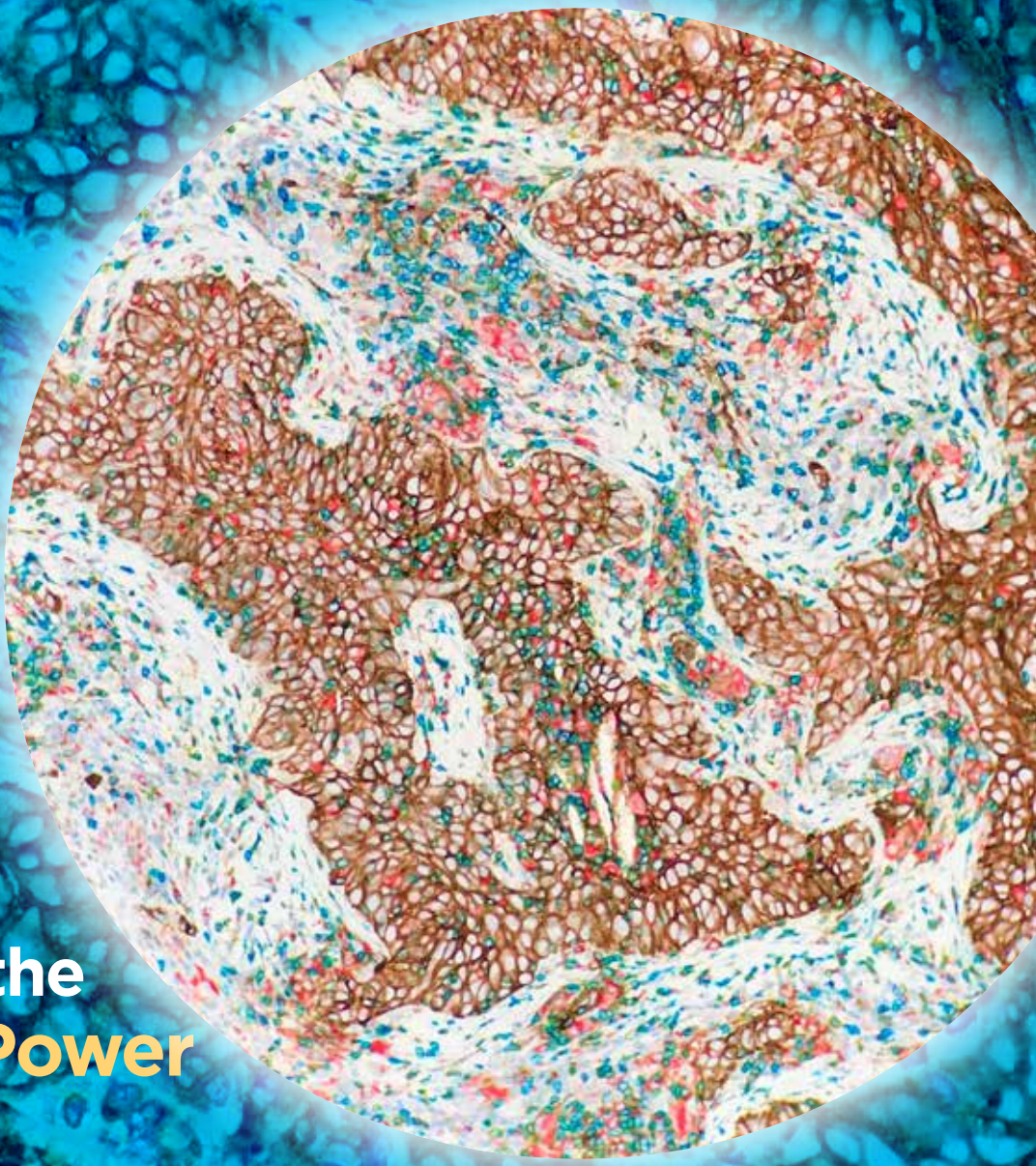
MSK PATHOLOGY REVIEW

Initiatives
Innovations
Accomplishments

1st Quarter 2020



Harnessing the Diagnostic Power of Proteins

Memorial Sloan Kettering is committed to fulfilling the promise of protein-based diagnostics.

Memorial Sloan Kettering Cancer Center

Commentary from the Department Chair

The current issue of the *MSK Pathology Review* continues our series of faculty research profiles, with Mauri Scaltriti, Jen Sauter, and Misha Roshal sharing their interests. We also examine our efforts in protein-based diagnostics, which have evolved from conventional immunohistochemical stains to multiplexed immunomorphology assays to mass spec-based protein detection and profiling. The new leadership of the autopsy program by Dilip Giri and Raj Murali is featured, as is our rejuvenated Grand Rounds program being led by Natasha Rekhtman and Hikmat Al-Ahmadie. These are all important topics that I hope will be of broad interest.

But of course, over the past three months, our attention has been focused on a topic of much broader impact to our patients, our staff, and our community–namely, the pandemic caused by SARS-CoV-2 and our response to the resulting illness, COVID-19. This disease has impacted everyone in some way, and our Department has been working continuously to adapt our activities, developing new workflows that allow for social distancing, experimenting with fully digital sign-out and telepathology, and piloting ways to work remotely. We have had to modify the close interactions we enjoy with our fellows, and we have had to devise new ways to ensure a robust educational experience for them. While most of the modifications to our processes are difficult to see as positive changes, the pressures of adapting to the pandemic have allowed some innovations that will hopefully persist beyond the immediate health emergency. The next issue of the *MSK Pathology Review* will be devoted to the Pathology Department's response to the COVID pandemic and will highlight how some of our new processes are actually helping us move forward initiatives like digital pathology and remote connectivity. But for now, we can take a break from the ongoing pressures of responding to this illness to enjoy stories that reflect an earlier time–which seems rather distant right now–when coming to work, looking at slides and data, conducting research, and teaching our fellows were the greatest challenges we had to consider!

