

MSK PATHOLOGY REVIEW

Initiatives
Innovations
Accomplishments

2nd Quarter 2020

Pathology in a
PANDEMIC



Memorial Sloan Ketterin
Cancer Center.

The current issue of the *MSK Pathology Review* is focused predominantly on our department's response to the COVID-19 pandemic. The impact of this public health emergency has been felt in every corner of our society, and the response from MSK introduced a range of new practices in an effort to keep our patients and staff safe while still delivering world-class cancer care. The challenges in Pathology were somewhat different from those in patient-facing units, but we were still required to retool many aspects of our practice. Initially, efforts were focused on physical distancing in the workplace since supplies of personal protective equipment were inadequate for universal masking. Unknowns about the mode of virus spread complicated planning – was it safe to handle gross specimens from COVID patients? How high was risk of viral spread from hard surfaces like glass slides or laboratory equipment? We made continual adjustments as new information appeared. One of the most notable changes was the discontinuation of dual microscope review between faculty and fellows. Remote microscopy was introduced instead, which allowed slide sharing over WebEx or Zoom. These platforms enabled ongoing interaction and education, but there is no question that the experience was diminished, and we are still struggling to replicate the sign-out experience we have long enjoyed. Some Pathology staff members were directly involved in the COVID efforts as they volunteered for redeployment (but don't worry – we did not have pathologists directly caring for patients – Pathology Department members were redeployed to important but not patient-facing roles!). COVID testing was performed in the Department of Laboratory Medicine, so our Department was not responsible for it, but some of our Molecular Diagnostics technologists joined the lab efforts and helped run the COVID testing. As the institution continued

to react to the crisis, all research labs were temporarily closed, making it very challenging to maintain the ongoing work in Pathology labs.

The reduction in cancer volume that occurred as MSK modified its clinical focus to treat our patients and employees with COVID led to a nearly 80% reduction in specimen volume in Pathology. This decrease enabled us to implement remote work arrangements for clerical, technical, and professional staff, ensuring that those who had to be on-site were able to socially distance. The lapse in case volume also allowed us to explore digital pathology technology further. The relaxation of some regulations – the requirement CLIA compliance for all work locations (such as physicians' homes), and the need to utilize only FDA-approved digital pathology devices – led us to study how we could implement remote digital slide review. Workflow improvements were initiated and equivalency studies were conducted, leading to provisional approval of our home-grown digital pathology system by the NY State Department of Health. As detailed elsewhere in this issue, an entire team collaborated to advance our digital pathology efforts very quickly, and we are now even closer to enabling primary digital sign-out for those so inclined – either within the hospital or from remote locations should circumstances again dictate working from home.

As we enter the autumn and winter seasons, we are well aware that the relatively low prevalence of COVID we enjoyed in New York over the summer could swing back, and that safety measures we have relaxed may need to be retightened. This time we are even better prepared, and we will continue to innovate to resolve our challenges and ensure the uninterrupted provision of top-notch cancer pathology care.

- David Klimstra, MD

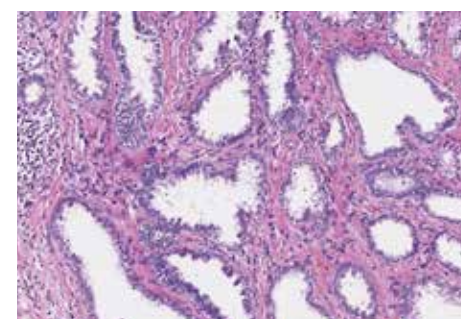
“The challenges in Pathology were somewhat different from those in patient-facing units, but we were still required to retool many aspects of our practice”

CASE HISTORY

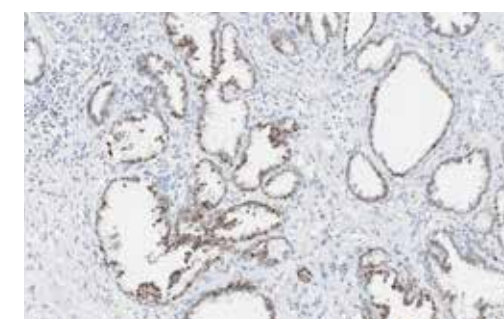
71 year old male, never-smoker with stage IIIc resected hilar cholangiocarcinoma s/p adjuvant chemotherapy approximately 2 years ago. Surveillance chest CT shows small bilateral lung nodules. He underwent a biopsy of the largest nodule in the right upper lobe measuring 2 cm.

The correct diagnosis will be provided in the next issue of the *MSK Pathology Review* and on Twitter at @MSKPathology

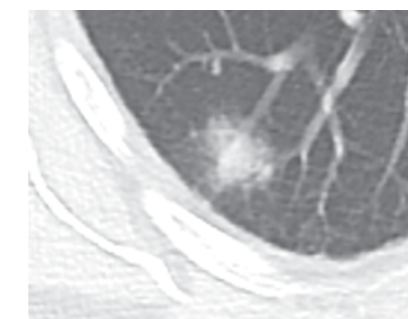
Scan the QR code to view digital slides available on mskcc.pathpresenter.com

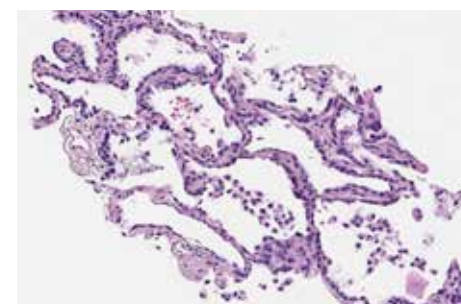
Cholangiocarcinoma



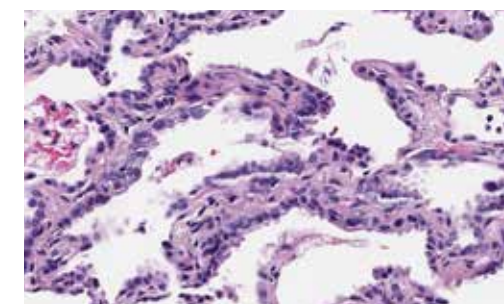
Cholangiocarcinoma TTF1-



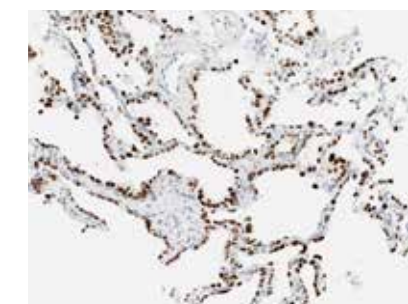
CT Scan



Lung Biopsy 1



Lung Biopsy 2



Lung biopsy TTF-1

CHOLANGIOCARCINOMA	LUNG BIOPSY
TP53 p.R248L	TP53 p.R248L
U2AF1 p.S34F	U2AF1 p.S34F
ARID1A p.A898T	ARID1A p.A898T
APC p.C2020Ffs*24	APC p.C2020Ffs*24
	9p21 (p16) homozygous deletion
	Deletion of ELF3 exons 1-7

DIAGNOSIS: LAST ISSUE

Ovarian mucinous carcinoma with malignant mural nodule comprised of sarcomatoid carcinoma



SAMSON W. FINE, MD

@rovingatuscap



Samson W. Fine, MD

By Kayt Sukei

Samson W. Fine, MD, a pathologist specializing in genitourinary cancers, has always been fascinated by the shapes, colors and architecture in life all around us.

“The variety of architectural patterns intrigue me,” he said. “Once I got to medical school and started taking courses in anatomy and histopathology, I realized that those sorts of patterns could also be observed on pathology slides under the microscope.”

This convergence led him to pursue pathology residency and ultimately a subspecialty in genitourinary pathology. Since his arrival at Memorial Sloan Kettering Cancer Center (MSKCC) more than 15 years ago, Dr. Fine has delved into many aspects of prostate cancer, publishing dozens of papers

on the disease that is the second leading cause of cancer death among American men.

“In the first few years of my career, I focused on studies defining histo-anatomy – especially the anatomy of the anterior prostate – and its correlations with biopsy features, grading and staging of prostate cancer, and lymph node metastasis, as well as patient outcomes,” he said. “In 2005, we learned that about half of all prostate cancers show gene rearrangement. We were able to parlay tissues collected and annotated in our work on anatomy and its clinicopathologic correlations into molecular studies of dominant anterior tumors.” Currently, he is preparing to publish the long-term outcomes of the anterior tumor cohort.

“... to do this kind of work, you first need outstanding colleagues who can help generate and refine important questions...having access to robust datasets – facilitated by MSKCCs large volume of patients – with long-term follow-up information, is especially important, since much of prostate cancer is indolent or progresses slowly after therapy. The combination of these data and collaborations allows us to focus on key pathologic features that may add to our understanding of the disease and have potential to change the way a clinician would treat a patient.”

