicians. What have you learned from them – and what do you hope they can learn from you?

I have always believed that learning is a two-way street. I try to learn from everyone – even the high school students who do summer internships in my lab. From the clinicians and medical residents, I work with, I try my best to absorb all of the clinical knowledge I lack. In return, I hope that my clinical colleagues gain a better understanding of the genetics behind the disease from my interpretations of test results – and from the conversations that we have when they don't understand the genetic basis of the established diagnosis.

I believe that all healthcare professionals must try to gain as much understanding as possible of the genetic and molecular aspects of any disease – most importantly at the level of the tissue and the cell. Many diagnoses – and nowadays even treatments – are based on the genetic diagnosis of a given tumor or disease.

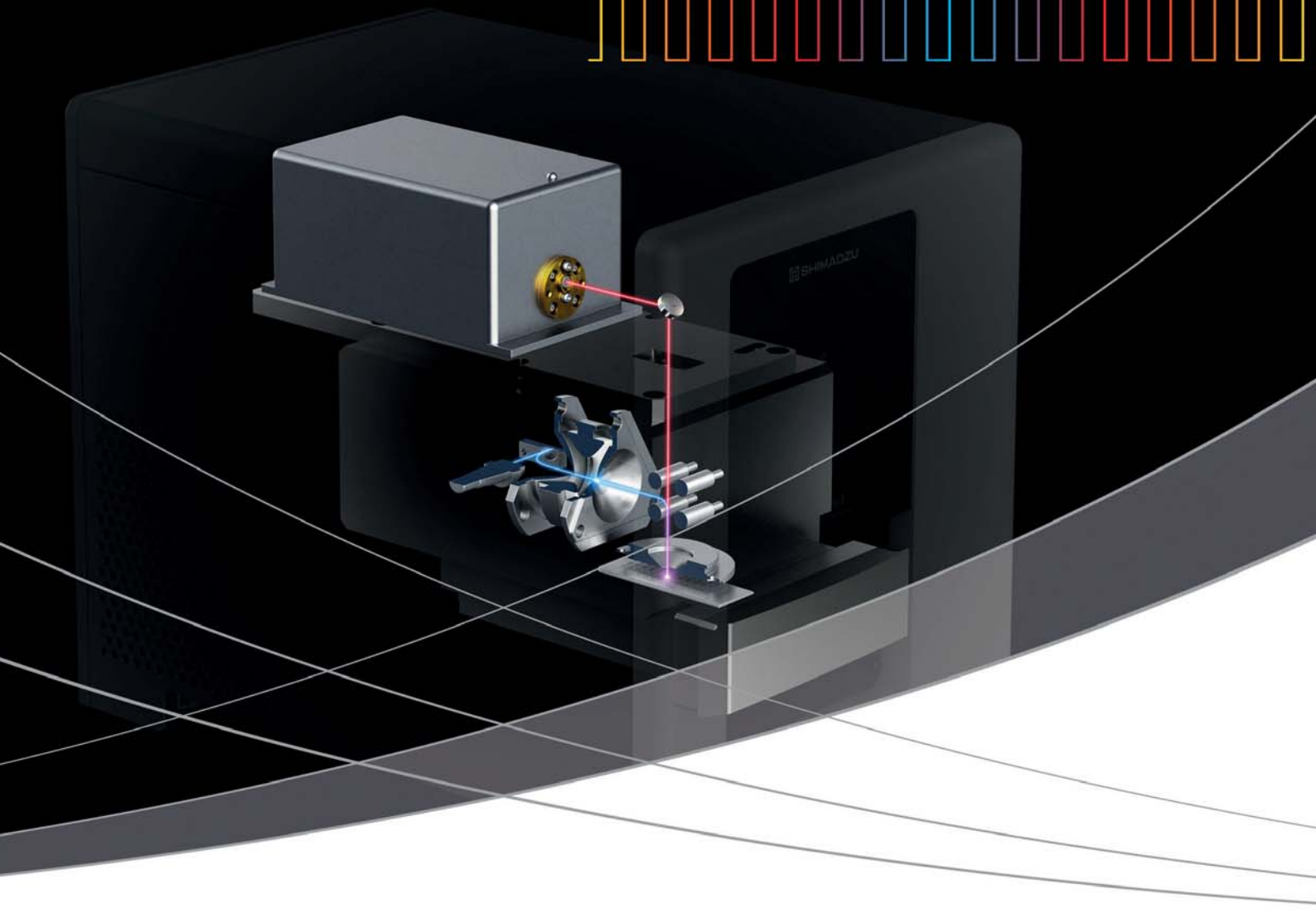
If you had not become a pathologist, what career would you have pursued instead?

I would most likely be in public relations! This is what my father saw in me. He even directed me to some job applications and interviews at big industries in Bangalore after I finished my master's. He always told me that I was a "people person" and that he could not picture me "isolated in a lab." While doing my master's, I attended night school at Bangalore University and got a diploma in public and industrial relations. I remember turning down two job offers in the field. If I had taken the first one, I would probably still be working for one of the largest employers in India. My dad was not pleased with me!

What one key message would you give early-career pathologists and laboratory professionals?

I tell all students, residents, and early-career pathologists who come my way, "Be persistent, never give up, and embrace repetitive practice – no matter how hard or boring it is." That's the only way to achieve their aspirations. I also tell them that perseverance and repetitive practice trumps intelligence. It's not enough just to work smart – you must work hard as well.

SHIMADZU
Excellence in Science



# Entering the digital age in MS

## Introducing the MALDImini-1 digital ion trap mass spectrometer

Shimadzu's first-of-its-kind MALDImini-1 digital ion trap mass spectrometer fits in a space the size of a piece of paper, allowing installation in places where mass spectrometers could not previously fit. It enables ion trapping up to 70,000 Da and the MS/MS and $MS^3$ functionality of the digital ion trap allows researchers to carry out comprehensive structural analyses with ease.

- **Fast, simple setup allows for a more convenient workflow**
- **Software allows switching quickly and easily between MS, MS/MS and $MS^3$ modes for seamless analysis**
- **Only device capable of MALDI-$MS^n$ in this compact size**
- **Space-saving lightweight design fits anywhere**

MALDImini-1

reddot winner 2021

**www.shimadzu.eu/maldi-dit**