- David Klimstra, MD

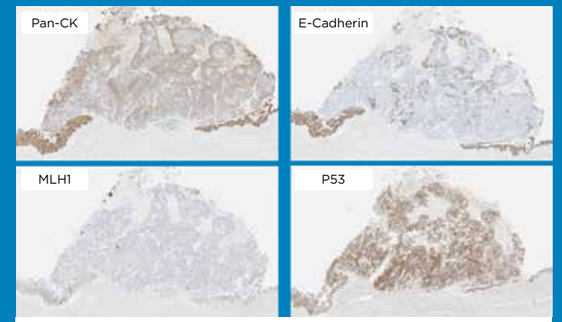
"The next issue of the *MSK Pathology Review* will be devoted to the Pathology Department's response to the COVID pandemic and will highlight how some of our new processes are actually helping us move forward initiatives like digital pathology and remote connectivity"

Case of the Quarter

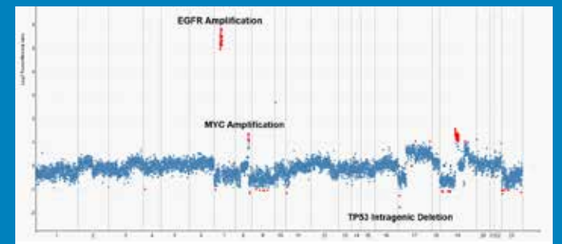
CASE HISTORY

21 year old female who presented with increasing abdominal distention and pain. Transvaginal ultrasound showed a 15 cm mid-pelvic mass reaching to the periumbilical region. Ca-125 was within normal limits. She underwent unilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection, omentectomy and appendectomy. The ovary consisted of a predominantly cystic mass with a solid mural nodule. Images are from the ovarian mass.

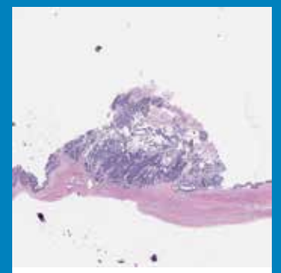
Scan the QR code to view digital slides available on mskcc.pathpresenter.com



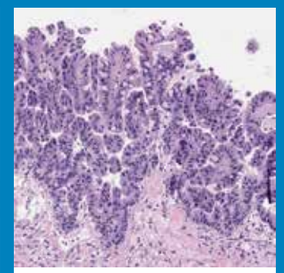
Ovary Immunohistochemistry



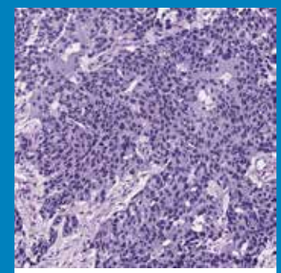
IMPACT Mural Nodule



Ovarian Tumor



Ovary Cyst Wall



Ovarian Mural Nodule

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

DIAGNOSIS: LAST ISSUE

Metaplastic (spindle cell) carcinoma arising from a malignant adenomyoepithelioma.

Maurizio Scaltriti, PhD, Dives Deep to Solve the Problem of Treatment Resistance

By Kayt Sukel

The research career of Maurizio Scaltriti, PhD, has been guided by one overarching question: Why do some tumors respond better than others to specific therapies?

Treatment resistance is a persistent challenge in addressing different forms of cancer. Some drugs simply don't work for every patient, even though, in theory, they should, said Dr. Scaltriti, principal investigator of the Human Oncology and Pathogenesis Program (HOPP) at Memorial Sloan Kettering Cancer Center (MSK).

"Many patients with the same genomic abnormalities should respond to a drug that works on those targets," he explained. "Yet even when the science tells us a group of patients with these characteristics should be sensitive to a given therapy, we often see that some are, and some are not. That begs the questions: What are the mechanisms of resistance in the people who do not respond to the drug? And what can we do about it so they can be more effectively treated?"

Dr. Scaltriti and his team spend their days trying to understand the wily ways of solid tumors and the mechanisms of resistance. The importance of this work can't be understated. While some patients may not respond to a given drug immediately, others will show modest improvements and then build up resistance over time. Once resistance to the go-to drug for a type of cancer occurs, there's not much clinicians can do, at least for the moment, to continue fighting the disease.

"Too often, the problem is not that we don't have an active drug to use. It's that it stops working at some point, allowing the disease to progress unchecked," Dr. Scaltriti said. Understanding why a drug is either not working or stops working offers researchers an opportunity to try new strategies.

DELVING DEEPER

Dr. Scaltriti and his colleagues use a variety of genetic and molecular techniques to understand how tumors cope with pharmacological pressure, or the consistent use of a drug over time. It is challenging work, he said—mostly because tumors are "very smart."

"Tumors evolve quickly, and can adapt to pharmacological pressure—really, to anything clinicians do to try to fight it—especially in cases of metastasis," he said. "Sometimes we outsmart them, sometimes they outsmart us. But to be in a better position to outsmart them, we need to understand, at the molecular level, how the tumor is adapting to the drug, radiation, or chemotherapy. There may be more than one mechanism of resistance. That's why it's so important to find ways that we can reliably identify each tumor's Achilles' heel, or heels."

By recognizing the vulnerabilities of certain cancer cells as well as the strengths that allow them to resist treatment, Dr. Scaltriti aims to provide new targets for more refined drugs, as well as increasingly personalized therapeutic strategies. His research has led to several breakthroughs on that front. As published in a 2019 *Nature Medicine* paper, he and his colleagues found that activation of the MAPK pathway is important in inducing resistance to TRK inhibitor drugs, commonly used to treat several cancer types.

"These drugs usually work very well for almost all patients," he said. "In some cases, the use of the drug activates other pathways. These are pathways that were not important to the tumor before, but once the drug is in use, the tumor finds them. We were able to take this finding and go back to the patients who were resistant and then give them a targeted therapy to turn off the MAPK pathway, and to reinstate a response to the treatment. That's the kind of personalized medicine that has a lot of clinical relevance."

Dr. Scaltriti has also studied the relationship of other pathways to treatment resistance in lung and breast cancers.

"Identifying these possible genetic causes of resistance is something that is very useful to the clinic," he said. "It can help doctors develop the best possible treatment plans for each patient."