IMPROVING RISK STRATIFICATION

A challenge of managing prostate cancer is that in a significant percentage of men, it’s fairly indolent, says Dr. Fine. “While there are patients who will need radical local and/or aggressive multi-modality therapy, others may be well-managed by active surveillance, which has gained increasing acceptance for very low/low risk and even some favorable intermediate risk cancers.” A particular emphasis of Dr. Fine’s work over the past decade has been examining ways in which pathologic features may more accurately stratify risk for patients.

In his work, Dr. Fine and colleagues have examined myriad prostate needle biopsy and radical prostatectomy specimens in an attempt to determine which features add information to well-known clinicopathologic variables and hence, enhance risk assessment. Working together with the prostate cancer outcomes group at MSKCC, Dr. Fine has investigated the value of Grade grouping in prostate cancer, the role of tumor quantification in prostate cancer across specimen types, as well as the impact of sub-categorizing prostate cancer margin status by quantity and grade.

A specific example is his investigation of the quantity of Gleason pattern 4 in Gleason score 3+4=7 (Grade group 2) prostate needle biopsies. This study showed that quantifying pattern 4 added information that would better enable clinician decisions – in that case between active surveillance and radical therapy. While some of studies have shown positive results, he is similarly satisfied with

determining that a particular feature does not add value, as was the case in a study of tumor volume measurements in radical prostatectomy patients. “Rigorous analysis of pathologic features in appropriately-sized cohorts offers richer information about which patients are better served by various management strategies,” he explained. “The idea is to highlight the features that can aid risk stratification and help our clinical colleagues provide the best quality care to patients. The idea should not simply be to add more features to pathology reports used in clinical assessment.”

CHARACTERIZING ADVANCED PROSTATE CANCER

Another thread of Dr. Fine’s research has involved improving our understanding of prostate cancer that develops after aggressive medical therapy. The advent of more potent anti-androgen therapies in the past decade has led to improved patient responses, yet many patients who respond to these drugs initially, eventually develop resistance to them. It is in this setting that “neuroendocrine prostate cancer” is most often identified.

“There’s a divide between clinicians and pathologists in how to define neuroendocrine prostate cancer,” he said. “Working with my GU Pathology colleague, Dr. Anuradha Gopalan, we have compiled a series of consecutive primary and metastatic prostate cancers that show neuroendocrine differentiation – with related therapeutic histories – to better define the spectrum

of morphologic findings in these tumors. We hope that this will facilitate correlation with molecular findings and ultimately, to identify subsets of patients with clinically-actionable patterns.” In a similar vein, he has also collaborated on Dr. Gopalan’s recent work using immunohistochemistry to better profile patients with an androgen receptor-null, non-neuroendocrine phenotype that is highly correlated with metastatic disease.

Dr. Fine highlighted the tremendous value in clinical and research collaborations that MSKCC is known for, as well as the large volume of data available for research use. “To do this kind of work, you first need outstanding colleagues who can help generate and refine important questions. I have benefited greatly from daily interactions with Dr. Victor Reuter and the GU Pathology team, as well as with clinician colleagues and epidemiologists/biostatisticians,” he said. “Having access to robust datasets – facilitated by MSKCCs large volume of patients – with long-term follow-up information, is especially important, since much of prostate cancer is indolent or progresses slowly after therapy. The combination of these data and collaborations allows us to focus on key pathologic features that may add to our understanding of the disease and have potential to change the way a clinician would treat a patient.”

Finally, Dr. Fine was an early adopter and champion of using social media for education in GU pathology. You can follow his #gupath explorations on Twitter at @rovingatuscap.



Matthew Hanna, MD, Ushers in Pathology’s Digital Revolution

By Kayt Sukel

Since the beginning of his career, Matthew Hanna, MD, has put faith in the potential of digital pathology to transform the standard of care for patients. A self-proclaimed tech junkie, he said his early education in biomedical engineering led him to quickly pivot to medicine — and a specialty in oncologic pathology.

“At the time, the giants in the pathology field looked at morphology and disease from a biology and process standpoint,” he said. “But even then, there were these new and emerging technologies and applications that were pointing to a revolution in pathology. I wanted to get into pathology to be part of that revolution — and change what pathologists could provide to patients in terms of diagnosis and prognostication.”

Since then, Dr. Hanna has been hard at work exploring ways to modernize the performance of pathology. Projects he and his colleagues are developing include new machine-learning algorithms that

have the potential to pick up signs of cancer on slides that may be invisible to even the experienced pathologist’s naked eye. They’re also working to create a meaningful workflow that can seamlessly integrate such tools into pathology labs around the country.

TAKING THE FIRST STEPS

Dr. Hanna said the first step toward incorporating digital pathology platforms is to establish a strong digital workflow that allows those tools to augment the work they are already doing without interruption or interference.

He feels fortunate that the pathology department at Memorial Sloan Kettering (MSK) was an early adopter of digital tools. “We are working hard to try new technologies as they become available and validate them at scale,” he said. “We want to use machine-learning models to create efficiencies for pathologists to help them find digital biomarkers that will help

“Our ultimate goal is to create novel and robust tools that pathologists can use to provide reliable, accurate diagnostics and pathology reports to patient-facing clinicians so we can improve the care and the outcomes of our patients. This kind of work is going to lead to the digital transformation of the entire field.”

them from both a diagnostic and prognostic standpoint.”

He said there is a lot of potential data hidden within the slides that pathologists rely on every day to grade and stage tumors. If new technologies can marry the pixels from the digital versions of pathology slides to patient outcomes, clinicians might not only be able to better predict survival — but select more targeted treatments to improve patient care.

To get to that point, however, Hanna admits there is much work to do, and a series of challenges to overcome. To start, in terms of machine-learning algorithms, it’s important that new models can work across different patient populations from multiple hospitals and institutions.

“Many different algorithms have been developed, but too often, we don’t know if

the machine-learning model one hospital creates based on its population works in another hospital,” he said. “There are a lot of different lab protocols and different patient populations, and a lot of research that still needs to be done to show how generalizable these models can be.”

Dr. Hanna and his colleagues recently published, in *Nature Medicine*, a proof-of-concept study for a clinical-grade computational pathology algorithm that was validated across a large group of patients across a variety of different institutions.

“We had good performance,” he said. “But less than 1% of these models that are created will be vetted on data that represents that level of patient populations. We need more of that.”

PILOTING THE POTENTIAL

Hanna credits the remarkable leadership and resources at MSK for his ability to move the digital pathology needle forward. Given the institution’s worldwide consultation service, the department can access and scan a remarkable amount of pathology slides.

The sheer number and variety of slides generated at outside labs, said Dr. Hanna, help him and his colleagues develop machine learning models that can be generalized for use at different hospitals. “With that much variability, we can minimize the noise and calibrate them to manage it. We currently have more than two million slides scanned, which are connected to patient data. The scale of data here is tremendous, enabling us to scale production of our platform very quickly with very good performance.”

In addition to advancements in computational pathology, as New York City began shutting down in response to the COVID-19 pandemic — including non-essential medical personnel — Dr. Hanna unexpectedly piloted a digital pathology workflow to enable pathologists who have been ordered to work from home on certain days, making it part of his research program.