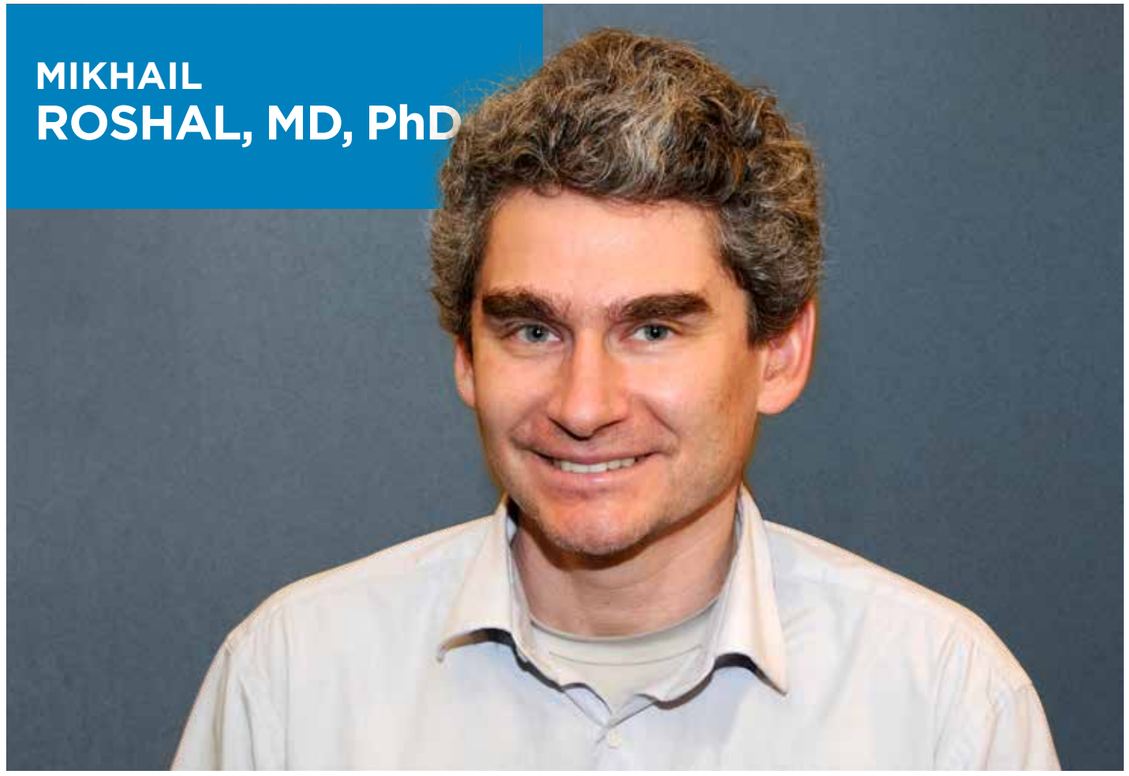
A TEAM EFFORT

While some may be surprised that Dr. Scaltriti finds himself as part of the pathology department at MSK, he said it was a good place for him to land. "When you do a lot of translational work, you need a lot of samples," he said. "For the kind of research I do, I need all types of specimens, from cell-free DNA to tumor biopsies."

He said his successes are due to strong collaborations with clinicians and other MSK staff—as well as working in an institution that sequences the DNA of almost every patient who walks through its doors.

"Having this kind of information available is invaluable in getting to know a tumor and understanding what its vulnerabilities might be," he said. "In finding the mechanisms of resistance, we can offer more benefits to patients who may no longer be responding to a particular treatment. Also, we may be able to help future patients avoid resistance by selecting a therapy that they are more likely to respond to. This is our goal for every project in my lab."

"Identifying these possible genetic causes of resistance is something that is very useful to the clinic," he said. "It can help doctors develop the best possible treatment plans for each patient."



Mikhail Roshal, MD, PhD, Looks for a "Needle in a Haystack" to Treat Recurring Blood Cancers

By Kayt Sukel

The American Cancer Society estimates that more than 60,000 new cases of leukemia, or cancers of the bone marrow and blood-forming organs, will be diagnosed in 2020. Traditionally, patients with this diagnosis are treated with chemotherapy—and approximately 70% will achieve a complete remission after completing a course of treatment. Unfortunately, said Mikhail Roshal, MD, PhD, a member of the Memorial Sloan Kettering Cancer Center (MSK) Hematopathology Service, relapse will happen for about half of those individuals. Worse, they'll often end up suffering with a much more aggressive form of leukemia or other cancerous disease.

"Those 50% are the patients who need additional therapies," said Dr. Roshal. "Unfortunately, it's difficult to identify them upfront. Finding ways to understand who is most likely to fail the initial therapy, and monitor them to figure out how their bodies are responding to that therapy, and what other types of treatment might be of benefit, could help us reduce the number of patients who go on to relapse after remission."

To find the patients who may need further treatment, Dr. Roshal is trying to correlate low levels of disease, which is often referred to as measurable or minimal residual disease (MRD) and is detected by flow cytometry and other molecular tests, with patient outcomes. MRD is the small number of lingering cancer cells that remain in the body after treatment and into remission. It's now established that the risk of relapse is proportional to the level of MRD in the body—and, as such, it is the major cause of relapse in diseases like acute myeloid leukemia (AML).

"The sheer numbers of samples that are available for study means we can not only look for things that may help us better tailor treatments for an individual patient, but also search for common factors that can help larger groups."

LOOKING FOR A NEEDLE IN A HAYSTACK

Dr. Roshal explained that trying to detect specific biomarkers that can be used to develop new targeted therapies for those patients most likely to remit is a challenge. The main reason? Leukemia is a heterogeneous disease by nature. Finding different genetic markers or proteins that might be an effective treatment target is a bit like looking for a very tiny needle in a very messy haystack.

"We tend to think about AML, for example, as a single disease. We even talk about it that way clinically," he said. "But it's really a large mixture of different diseases with heterogenous behaviors—and heterogenous outcomes. Developing therapies for AML and even just looking for biomarkers that can help us detect residual disease is difficult due to the number of different entities all grouped together. We want to find biomarkers and approaches that suit the largest number of patients—but it takes time."

Many patients who relapse or develop other forms of cancer after AML treatment face a bleak prognosis. With more targeted therapies available, said Dr. Roshal, those patients are more likely to be successfully treated the first time around—avoiding potentially deadly recurrences altogether.

WORKING TOWARD A COMMON GOAL

Dr. Roshal credits his extensive collaborations with other researchers at MSK and scientists at outside institutions with helping to identify some of those markers. In fact, some of their work has initiated the development of a targeted antibody therapy that may one day be used to help treat AML patients. The ability to form those collaborations is one of the reasons why he is happy he came to MSK eight years ago.

"There are plenty of strong research institutions," he said. "But MSK's research resources are exceptional. I have spectacular colleagues, both in hematopathology and in the medical oncology service here. But MSK also offers us a cooperative and supportive research environment. It's an atmosphere that really facilitates new ideas and people trying to work to the highest level of their fields."

It is also a benefit that MSK's hematopathology service runs such a high volume of samples. Tens of thousands of hematological biopsies and flow cytometry cases are handled in the service each year—and many patients consent to have those samples used in research projects like Dr. Roshal's. The more samples available to Dr. Roshal and his colleagues, the more opportunities they have to identify the critical molecular markers they seek.

"We see things here that are rarely seen at other institutions," he said. "The sheer numbers of samples that are available for study means we can not only look for things that may help us better tailor treatments for an individual patient, but also search for common factors that can help larger groups."

Dr. Roshal enjoys his work immensely—and is driven by the stimulation that comes from working with innovative technologies that allow more precise molecular and protein-based characterization of MRD cells.

"Progress will always be incremental—and it will always require a team approach," he said. "But with such spectacular collaborators and resources, I'm able to investigate novel targets that I might not be able to otherwise. In doing so, I get to play a role in helping better treat patients with leukemia in the future."

HARNESSING THE DIAGNOSTIC POWER OF PROTEINS

Memorial Sloan Kettering is committed to fulfilling the promise of protein-based diagnostics.

By Kayt Sukel

Over the past decade, the medical and scientific communities have been working to promote truly personalized precision medicine. At the completion of the Human Genome Project, the hope that oncologists would be able to examine the genetic changes in a patient's cancer and then select the best treatments to address those changes grew. Yet genes alone can't tell the whole story of a tumor, said Travis Hollmann, MD, PhD, Director of Advanced Immunomorphology Platforms at Memorial Sloan Kettering Cancer Center (MSK).

True precision medicine, both at the diagnostic and treatment levels, will require taking a closer look at proteins.

"A protein is the functional end product of a gene. It's the part that is essentially doing a gene's business in the majority of cancer cases," he said. "While we have accrued a lot of data on genomics, as well as expression data on RNA, protein data has been more difficult to assess—and that's the type of data that could make our diagnoses and subsequent treatments more precise."

Proteomics, the large-scale study of proteins, is an emerging field with much to offer in terms of pathology and cancer diagnostics. For more than a century, physicians have used different proteins as simple diagnostic markers in a variety of medical conditions, including various types of cancer. Yet despite the millions of protein molecules estimated to be housed in a single cell, it has been a challenge to expand this important portfolio of biomarkers into a higher level of precision care. Michael Roehrl, MD, PhD, gastrointestinal pathologist and director of MSK's PPBC, said identifying the proteins that may be most useful for diagnostic purposes remains a challenge.

"People thought for a long time there was a direct relationship from DNA to RNA to proteins. There's a mutation in a gene, that mutation makes it into the RNA, and then that produces a mutated protein," he explained. It was presumed that an amount of RNA is correlated with the amount of protein but, he added, "that doesn't really hold up. We now understand that trying to predict which genetic aberrations at the DNA/RNA level actually make it into the protein domain is quite difficult. But since these proteins actually carry out the biochemistry, those functional things that happen in a cell, and ultimately, in the processes that lead to cancer, these are the components we need to track in order to understand what is driving disease."

That's why MSK's pathology department is committed to developing and validating innovative protein-based diagnostic tests using state-of-the-art methods and tools. The department's new Clinical Proteomics Laboratory now offers the first clinical laboratory in New York State to do comprehensive proteomic phenotyping of human cancer tissues. Ahmet Dogan, MD, PhD, chief of hematopathology, argued the addition of proteomic results to more traditional diagnostic methods has the strong potential to enhance patient care—and provide the kind of precision medicine clinicians and patients seek.

"Protein-based diagnostics identify the consequences of genetic changes related to cancers," he said. "Precision medicine drugs could target those proteins, not the genes, for a better result."

IMPROVED DIAGNOSTIC METHODS

One area in which a more comprehensive understanding of proteins can assist with diagnosis is in improved immunohistochemistry techniques. Pathologists all over the globe rely on this technique, which utilizes antibodies to identify antigens of interest in a tumor to make accurate diagnoses, said Achim Jungbluth, MD, PhD, an attending pathologist at MSK.

"The rise of immunohistochemistry as a robust diagnostic method only began in the late seventies with the introduction of monoclonal antibody technology by Kohler and Milstein. Earlier, animal sera containing the antibodies of interest were commonly used but mostly in a research setting. Today the mostly monoclonal antibodies we use in these tests are sensitive tools which are able to distinguish different molecules, mostly proteins, which enable the pathologist to differentiate different tumor types," he explained. "With classical chemical staining methods such as hematoxylin/eosin, there is only so much you can say about a tumor. But tumor research reveals that certain types of tumors express certain types of proteins—so an 'in-situ' protein expression analysis done on a tumor section can give you a lot of information to further define the tumor and put a clear label on what disease is actually there on the slide."

With so many potential proteins or other molecules of interest that can be detected by antibodies in different cancers, Dr. Jungbluth said "specificity is key." He and his team are working to create specialized protocols so only the appropriate and desired proteins are stained. In doing so, they can move such tests more quickly from the bench to the bedside.

"The most important thing is to make sure the method you use is actually detecting the proteins it's supposed to be detecting," he said. "My lab's goal is to establish standardized, reliable immunohistochemical protocols that can be used in our clinical immunohistochemistry labs to provide the kind of specificity required for accurate diagnosis."