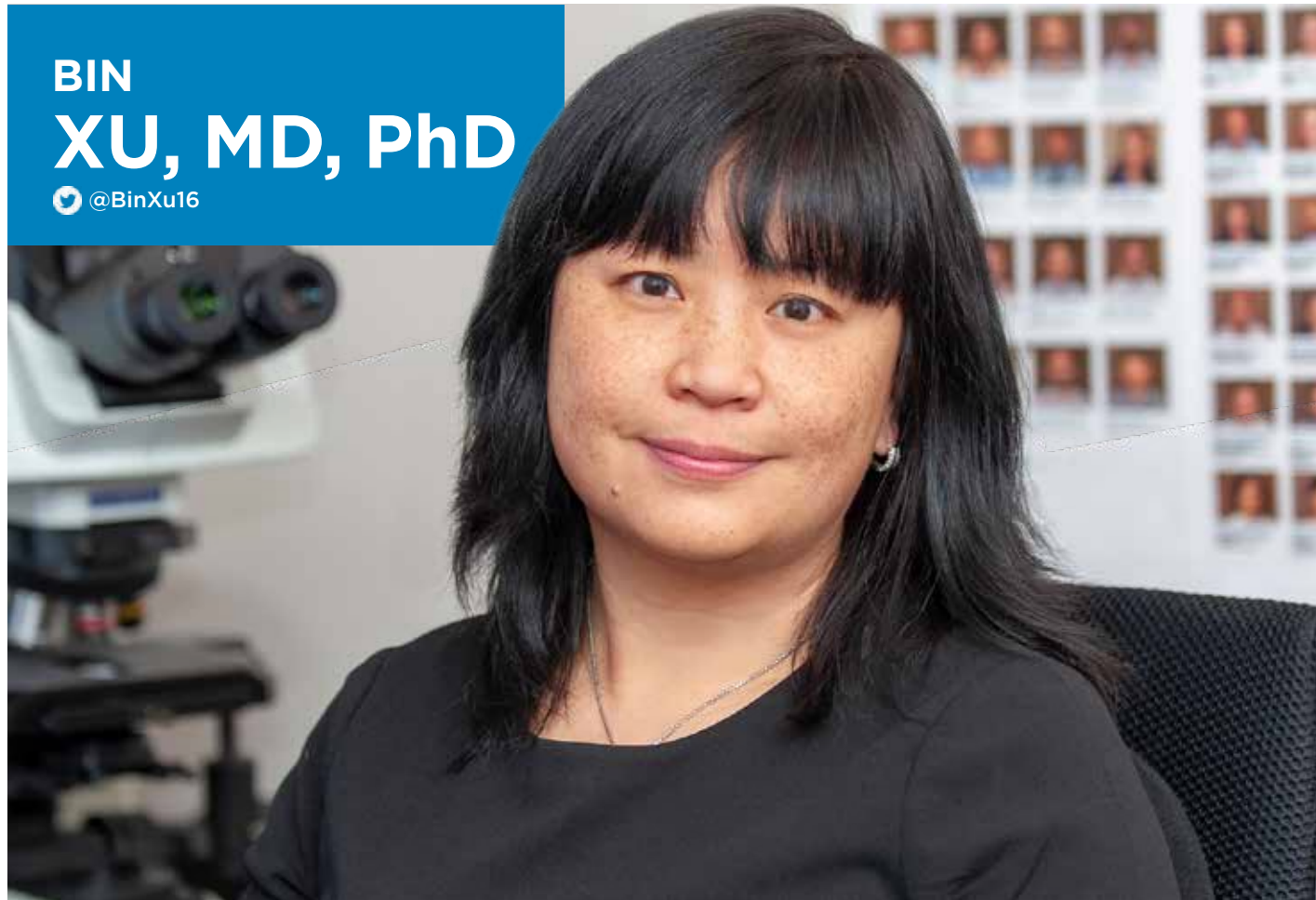
“All systems used for patient care should be clinically validated, whether cleared by the Food and Drug Administration or not,” he said. “We are having some of our pathologists do a remote sign-out of cases that they will review at home and then do the final diagnostic work back in the hospital. These times highlight the tremendous value of digital pathology so we can protect pathologists if we are on a city-wide lockdown, while still ensuring we are providing the best possible care to our patients no matter what’s happening.”

Moving forward, Dr. Hanna plans to continue his work in machine learning and digital workflow development to help provide robust clinical decision support in a seamless fashion for pathologists at MSK and across the globe.

“We want to develop technologies that can provide strong clinical decision support — but we need to ensure that those systems are safe and effective,” he said. “Our ultimate goal is to create novel and robust tools that pathologists can use to provide reliable, accurate diagnostics and pathology reports to patient-facing clinicians so we can improve the care and the outcomes of our patients. This kind of work is going to lead to the digital transformation of the entire field.”

**BIN
XU, MD, PhD**

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**Bin Xu, MD, PhD,
Unravels the Mysteries
of Anaplastic Thyroid
Cancer**

By Kayt Sukel

Anaplastic thyroid cancer may only affect one in a million people, but of all forms of thyroid cancer it's the most aggressive, and the most lethal, said Bin Xu, MD, PhD, a pathologist with the Head and Neck Pathology team at Memorial Sloan Kettering (MSK) Cancer Center.

"Most people who develop this disease die within a few months — about 80% of those patients won't survive one year after diagnosis," she explained. "But it has not been clear why this type of thyroid cancer, compared to other types, has such fatal outcomes."

During her fellowship in oncologic surgical pathology at MSK, and now in the year-plus since she's returned to the institution, Dr. Xu has embarked on research projects that run the gamut of head, neck and endocrine tumors. She is driven by her desire to understand the pathogenesis behind these different

conditions and provide vital information to help clinicians better manage patients' treatment regimens after diagnosis.

"I enjoy being able to find the different pathologic parameters that shape how we give a diagnosis and can help us better understand how a patient will do after that diagnosis," she said. "When we can better understand the different features of these diseases, we can better stratify patients and make sure they get the most effective intervention for them."

LOOKING FOR CLUES

With regard to anaplastic thyroid carcinoma, Dr. Xu and her colleagues set out to better characterize the pathological features of this rare and deadly tumor type. "We gathered the largest cohort in history of anaplastic thyroid carcinoma tumor samples from more than 300 patients," she said. "We then carefully studied the

pathology and molecular features of those samples so we could provide more clues about diagnosis and prognosis."

As they delved into the data, Dr. Xu's team discovered that patients with this rare condition carry unique, specific genetic mutations that can help clinicians not only better identify them at diagnosis, but also provide them with an appropriate survival prognosis.

"This is the first time we found a molecular prognostic marker in this disease," she said. "But, more than that, we also found that there are biomarkers that differentiate those who will survive the disease." While it's still, sadly, true that many people with this cancer die within a year, Dr. Xu's research provides evidence that there's a small cohort of patients who will survive longer. "We found that when patients have a smaller tumor size or when the margins are clear, or the tumor is completely taken out during surgery, they do better. These pathologic parameters will offer clinicians the kind of predictive information that can help them better manage the care of the patient."

That includes the use of already Food and Drug Administration-approved inhibitor drugs that target oncogenes like BRAF, in certain patients who will most benefit from them.

"With this pathology information, we can see which patients may be responsive to new adjuvant targeted therapies," she said. "We see that patients with a particular profile have a great response to these drugs. So, when we can identify them early using

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A RICH RESEARCH ENVIRONMENT

The ability to collect such a large cohort of patient samples is one of the reasons Dr. Xu wanted to return to MSK after spending a few years working in her native Canada. She also appreciates being in the kind of supportive, collaborative environment that allows her to pursue her research interests. She said MSK provides that kind of environment.

"There is a lot of support for our research endeavors. Our service time is evenly spaced out so there is time for us to do our research, and we have a strong multi-disciplinary team that collaborates on a variety of different projects," she said. Not only that, but "MSK has the best cases. We have a very high case volume, and because so many people with rare cancers come here for clinical trials, we have access to those samples." That richness

in number and variety make the kind of research Dr. Xu does on anaplastic thyroid carcinoma feasible and rewarding.

Moving forward, Dr. Xu wants to continue researching what features denote long-term survival in anaplastic thyroid carcinoma. "We want to look at this unique cohort to see what allows them to live longer as compared to other patients with this condition," she said. "If we can identify the right patterns in these tumors, we can stratify patients for different treatments. But we may also uncover new avenues we may be able to exploit to help others survive better."

It is Dr. Xu's hope that, through these research projects, they will be able to identify actionable pathologic and molecular targets to fuel future drug discovery.

"When we can characterize these diseases better and provide diagnostic and prognostic clues to help classify them better, we are in a position where we can really help our patients," she said. "That's why we all do what we do."



PATHOLOGY IN A PANDEMIC

If there's a silver lining to the shutdown around COVID-19, it's the way the pathology department has nearly seamlessly shifted to digital platforms without sacrificing patient care.

By Kayt Sukel

Early in the year, physicians across Memorial Sloan Kettering (MSK) Cancer Center began hearing of a novel coronavirus spreading through China. As January turned to February, concerns mounted that the deadly virus, dubbed COVID-19, had reached the United States. At the same time, Pathology Department chair David Klimstra, MD, and his colleagues at MSK were preparing for the United States and Canadian Academy of Pathology (USCAP) meeting in California, scheduled for the first week of March. "There was a lot of discussion in the weeks before USCAP whether the meeting would happen at all — and, if it did, whether it was safe to go," said Dr. Klimstra. "That's right around the same time the first cases appeared in New York City."