PROTEOME PROFILING

With advances in proteogenomics, Dr. Roehrl's lab studies how proteome signaling in cancer changes over time. Those biomarkers can then better inform diagnosis and treatment selection.

Jessica Chapman, PhD
Director, Clinical Proteomics

Ahmet Dogan, MD, PhD
Attending Pathologist
Chief, Hematopathology Service

Travis Hollmann, MD, PhD
Associate Attending Pathologist

Achim Jungbluth, MD, PhD
Attending Pathologist

Michael Roehrl, MD, PhD
Associate Attending Pathologist
Director, Precision Pathology Biobanking Center (PPBC)

"Once you start treating a patient, you are basically perturbing the protein network," he said. "So if you can measure the proteins and see what happens to them quantitatively, their chemical activation state, and how they are interacting with one another, both before and after treatment, you can get a better idea of whether or not that treatment is working."

Using a variety of biochemical tools including high-resolution mass spectrometry, he and his lab colleagues have discovered novel proteins in colorectal cancer that correlate with its propensity to metastasize, and his lab is developing pan-proteome profiling of cancers.

"Understanding the dynamics of the proteome requires precise quantitative measurements," he said. "Our technologies have the potential to transform pathology and bring proteome-driven diagnostics and treatment monitoring to patients."

DIGITAL PATHOLOGY

With so many proteins circulating in a single cancer cell, it can be difficult to identify which have the most clinical relevance. Today, diagnostic pathologists generally assess 1-2 proteins on a single slide and sometimes between 10-20 slides per patient to fully interrogate the expression of proteins in a tumor and the tumor's microenvironment (the blood vessels, immune cells, fibroblasts, and other signaling molecules that surround the tumor) for a diagnosis.

Dr. Hollmann's laboratory is examining ways to simplify that work so that pathologists can do these assays on a single tissue slide, reducing the time, effort, and valuable patient tissue used to derive the information required for diagnosis.

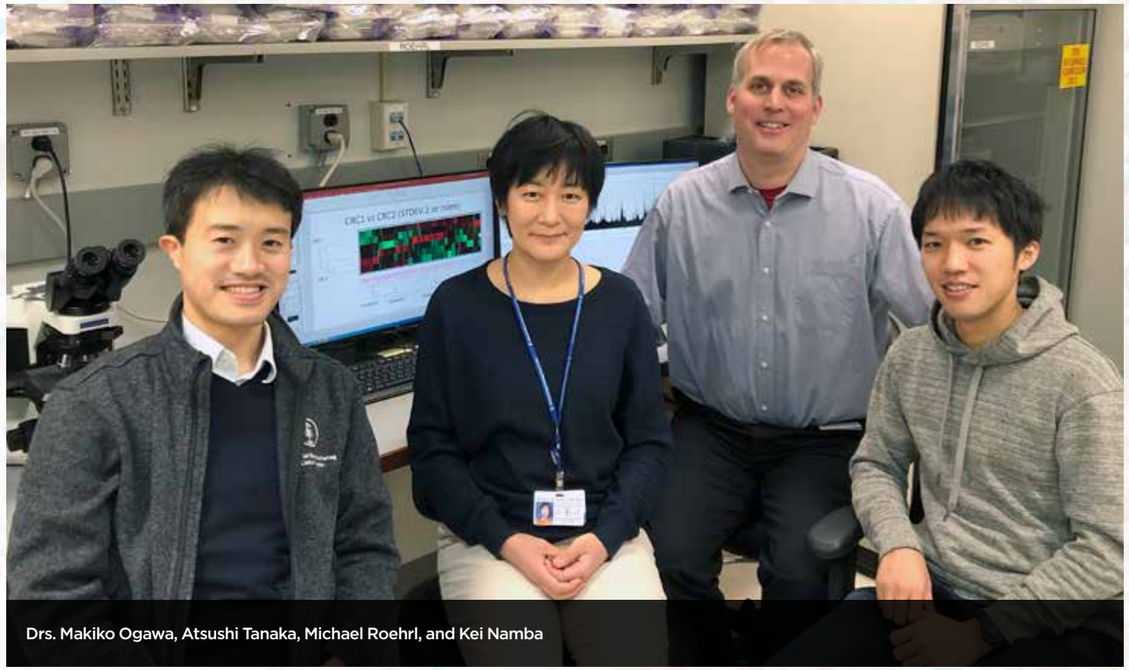
"The benefit of having many markers on a single slide is that you retain co-localization and the subsequent quantification of coexpression and proximity," said Dr. Hollmann. "Much of this technology is reliant on new digital detection devices using more sophisticated microscopes than what pathologists use today. The The pathologist can then use digital tools on their computer to assess images, quantify, and make the diagnosis."

Reaching that point, however, will require more work. Dr. Hollmann said pathologists interested in furthering protein-based diagnostics need to study results from tissues used in prior clinical trials to associate proteomic discoveries with patient outcomes, as well as do more comparability projects with the current gold-standard being conventional immunohistochemistry.

"This is a good time to expand our digital pathology tools to include the analysis of protein-based tests. This will certainly improve quantitation in diagnostic pathology. These advances should ease a pathologist's job so they can accomplish more in less time, freeing them up to do more clinical or translational work," he said. "It also reduces the subjective element in diagnosis, which can improve our accuracy and reproducibility."

A PROTEIN-BASED TEST FOR AMYLOIDOSIS

Unfortunately, cancers often travel with other conditions which can directly affect a patient's outcomes. One of those disorders is amyloidosis, a condition in which misfolded protein is deposited extracellulary, displacing healthy tissue. A subset of patients with blood cancers will develop amyloidosis, which is quite difficult to diagnose. Recently, however, MSK developed and validated the first clinical assay to diagnose amyloidosis. This is highly significant, says Dr. Dogan: "It is the first time such an assay has been clinically implemented in New York State and the Northeast."



Drs. Makiko Ogawa, Atsushi Tanaka, Michael Roehrl, and Kei Namba

Jessica Chapman, PhD, director of MSK's Clinical Proteomics Laboratory, said this protein typing test, using formalin-fixed paraffin embedded (FFPE) tissue, can identify the protein responsible for amyloidosis before too much damage has been done—and can help clinicians better select the right course of treatment for patients.