USCAP took place, and by the time Dr. Klimstra and others from the pathology

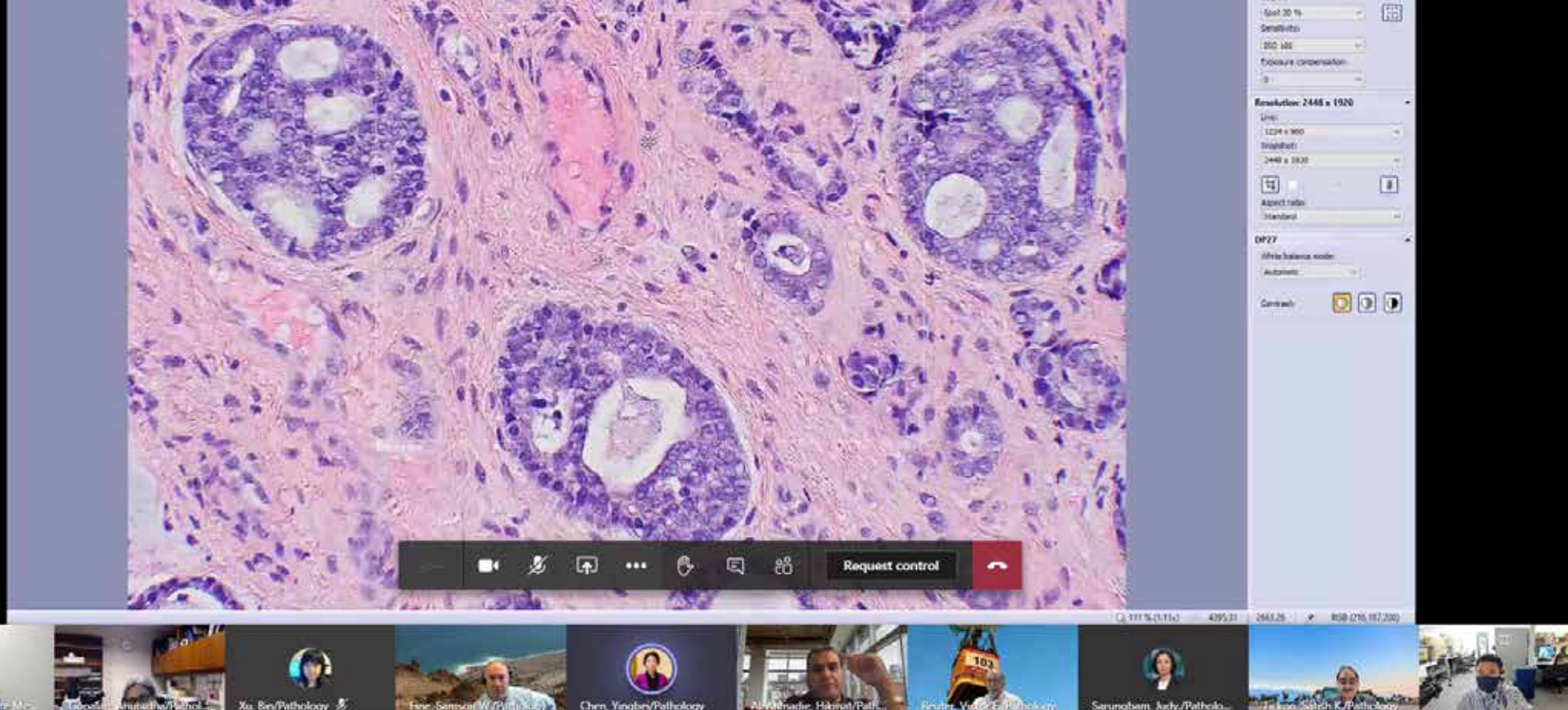
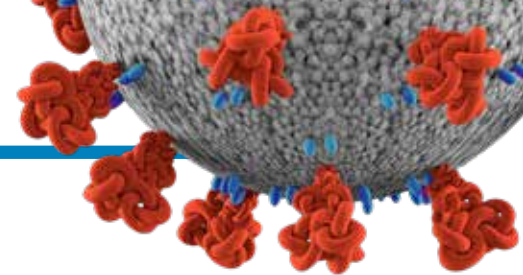
department returned, the number of COVID-19 cases in the city was steadily rising. Soon after, the World Health Organization declared a global pandemic. Within days, New York City was under a shelter-in-place order, with strict social distancing guidelines in effect at essential workplaces like healthcare facilities. Christine England, Senior Director of the department, said she and other department leaders immediately put new policies in place to protect the health of both patients and providers across the institution.

MSK, like other healthcare institutions, had an emergency preparedness plan — but it had been developed to address more predictable and commonplace events like snowstorms and hurricanes. It soon became clear that the facility would need a more focused, sustained strategy to deal with the pandemic.

That included pathology. "Most of us are not patient-facing, like the majority of other physicians here," said England. "But we do play a pivotal role when it comes to continuity of care. We had to be sure that patients who truly needed cancer care were not forgotten. The question became: how could we, with minimal staff on-site, offer patients diagnoses and treatment recommendations across the different pathology services during this time? And how we could do that when the world's understanding about this virus and how it spread changed from week to week?"

RETHINKING PROTECTION, TIME, AND SPACE

The first step, said Ahmet Dogan, MD, PhD, chief of the Hemopathology Service, was to introduce a variety of vital public health practices into the pathology department's



Reuter, Victor E./Pathology



Remote Sign-out, Realized

How MSK pathologists helped make digital pathology a reality

by Kayt Sukel

As the novel coronavirus hit New York City, the volume of pathology cases dropped by approximately 75% as care at Memorial Sloan Kettering (MSK) Cancer Center was redirected toward COVID-19 patients.

“The silver lining here is that

it gave us the opportunity to pilot remote sign out and digital pathology in a way that would not have been possible if we were doing our normal routines,” said David Klimstra, MD, Chair of the Department of Pathology at MSK.

Yet that opportunity required

a lot of behind-the-scenes work. S. Joseph Sirintrapun, MD, MSK’s Director of Pathology Informatics, said it’s never simple to transform a process that has been done largely the same way for the last century.

“Many laboratories in Europe have now gone completely digital,” he explained. “But we’ve been held back, not only by figuring out the right workflows, but by regulations saying we need be physically present in a Clinical Laboratory Improvement Amendments (CLIA)-certified facility.”

As the president-elect of the Association of Pathology Informatics, Dr. Sirintrapun launched a grassroots movement to lift the CLIA certification so that pathology could continue its work during the pandemic. He created a petition and collected

more than 10,000 letters from pathologists across the country to send to the United States Senate. The aim was to highlight the need for remote sign-out and digital pathology capabilities.

“It was important they understood that our entire workforce was at risk, and our campaign did that,” he said. By late March, the announcement came: CLIA would relax regulations and allow remote sign-out. “That really opened the door for us, as a department that is leading in the digital space, to get New York State approval and really put our digital capabilities into place.”

Dr. Sirintrapun didn’t effect this major change on his own; he gives credit to the entire pathology department, particularly the efforts and support of key individuals like Matthew Hanna, MD, Orly Ardon, PhD, MBA and

Dr. Klimstra, as well as dozens of others who helped find the right digital tools to support the department during the COVID-19 crisis.

“We are discovering the boundaries of what’s required for this to work,” said Dr. Sirintrapun. “What technologies do we need? What’s the right equipment to use at home? What kind of bandwidth is necessary? What do we need from both a technical and an operational standpoint to do this, and do it well? As a team, we were able to answer those questions and develop a workflow that did not diminish the quality of our results. We’ve long wanted to embrace the power of digital pathology, and in the face of this crisis, we were able to go full force and show how it can be done.”

workspaces and workflows. While healthcare organizations across the country faced shortages of personal protective equipment (PPE), “we were lucky in that we had our own little stockpile of PPE,” he said. The key was to take a careful inventory and then develop policies for its use among those working on-premises. Devising those policies was a challenge, said Dr. Dogan. “We didn’t know what the risk really was in pathology. Could the virus spread from slides? We had to come up with policies and then adjust them as we learned more.”

The department also had to put social distancing measures in place. An impediment to maintaining the recommended six-foot separation is the lack of space. MSK doesn’t have much square footage to spare — and laboratory technicians cannot gross or slice samples from home.

“Laboratories tend to be in confined spaces around the hospital,” said England, with technicians and technologists working physically close to one another. “We had to think about which areas were critical to have staff working on-site — and then figure out how to make sure they could work far enough apart.”

The solution was staggered shifts, said Dr. Peter Ntiamoah, Manager of the Surgical Pathology laboratory. Rather than a daily 9-to-5 schedule, staff members would work 12-hour shifts on different days each week. “Finding the space for staff to prepare the slides the pathologists need to make their diagnoses while minimizing their exposure to COVID-19 was a top priority,” he said. “We worked hard to minimize foot traffic in the lab but also talked to all the lab members so we could move to shifts that would not overburden them.”

Ntiamoah also coordinated with MSK’s morgue to make sure it could remain fully functional during the crisis. “At one point, the morgue was full,” he said. “We worked together to ensure that if it were to become full again, there would be other places we could safely place the deceased.”

The need to maintain appropriate distance did not just affect laboratory spaces. Many of the pathologists, as well as their training fellows, utilize two-headed or multi-headed microscopes in their daily tasks. Meera Hameed, MD, chief of the Surgical Pathology Service, said protecting vulnerable cancer patients was, of course, always the department’s top priority. But the department also strove to protect its pathologists.

“We needed to find a way to balance

out shifts in a way that we could maintain coverage as well as the overall quality of our work,” she said. “I lead one of the largest divisions within the department, with more than 60 faculty members. We came up with a plan to stagger who was coming in when.” With everyone’s input, the schedule Dr. Hameed and her team created allowed for distance without sacrificing the level of quality expected from MSK.