"Amyloidosis is underdiagnosed because it comes with a tricky set of symptoms. This test can help," she said. "It starts when a pathologist reviews a case and considers it suspect for amyloid deposits. We then review it to see how much material we need for the test and I work with the surgical pathology labs to get the specimens in the way we need them. Then a clinical proteomics technologist will perform laser microdissection, protein extraction and then analyze those on the mass spectrometer."

When Dr. Chapman first came on board at MSK, her primary role was to get the test validated for clinical use, a task that took significant time and effort. She and her colleagues instituted comprehensive quality-control systems and standard operating procedures to meet New York State's vigorous regulations.

"It's just a mix of 15 peptides but there's a certain way they look when they come off the instrument," she said in reference to the daily quality standard they run on the mass spectrometer. "We make sure that we are running these tests under the correct parameters, so we know we are giving pathologists the right information to make decisions."

While the amyloidosis test was the first validated in the Clinical Proteomics Lab, Dr. Dogan said it will not be the last. They hope to validate a novel assay to assess minimal residual disease (MRD) in myeloma after treatment, to replace invasive bone marrow biopsies. They are also developing tests for diagnostic biomarkers in rare carcinomas and comprehensive typing of immunoglobin repertoires to assess the tumor microenvironment in different cancers.

"It is hoped that these novel assays will have broad applications, not only in the diagnosis of cancer but in predicting a patient's response to therapy," Dr. Dogan said.

MOVING FORWARD

Dr. Chapman said that finding ways to integrate proteomics into validated diagnostic tools will be a challenge. But with its addition to information pathologists currently collect regarding DNA, RNA, and other clinical features of disease, it should allow for more precise diagnoses and more informed evidence-based clinical decisions regarding treatment.

"Being able to give the most accurate diagnosis is the foundation to making sure that a patient is getting the proper care," she said. "There are a lot of challenges to both developing and then validating these tests. But when we can give clinicians relevant information, they have the ability to make sure patients aren't having to try different treatment protocols or go through extra procedures."

As research in proteomics progresses and leads to the identification of new biomarkers, it is likely to also play a role in the development of newer, more precise treatment regimens, added Dr. Hollmann. Current drugs don't affect genes, they affect targeted proteins. By knowing what proteins have changed in the tumor or the tumor microenvironment, there is the potential to develop more effective pharmacological interventions.

"Many patients will receive some type of combination therapy," he said. "But a lot of the current combinations that are being pushed through are not necessarily based on the specific biomarker profile of the tumor. In the future, we can use this technology to guide combination therapy. We can use proteomics to direct the patient to the correct clinical trial at the correct time in their therapy. We can use it to find new proteins we may not have considered before in drug development. There's a lot of potential there."

Dr. Chapman agreed. "Protein-based diagnostics is an area where we can have a lot of impact on clinical care," she said. "At the end of the day, I think that's why most of us do what we do here."

The protein-based diagnosis team at MSK has been fortunate and grateful to receive generous grant support from the Farmer Family Foundation.

Dr. Travis Hollmann

"This is a good time to expand our digital pathology tools to include the analysis of protein-based tests. This will certainly improve quantitation in diagnostic pathology."

Grand Rounds are Back, and Better Than Ever

Memorial Sloan Kettering Cancer Center's Pathology Department relaunched its grand rounds program to better meet the needs of its trainees and faculty.

By Kayt Sukel

Medicine evolves constantly, and continuing education is a key way clinicians can keep abreast of the latest advances in methods,tools, practice-based guidelines, and clinical trial results. And while physicians and other medical staff subscribe to academic journals and attend conferences to stay on top of new developments, few options for continuing education parallel Grand Rounds programs. These events—formal presentations of thought-provoking medical content by prominent experts in the field coupled with active discussions—offer physicians, trainees, scientists, and medical students another avenue to gain critical knowledge. That's why, David Klimstra, MD, the Pathology Department Chair, requested volunteers to reboot the program to better reflect the evolution of the field. Natasha Rekhtman, MD, PhD, a thoracic pathologist and cytopathologist, and Hikmat Al-Ahmadie, MD, a genitourinary pathologist, gladly heeded the call. The new team was charged with coordinating the Grand Rounds program as well as the nominations for the annual Gerald and Stewart awards, with Dr. Rekhtman as a lead for the Grand Rounds and Dr. Al-Ahmadie for the award nominations.

Clinicians in the Pathology Department can derive huge benefit from regular Grand Rounds presentations. "There are so many doctors and scientists who really are working at the cutting edge of their fields," Al-Ahmadie said. "When we can learn more about that work—what they've done, how they are approaching medicine's bigger problems, and how it might apply here at Memorial Sloan Kettering Cancer Center (MSK)—it really is of great benefit." Beyond those advances, the MSK Pathology Department has grown by leaps and bounds over the past few years. With so many new faces, there was also a need for new ways to bring people together in a collegial, educational atmosphere. "Beyond our faculty, a robust Grand Rounds program is tremendously beneficial to our fellowship program. It exposes our trainees to different perspectives held by experts from other institutions and provides fellows an opportunity to engage with them directly during the dedicated slide session or fellow lecture later in the day." said Dr. Rekhtman.

By organizing regular, ongoing presentations, at a more convenient time of day, pathologists, pathology trainees as well as other interested clinicians outside the department would be more likely to be able to fit the sessions into their busy schedules and directly benefit from attendance.

With logistical support from Sarah B. Virgo, the department's Education & Communications Manager, Drs. Rekhtman and Al-Ahmadie worked to revamp the department's Grand Rounds program to provide regularly scheduled monthly talks. Grand rounds speakers were selected after soliciting recommendations from members across the department. The new program also moved the sessions to a larger space and scheduled the talks at midday, with food provided for attendees, to make it easier for more people to attend.

"We asked each sub-specialty team to propose the names of people who are doing interesting and important work relevant to our field—and we reviewed those recommendations in an ordered, systematic way to coordinate a great program," said Dr. Rekhtman. "The goal is to invite people who are great educators or who are doing groundbreaking research."