RETHINKING WORKFLOW VIRTUALLY

Staggering schedules doesn’t just alter what time people come and go to work; it shifts the usual ways pathologists in different services handle their typical workflow with laboratory personnel and each other. For example, said Dr. Dogan, traditional sharing of different slides and samples could no longer be supported thanks to COVID-19.

“We ended up moving all of our meetings and consults to virtual platforms. We have a variety of formal and informal processes across the department, and we needed online platforms that could support them all.”

The department quickly pivoted, using Microsoft Teams, Zoom, and other virtual tools. This allowed pathologists to continue their work, both at home and in the laboratory, without fear of compromising patient care or their own personal safety.

“MSK is a very progressive organization when it comes to technology so it did not take long for us to move to these kinds of platforms to support our work,” said Matthew Hanna, MD, a pathologist who has been working on implementing digital pathology workflows throughout the department. “It made all the difference to how quickly we could stand these things up.”

CONTINUING EDUCATION

MSK is a teaching institution, so figuring out how to continue to educate fellows was another important priority, given that COVID-19 erased the ability of attending pathologists to physically sit with their trainees during slide review.

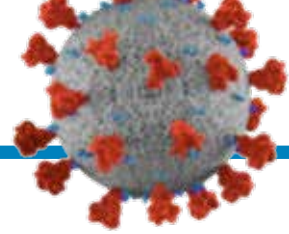
“Our fellows are accustomed to preparing a case and then submitting it to the attending for review,” said Dr. Klimstra. “Normally, the fellow is sitting with the report open on the computer and the attending is sitting at the two-headed microscope looking at the slides with them so they can make any needed changes as they go. Obviously, that doesn’t work with this virus. So, we had to ask ourselves, how can we continue to do those reviews? How can we give the fellows



S. Joseph Sirintrapun, MD



Matthew G. Hanna, MD



Put to the Test

Up for the challenge, Memorial Sloan Kettering Cancer Center's Department of Laboratory Medicine raced to develop viable COVID-19 tests

by Kayt Sukel



The Department of Laboratory Medicine at Memorial Sloan Kettering (MSK) Cancer Center did incredible work in quickly developing a COVID-19 test — one of the first to receive Food and Drug Administration (FDA) clearance, said pathology department chair David Klimstra, MD.

It was vital to have an RNA-based test that could determine who had COVID-19 and find ways to minimize the spread of the virus. "That allowed us to be one of the first hospitals to set up a COVID-19 floor for patients, and then also make sure that sick employees were sent home right away," she said. "We were able to limit the amount of infection because we had that tool at our disposal," said Melissa Pessin, MD, PhD, Chair of Laboratory Medicine.

Moving quickly was a challenge. Esther Babady, PhD, a microbiologist who specializes in the molecular diagnosis of infectious diseases, said the team hit several regulatory and supply roadblocks. But they also had an advantage in MSK's strong molecular section. "We had all the right instrumentation and skills for developing everything we needed with the exception of the reagents required for the assay." Eventually, Babady and her team modified the Centers for Disease Control and Prevention's COVID-19 test, validated it, and received approval from the FDA and New York State Department of Health. The test was in use by March 10, 2020.

At the same time, Lakshmi Ramanathan, MD, chief of the Clinical Chemistry Service, and her colleagues were at work on a COVID-19 serology test. Different from the assay, this test detects the specific antibodies that are produced after exposure to the virus. Ramanathan's group was able to use the already validated RNA



Esther Babady, PhD, D(ABMM), FIDSA, Director, Clinical Microbiology Service

test to bolster their efforts, because they could collect specimens from patients who had tested positive for COVID-19.

"We also looked at our validation banks of normal blood specimens because we needed to look at pre-COVID specimens," she said. "We also took blood specimens from MSK employees who had previously tested positive for COVID-19 and were getting ready to come back to work." The serology test went live on April 27.

Pessin said Laboratory Medicine's swift and dedicated efforts helped to put MSK in a position to better protect its patients and employees from the spread of COVID-19 — and make sure that it could continue to fulfill its mission to provide the highest quality cancer care.

"We are continuing to develop better tests, including saliva-based screens that don't require nasal swabs, so we can continue to screen employees on a routine basis, as well as new technologies to run those tests on," she said. "We've had to learn a lot on the go. But Laboratory Medicine has the right mix of skills and expertise to make sure we were in and will continue to be in a position to effectively contain and treat this virus at MSK."

good feedback about something they may have missed on a slide without being right there? What can we do from afar that offers the same level of guidance as before?"

Daily didactic sessions represented another challenge to the educational mission, said Victor Reuter, MD, director of genitourinary pathology. The department didn't want to jettison these sessions, which are comprised of a series of lectures and educational programs. Yet with only essential personnel on-site, the department required a good virtual solution to continue those endeavors.

"We moved from giving a group presentation in a multi-headed scope room, or from meeting in the conference room, to doing things via Zoom," said Dr. Reuter. "We needed to share digital images with resolution similar to what the fellows would be able to see on slides." It took a little time and ingenuity to be able to offer fellows high quality of input, but now, "we send emails about different cases where we feel they may have missed something, and we use Zoom or other conference tools to share the slides and highlight the areas we are talking about, so we can fulfill our responsibilities with regards to training the next generation of pathologists to the level we at MSK have always done."

DIGITAL PATHOLOGY TO THE RESCUE

Another digital tool that allowed the department to pivot so ably in the face of the crisis was their homegrown digital pathology platform. Dr. Hameed said the COVID-19 pandemic has provided an opportunity for the team to test out technologies that allow pathologists to review cases remotely.

"With so many of our pathologists working from home, we needed to find a way to make digital pathology not only possible, but efficient and workable for them," she said. "If there is a silver lining in all of this, it's been that we have been able to get team members to mobilize and try these new tools, growing their skills and level of comfort with working outside the lab so we can better respond to public health emergencies."

The federal government requires pathology laboratories that provide diagnoses to be Clinical Laboratory Improvement Amendments (CLIA)-certified before they can accept human samples for review and testing. In response to the COVID-19 crisis, the Center for



Izabela Maciejkowicz, Cytology

Medicare and Medicaid Services loosened those guidelines, permitting pathologists to review and report on pathology specimens to make cancer diagnoses outside of CLIA-certified facilities.

"This was unheard of before," said Dr. Hanna. "A temporary non-enforcement of CLIA regulations offered us an opportunity to let pathologists remotely sign out cases using our digital pathology platform so they can do their work from home."

New York, however, requires that any diagnostic tests be approved through a state regulatory body. Dr. Hanna and Orly Ardon, PhD, MBA, Scientific Manager for Digital Pathology Diagnostics, quickly got to work to validate their system, which includes hardware that has not yet been approved by the Food and Drug Administration, in order to get that approval. As part of the painstaking process, all glass slides used for routine surgical pathology sign-out were scanned on a high-resolution scanner and then fed into the digital pathology platform, as well as integrated with the laboratory information system, for remote review. A dozen of the department's pathologists from different subspecialties volunteered to do reviews. With that level of participation, Dr. Ardon said they were able to quickly determine the use of the platform at home was equivalent

or superior to a normal microscopic session in the lab.

“This kind of platform can help us modify the way our pathologists work, and still make sure we can keep up with our caseloads while meeting the required turnaround time in surgical pathology”

"We looked at everything from the different metrics and measurements used for diagnosis, to compare what the pathologist saw on screen while reviewing at home versus what they would see in the microscope," she said. "In many ways, we were looking for problems — we needed to make sure they had the adequate bandwidth and hardware to access the images on their home office equipment. There are many variables between the kind of set-up one pathologist might have at home versus another. We wanted to see how far we could push the platform's use and still have everything go smoothly."

That work paid off. After preparing a more than 500-page document for the state regulatory authority, the pathology department was granted provisional approval, the first in the state, to use their

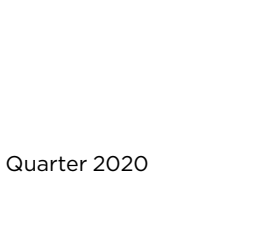
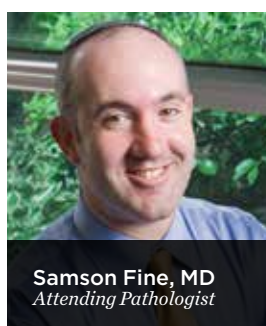
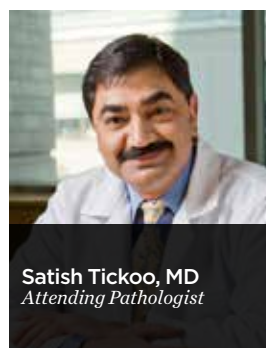
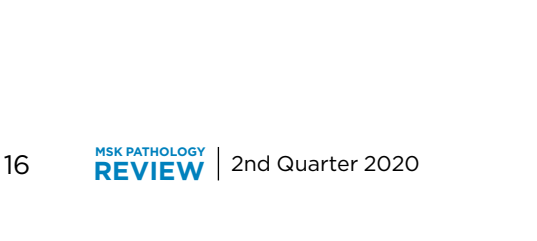
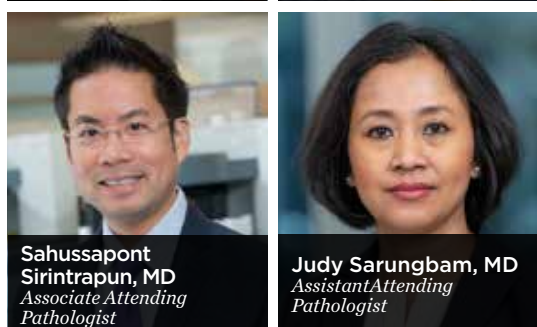
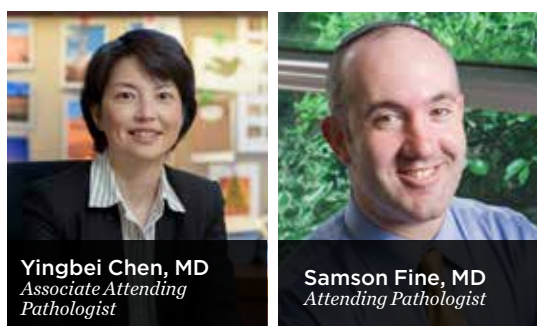
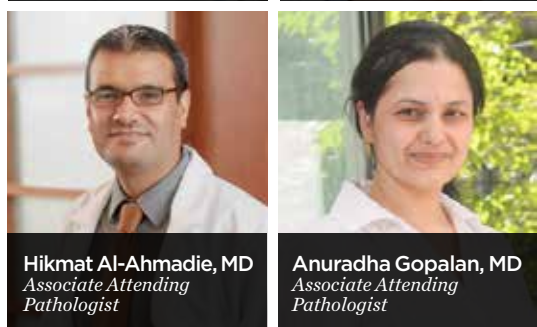
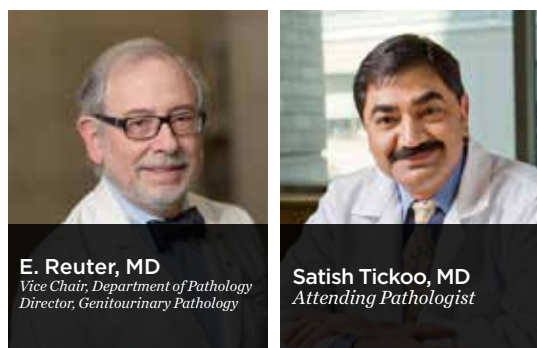
digital pathology platform for primary diagnosis during the pandemic. Within a few weeks, they should know whether that approval will be extended so they can continue to use their digital pathology platform in the future as well.

"This kind of platform can help us modify the way our pathologists work, and still make sure we can keep up with our caseloads while meeting the required turnaround time in surgical pathology," said Dr. Hanna. "It really is a testament to everyone in the department that we were able to get this done so quickly. It was an institution-wide effort and it shows the important role that digital pathology can play in the face of an emergency."

MOVING FORWARD

With experts predicting a second wave of COVID-19 in the fall, Dr. Klimstra is confident that the Department of Pathology will be ready with the tools necessary to fulfill both patient care and educational duties. "We are learning as we go," he said. "Our ability to care for our patients is improving as we learn about all the different complications of this virus and how to best treat them. Our hope is that, if it does come back, we will be able to mobilize the department quickly to work remotely and still make sure we are providing the highest quality clinical care to anyone who walks through MSK's doors."

Genitourinary Pathology



Team of Excellence

by Kayt Sukel

At the time Victor E. Reuter, MD, completed his fellowship in surgical pathology at Memorial Sloan Kettering (MSK) Cancer Center, one of his main inspirations was Willet F. Whitmore, Jr., MD, a pioneer of urologic oncology, then-chief of MSK's urology service. Dr. Whitmore, known for his "Whitmore-isms," helped show him the value of specializing in this sometimes-overlooked area in pathology. That was nearly 40 years ago, and Dr. Reuter hasn't forgotten what got him here.

"When I first arrived at MSK, while I was committed to cancer care, I was not sure where to focus my efforts," he explained. "But Dr. Whitmore, a true Renaissance man, inspired me to pursue urologic pathology. He had this uncanny ability to make everyone around him feel important and he made sure we all knew no one doctor could battle cancer alone, but that it took a village — a real team effort."

Together with his Pathology mentors Drs. Myron Melamed and Philip Lieberman, Dr. Whitmore spurred him to specialize in genitourinary (GU) pathology in MSK's pathology department. And over the course of the next several decades, Dr. Reuter built a remarkable subspecialty team to work alongside him.

"I have been blessed to work at an institution that is rich in clinical expertise, rich in patients, and rich in basic and translational research. For many years, I was the only person in the service — but that allowed me to work with many investigators from all sorts of different fields and learn a great deal," he said. "As the service has grown, we have been able to recruit many dedicated surgical pathologists with expertise in a variety of GU cancers, so that we now have a great core providing diagnostic excellence as well as excellence in translational research studies."

That "team of excellence," as Dr. Reuter refers to his fellow members of the GU team, is well-equipped to manage the ever-increasing volume of pathology samples, and to move the field further with their innovative translational research efforts.

BALANCING VOLUME AND RESEARCH

After breast cancer, the GU team takes on the largest volume of Pathology cases at MSK, a number that is only growing. The team reviews thousands of biopsies and resections from patients each year, including cases involving kidney, adrenal, prostate, bladder, ureter, urethra, and testicular cancers.

"After adjusting for departmental consults, we had an increase of 7 percent in the volume of cases we reviewed last year compared to the year before," he said. "The sheer number of slides reviewed by our team is extraordinary, especially when you consider that many of the cases we see are relatively complex tumors that come to MSK for a second opinion."

The pathologists on Dr. Reuter's team help establish the correct diagnosis for different types of cancer, as well as provide a thorough characterization of stage and grade of the tumor, among other pathologic parameters. Despite handling the service, Dr. Reuter said, the team has distinguished itself at the global level

with its research efforts.

"If we could concentrate solely on research, we would still be extremely busy," he said. "But finding ways to balance that work with an active clinical service is quite difficult. It's a testament to the talent on our team that we manage it as well as we do."

Over the past few years, the team has contributed to new advances in the classification and discrimination of different types of kidney cancers, describing the biology and molecular pathology characteristics of newly recognized sub-types. They have also contributed to advances in the characterization of different urothelial and prostate tumors. The combined research into molecular and genetic abnormalities, and their association with unique pathologic features, is helping the team identify markers that can better aid clinicians in determining diagnosis and prognosis. This work may even identify potential targets for future treatments.

"This isn't just a better understanding of the morphology of these tumor types but also a deeper look at their molecular phenotypes," said Dr. Reuter. "Our pathologists have published remarkable studies on prostate, urothelial and kidney cancers. Recently, some of the team's members described a special type of prostate cancer, called androgen-receptor null, a rare but important variant which can now be defined pathologically with the use of ancillary studies. We also have a high level of expertise in testicular cancers. In fact, our team was instrumental in the publication of *The Cancer Genome Atlas for Testicular Cancer*."

Dr. Reuter is understandably proud of his team's accomplishments and appreciates how much each team member contributes to our understanding of specific tumor types and the best ways to effectively treat them.

COLLABORATION IS KEY

Dr. Reuter said the unique collaborations that led him to decide to sub-specialize in GU pathology are still strongly in place today. He and the other GU team members work closely with researchers, medical, surgical and radiation therapy colleagues to help provide the highest quality care for every GU patient that walks through MSK's doors.

"Everyone is very busy, so finding the time to collaborate can sometimes be a struggle," he said. "Yet we work hard to support our clinical and research colleagues while pursuing our research interests".

As someone who has stayed at MSK for the bulk of his career, Dr. Reuter said he appreciates the fact that pathology takes such a central role in both care and research at the institution.