The field of pathology has evolved pretty dramatically over the past decade, added Dr. Al-Ahmadie, with new methods and tools regularly coming online. Pathology team members wanted more ways to keep up with those innovations. "With so many new advances in medicine in general, as well as in pathology and genomic medicine, the way we understand how to diagnose and characterize disease has changed and will likely continue to change," he said. "With such a large department, with such diversified specialties and backgrounds, a Grand Rounds program that looks at the bigger picture, so to speak, is something that we hope will appeal to everyone."

Grand Rounds relaunched in September. Since then, said Dr. Al-Ahmadie, the sessions have been a "resounding success," with both attendance and engagement high. The first few gatherings featured invited speakers from outside institutions, but Dr. Al-Ahmadie said some of them had a connection to MSK. "Some were former trainees or colleagues who went on to become experts in their particular field," he said. "They set the bar quite high for the content and quality of their presentation, which is something we want to continue. If we are asking our colleagues to give up an hour of their time, we want to make sure it is worth it."

Dr. Rekhtman agreed. With the Grand Rounds team's new means of soliciting and vetting speaker nominations, however, she is not worried about finding qualified candidates. And as they move forward with the program, she and Dr. Al-Ahmadie are already thinking about ways to improve it for the department and the larger MSK community.

"Attendees' feedback has been overwhelmingly positive," she said. "It's been a great way for the whole department to come together at a regular time and learn about what's new and exciting in our field. In the future, we hope to include internal speakers as well as to develop educational seminars. The last few months are just the start. It's the foundation that we hope to keep building upon to make Grand Rounds indispensable for everyone."

Natasha Rekhtman, MD, PhD
Associate Attending Pathologist

2019 Grand Rounds Lectures

September 24
Characterizing and Targeting Epigenetic Dysfunction in Malignant Glioma
Jason T. Huse, MD, PhD
The University of Texas, MD Anderson Cancer Center
Departments of Pathology, Anatomical and Translational Molecular Pathology

November 5
Artificial Intelligence & Cytopathology
Liron Pantanowitz, MD
Professor of Pathology and Biomedical Informatics
University of Pittsburgh Medical Center

December 3
Three Reasons You Should Care About Breast Myoepithelial Cells
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January 21
Where are We Going? One Person's View of a Future for Molecular Diagnostics in Cancer
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Jennifer Sauter, MD Puts Mesothelioma Under the Microscope

By Kayt Sukel

Just over three years ago, Jennifer Sauter, MD, finished her fellowship work and embarked on a position in thoracic pathology at Memorial Sloan Kettering Cancer Center (MSK). As someone driven by delving deeper into histologic factors involved with pleural mesothelioma, an aggressive tumor that effects the lung's pleura, she knew MSK had unparalleled resources to help her in that mission.

"There are so many phenomenal resources at MSK that it seemed like a natural fit for me," she said. "MSK Pathology houses a large number of archival cases we can study and learn from. We have tremendous assets like next-generation sequencing (NGS) technologies so we can obtain robust molecular data and active clinicians who want to collaborate on innovative research projects. It felt like coming to MSK would put me in a good position to study the pathology of mesothelioma in a really comprehensive way—and to advance the field."

Mesothelioma affects approximately 3,000 people, mostly men, each year and is an aggressive disease with very poor overall survival. Dr. Sauter is committed to discovering microscopic clues that can improve clinical management for patients with mesothelioma.

"Traditionally, mesothelioma is diagnosed by histologic subtype. We identify the tumor as either epithelioid or sarcomatoid, or biphasic, tumors that contain both epithelioid and sarcomatoid components," she explained. "But we are finding we can become more granular in our histologic reporting to identify tumors within the epithelioid subtype that will likely behave more aggressively to help clinicians better stratify patients."

PINPOINTING MOLECULAR MARKERS

Going beyond the classic subtyping of mesothelioma and providing more information, including the nuclear grade of the tumor, may change the way a patient is treated. Dr. Sauter added that identifying unique histologic patterns, as pathologists do for lung adenocarcinomas, has the potential to better inform clinical decision-making.

"For example, patients with epithelioid mesotheliomas with a lower nuclear grade have a better prognosis than those with a higher nuclear grade, whereas epithelioid mesotheliomas with a pleomorphic component tend to behave more aggressively," she said. This information is useful to oncologists in making management decisions for these patients. But there is still much to learn.

"Currently, there are some subtypes of mesotheliomas where the data are unclear, particularly with rare features that we do not often encounter, so it will be important to accrue more data to determine what they may mean for the patient. The hope is that by including more histologic data in our reporting we can help clinicians better manage patients."

BETTER BIOMARKERS

Dr. Sauter's research is also directed toward identifying more effective biomarkers that can be used for targeted immunotherapy in mesothelioma. Oncologists are beginning to utilize immunotherapy to combat this disease, but outcomes have been mixed. PD-L1, for example, is a biomarker used across a variety of tumor types to help select immunotherapies. But that same pathway may not work as well for pleural mesothelioma. Dr. Sauter and her colleagues recently studied V-domain Ig-containing suppressor of T-cell activation (VISTA), a protein that is highly expressed in mesothelioma tumors and may be a more apt target for this disease.

"We now have anti-VISTA antibodies that can be used to target tumors that express VISTA," she said. "Alternative targets, beyond PD-L1, may be more useful in treating mesothelioma since the majority of mesotheliomas do not express PD-L1 and mesotheliomas generally have a low mutation burden. VISTA may be a better target for immunotherapy in pleural mesothelioma. Here at MSK we recently started a clinical trial that utilizes a combined anti-PD-L1 and anti-VISTA regimen for patients with mesothelioma."

Dr. Sauter discusses her ongoing work with a mixture of hope and enthusiasm. At the end of the day, she's genuinely excited to be at her microscope learning about thoracic tumors and trying to find ways to improve cancer care for our patients.

"It's thrilling to be able to actively participate in collaborative work with our colleagues throughout the institution that can be translated into improving cancer care for our patients," she said. "The work we are doing will help us better understand tumor biology in a more detailed way and can help our clinicians develop or utilize new targeted therapies for these hard-to-treat tumors."