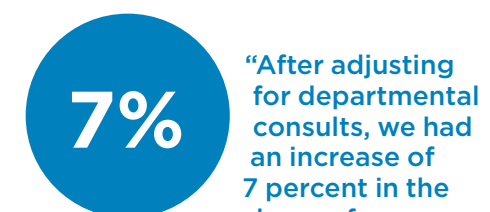
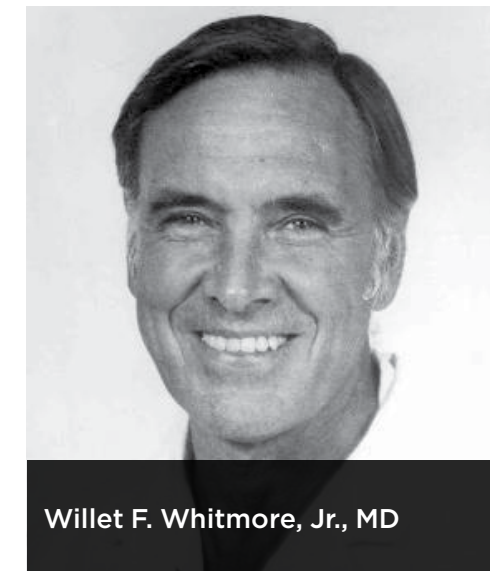
"Often, I hear from colleagues who have moved on to other institutions that it's not the same way there," he said. "Once they leave, they realize that they took the way we do pathology here a bit for granted. The kind of excellence we provide to the clinical care and research at MSK is very different from what you see in other places. It speaks volumes about the way we are respected by our oncology colleagues."

As cancer care in general and the GU team in particular continue to evolve at MSK, Dr. Reuter sees further adoption of digital tools and artificial intelligence algorithms to help them keep pace with both their case volume and their research efforts. With the department now scanning tens of thousands of slides per week, the GU team will have access to an immense digital archive that can help them with their translational work, as well as to make more timely and accurate diagnoses for patients.

"More and more, the classification of tumors is not going to be based solely on what we see under the microscope but is also going to require a thorough understanding of the tumor's molecular profile," he said. "The way we classify and treat tumors is going to change and probably change quite a bit."

That said, Dr. Reuter has full confidence that his team is more than ready for whatever the future may hold.

"I consider myself extremely fortunate, in both the place that I work and the team that I work with," he said. "Like Dr. Whitmore said, it really does take a village. And our village in the GU team is smart, experienced, and poised to do a lot of great things in the future."



7% "After adjusting for departmental consults, we had an increase of 7 percent in the volume of cases we reviewed last year compared to the year before," he said. "The sheer number of slides reviewed by our team is extraordinary, especially when you consider that many of the cases we see are relatively complex tumors that come to MSK for a consult or second opinion."

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New Pathology Faculty



Leonardo Boiocchi, MD
Assistant Attending Pathologist, Hematopathology Service



Amy Duffield, MD, PhD
Associate Attending Pathologist, Hematopathology Service



Mark D. Ewalt, MD
Assistant Attending Pathologist, Molecular Diagnostics Service and Hematopathology Service



Ying Liu, MD, PhD
Assistant Attending Pathologist, Diagnostic Molecular Service and Hematopathology Service



Dianna Ng, MD
Assistant Attending Pathologist, Cytology Service



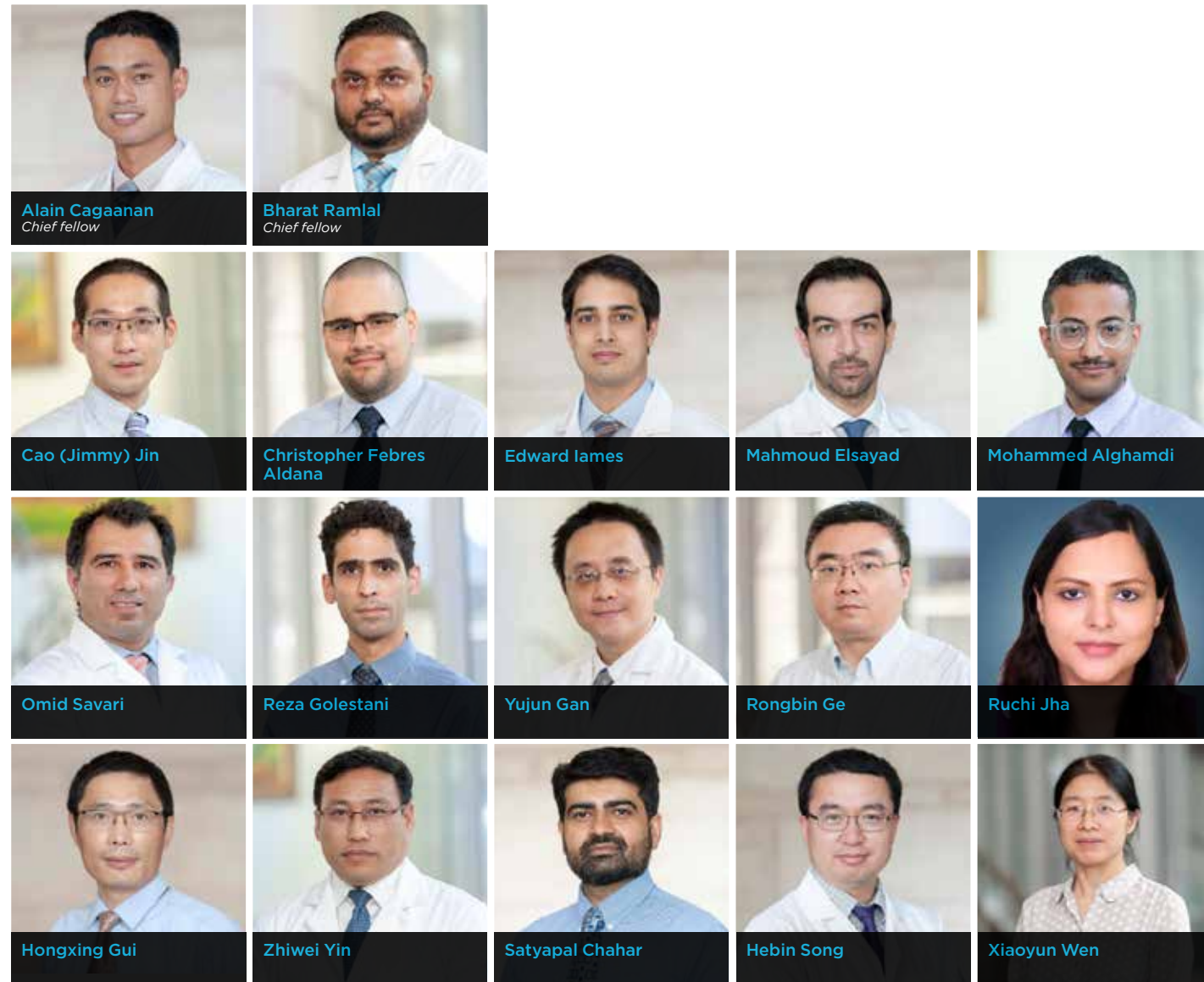
Panieh Terraf, PhD
Assistant Attending Molecular Geneticist, Molecular Diagnostics Service



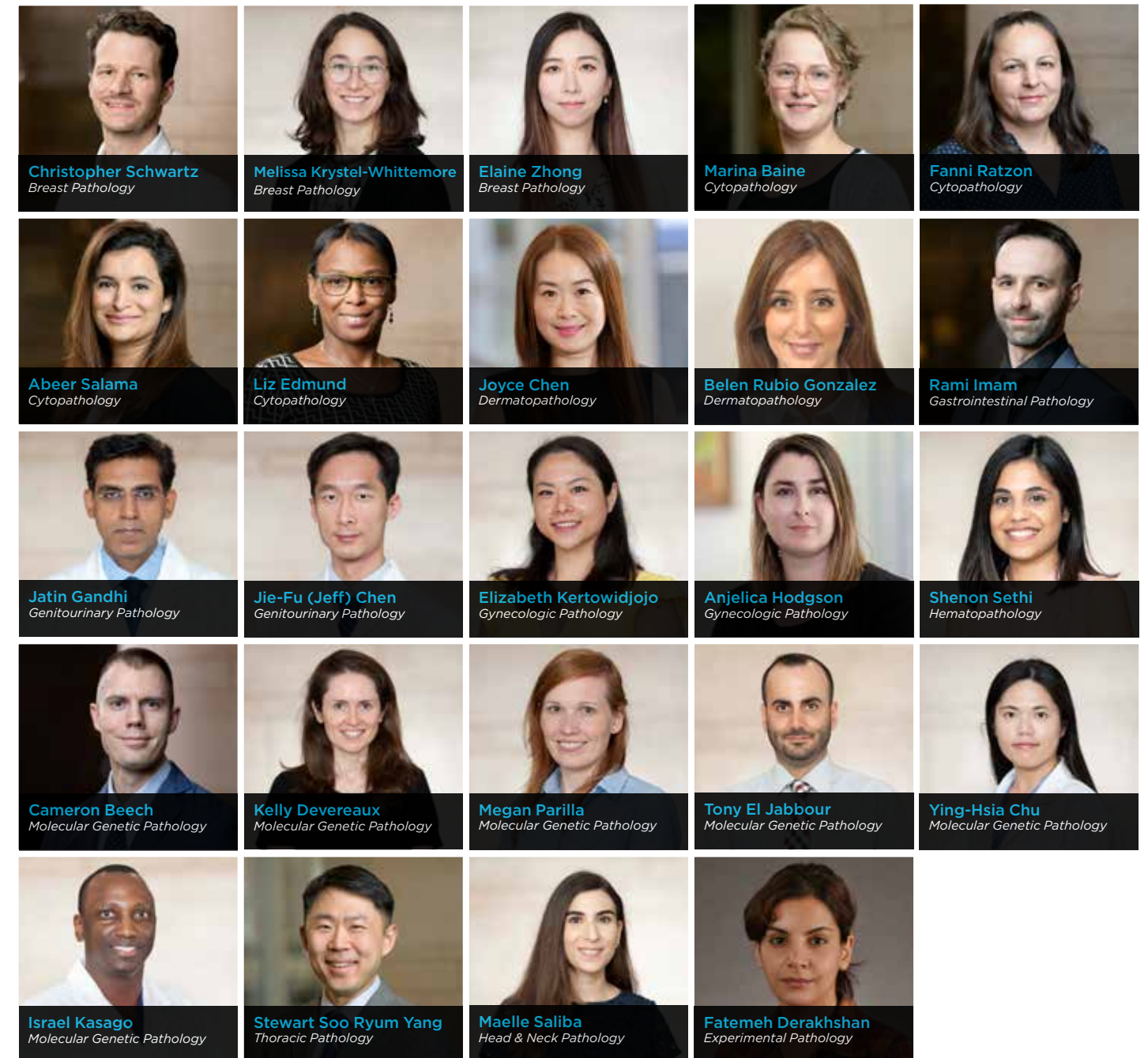
Menglei Zhu, MD, PhD
Assistant Attending Pathologist, Molecular Diagnostics Service and Hematopathology Service

2020-2021 Fellows

Oncological



Specialty



2020 Summer Students

The Department of Pathology Summer Student Program provides an opportunity for students to spend the summer at Memorial Sloan Kettering Cancer Center working side-by-side with laboratory professionals and senior administrative leadership. Students who are knowledgeable, self-motivated, and passionate about a career in healthcare are encouraged to apply for the 2021 cycle.

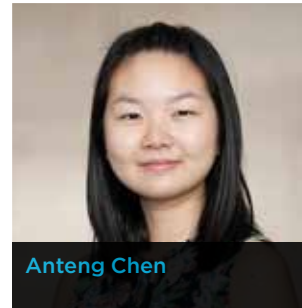


If you are interested in applying to the Department of Pathology Summer Student Program, please visit:

<https://www.mskcc.org/departments/pathology/summer-student>

Please note that applicants must meet the following criteria:

- 3.0 grade point average
- A genuine interest in healthcare career opportunities and laboratory sciences
- Must be 14 or older by June 15, 2021
- Eligible to work in the United States
- Must be able to make a six-week, full-time commitment (37.5 hours per week) to the program from July 5, 2021 to August 16, 2021
- Submission of application materials by April 1, 2021



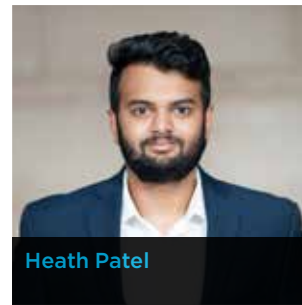
Anteng Chen



Jeremiah Ntiamoah



Michelle Moe



Heath Patel



June Kim

Q&A

Pathology Department Molecular Diagnostics Laboratory Technologists

Nana Yaa Mensah, Utsav Patel, Coleman Spence, Tanaz Dahya, Meiyi Wang, Zarina Yelskaya, Jada Barbee and Daniela Elezovic

By Kayt Sukel

Editor's Note: While the Pathology Review Q&A typically features one outstanding individual discussing their work, we're highlighting here the phenomenal contributions of our laboratory technologist team. These pathology department professionals ably assisted Memorial Sloan Kettering (MSK) Cancer Center's Department of Laboratory Medicine as they rolled out COVID-19 viral and antibody testing.

Q How did the pandemic change your day-to-day duties as a laboratory technologist?

Zarina Yelskaya: As a technologist, I test patient samples and patients' family members for germ-line DNA alterations that may predispose them to cancer. I do this using molecular diagnostic techniques, among other things. With the rapidly evolving COVID-19 situation, MSK had to take critical steps to minimize risk and exposure to the virus for patients and employees. The microbiology laboratory was overwhelmed with incoming testing, in addition to having to carry out thousands of novel COVID-19 tests. As a New York State licensed clinical laboratory technologist, I felt I was in a unique position to help the microbiology lab with testing without leaving my own lab short-handed.

Q What were some of the biggest challenges of supporting Laboratory Medicine as they developed COVID-19 testing?

Nana Yaa Mensah: Because of the novel character of the virus, and the lack of understanding of its functionality, it was quite difficult to work with. We are still working to understand its mechanisms. Molecular testing techniques will bridge anatomic pathology as research continues to yield more information about the virus.

Because it is so new, we all took great care to remain safe and avoid cross-contaminating any samples. We also faced the challenge of having a large number of samples since the traditional workflow of Laboratory Medicine remained quite high while we were completing COVID-19 tests. And since social distancing was a concern, staff presence was reduced, too. We overcame these challenges by working as a team to modify our workflows to get what we needed done.

Q How did it feel to contribute to this undertaking?

Coleman Spence: It gave me an immense sense of pride to be able to assist with this effort. I also felt very supported by my supervisor and co-workers in Pathology. It was amazing to see the community and hospital show their support, too. My usual role at MSK is in research, and I am still fairly new to the organization, but it was eye-opening to see how expansive this institution is and have the exposure to the clinical lab space in microbiology. I spent three weeks organizing samples and doing the rapid assay test for COVID-19. I left knowing that I was able to lend my skills and help during this crazy time. It felt good to be able to do something to help curb this pandemic.

Q How will this experience change the way you work at MSK?

Daniela Elezovic: I believe this pandemic has led many of us to start thinking outside the box and contribute more ideas to better ourselves, not just in the lab, but across MSK. I think it would be very useful to cross-train laboratory technologies across different departmental teams to help other team members understand workflows they aren't familiar with, bring in new ideas, and provide a helping hand when unexpected conditions arise, such as in a pandemic like this one.

Q How has this changed the way you see your role, both inside and outside of a pandemic?

Nana Yaa Mensah: I have always seen myself as an integral part of a team dedicated to the eradication of cancer in all its forms around the world. The COVID-19 pandemic, however, has put a new spotlight on the role of global health in our society. I believe that our hospital systems will be able to better save lives on a worldwide scale as we continue to work together as a team to control this new virus.

Pictured below left to right: Tanaz Dahya, Coleman Spence, Jada Barbee, Zarina Yelskaya and Nana Yaa Mensah (not pictured: Utsav Patel, Meiyi Wang, Daniela Elezovic)



Sixth Annual
**Translational
Research
in Pathology**

April 1, 2021
VIRTUAL EVENT

**The Pathology of
Neoplastic
Diseases**

May 3-7, 2021
VIRTUAL EVENT

**Medical Laboratory
Professional's Week**

April 26-30, 2021
VIRTUAL EVENT



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ICYMI: @MSKPathology's #CaseoftheQuarter featured in the #MSKPathologyReview courtesy of @MGHannaMD. Diagnosis provided in our next issue and on Twitter and Instagram. #breastpathology #pathpresenter #MSKPathology

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Today marks the "first day" anniversary for some of our most distinguished alumni: Drs. Frank Foote, Jr. (1959), Patrick J. Fitzgerald (1972) and Myron Melamed (1979). Today we also welcome the new 2020-2021 class of @MSKPathology fellows @sloan_kettering #MSKPathology

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We are sad to share news of the death on July 7 in Milan, Italy of Juan Rosai, MD, who served as the James Ewing Alumni Chair and Chairman of @MSKPathology at @sloan_kettering from 1991 to 1999. One of the most influential figures in #surgicalpathology of the last 50 years, whose broad diagnostic expertise was recognized worldwide, Dr. Rosai's impact on clinical care, research, & education cannot be overstated. For much of his career, he served as a consultant to the international pathology community, providing expert second opinions and making enormous contributions to direct patient care. A world-renowned pathologist, as well as a treasured friend to many, his generous spirit and ability to build consensus are as much a part of his legacy as his unparalleled expertise. We are grateful to have known him and extend our heartfelt condolences to his family. #JuanRosai #MSKPathology

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Earlier today, members of #CookiesvsCOVID from @SARHighSchool delivered these for @MSKPathology staff! Our #healthcareheroes continue to work diligently around the clock for our @sloan_kettering patients and these treats were very much appreciated!! Thank you!!

INQUIRIES about the *MSK Pathology Review* should be addressed to

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Hematopathology

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