> "What we're doing now is helping us to understand tumor biology in a much more detailed way, which will one day help our clinicians develop or utilize new targeted therapies for these hard-to-treat patients."

AUTOPSY PROGRAM

Rajmohan Murali, MBBS, MD, FRCPA
Associate Attending Pathologist
Director, Last Wish Program
Co-Director, Clinical Autopsy Program

Dilip Giri, MD, FACP
Attending Pathologist
Director, Clinical Autopsy Program
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Clinical Insight: the Ultimate Gift

The Autopsy Program of the Department of Pathology provides clinicians and researchers with unique, invaluable insights into the nature of cancers.

By Kayt Sukel

Modern medical knowledge is built upon discoveries revealed by autopsy, the external and internal examination of a cadaver to determine the cause and manner of death. In fact, before the advent of innovative imaging technologies, autopsy was the only way clinicians could unravel the mysteries of human anatomy or track the physiological consequences of different disease states.

Rajmohan Murali, MBBS, MD, FRCPA, Director of the Last Wish Program and Co-Director of the Clinical Autopsy Program at Memorial Sloan Kettering Cancer Center (MSK), emphasizes the great value to science of performing these posthumous procedures. Autopsies aren't only of use to reveal the cause of a suspicious death. The development of innovative genetic and molecular tools make autopsy a remarkable tool to help clinicians and scientists better understand how different cancers and their treatments affect the human body.

"Over the last 150 years, we've seen the number of autopsies decline significantly for a variety of reasons," said Dr. Murali. "But autopsy, especially in cancer patients with disease-and treatment-related changes, can provide insights that can help us determine how to better manage cancer care in the future. Many of those insights would simply not be available to us without performing this kind of examination."

NOVEL CLINICAL INSIGHTS

Dilip Giri, MD, FACP, who directs the Clinical Autopsy Program, said the program provides both clinical and research autopsies to support different needs and programs at MSK. For example, clinicians may request an autopsy after a patient passes away to understand the exact cause and circumstances of death.

"The doctor may not know what exactly led to a patient's demise," he said. "Often, we are able to provide that answer by doing a complete autopsy. We then present those cases in a multidisciplinary conference so the requesting physician, as well as other clinicians, can better understand if the death resulted from clinical progression of cancer or from some other unsuspected or undetected factor."

Such information is of huge help to clinicians and can bring up new issues that they should consider in order to better manage the care of similar patients.

"We are trying to increase awareness, among both doctors and patients, about the importance of autopsy and what it offers to potential research studies."

"Many patients may have received different types of treatments over several years," said Dr. Giri. "They may have developed complications from such treatments. There are a lot of complicating factors that may have contributed to a patient's death. An autopsy can help pinpoint some of those factors by closely examining the different tissues. The autopsy findings can better inform future clinical management of patients. Physicians appreciate having that information, especially as they make decisions about how best to treat the patients."

Dr. Murali agreed. "Autopsies can also inform us about what a particular drug may be doing besides targeting the tumor. For example we may see, during autopsy, that a drug given to treat a patient's cancer had an unusual effect on the liver. Then, we connect that liver injury back to the drug. That is important information which can help clinicians make optimal treatment decisions for their patients.

NEW AVENUES FOR RESEARCH

Autopsies don't just offer clues to the cause of death—they also provide tissue samples critical to innovative research projects. Clinical biopsies only provide small amounts of tissue, which limits the types of tests or experiments researchers can perform. For example, Dr. Giri said one big question for cancer researchers is why treatment response for a certain drug or intervention may change over time in a single patient.

"Very often, for patients, the initial treatment response is great. They go into remission and have a good life for several years," he said. "But then the cancer comes back and the treatments no longer work on that recurring disease. Why is that?"

The question can be better answered when researchers can access tissue from both biopsies and autopsies. The tissue samples harvested from autopsies provide more of the vital material scientists require to follow the progression of disease, as well as to use innovative investigative methods like genetic and molecular approaches to understand what pathways a certain treatment acted upon—and where that treatment may have failed.

"It offers us a whole new way of exploring the treatment of cancer," said Dr. Giri. "That autopsy tissue may potentially offer researchers new molecular pathways to explore, and these may lead to future novel treatment."

There are many other research questions that can be investigated with autopsy-harvested samples, from why some patients never respond at all to treatment to how tumors metastasize in the body. Dr. Murali added that autopsy samples offer researchers the ability to directly compare different tissues or tumors in a single patient as the harvested samples provide them a lot more material to work with than what can be obtained through biopsies or other clinical means.

"Autopsy samples allow researchers to be much more comprehensive and clinically effective in their studies," he explained. "We can take multiple pieces of tissue from the tumor, from other tumors that may be also present in the body, and then from other organs or tissues as well. Studying these samples can help us understand how cancer develops, progresses and spreads. We can even look at how each of those individual sites respond to different treatments. It really expands what kinds of questions researchers can ask and what they are able to do in their studies."

MAKING A LAST WISH

Under the leadership of Christine Iacobuzio-Donahue, MD, PhD, MSK launched an initiative in 2015 aimed at gently encouraging more patients, and their families, to donate their bodies for autopsy. Over the past five years, the Last Wish Program has conducted over 150 autopsies, which have yielded around 12,000 tissue samples. Those samples are carefully stored in a tissue bank, a tremendous resource that scientists can tap for a variety of research purposes.

"It is a tremendous resource," said Dr. Murali. "We are trying to increase awareness, among both doctors and patients, about the importance of autopsy and what it offers to potential research studies."

That said, broaching the subject of autopsy with patients can be a challenge, said Dr. Murali. But he feels that awareness of programs like Last Wish is important because it has the potential to bring about new discoveries regarding how cancer should be both diagnosed and treated.

"It is an extraordinary program that offers so much potential for discovery," he said.

"Our patients are agreeing to give us the ultimate gift of their bodies at one of the most difficult times in their lives, to help further cancer research. These donations have already revealed new insights into the biology of tumors. We are immensely grateful for the generosity and altruism of the patients who consent to donate their bodies. It really is fundamental to enabling us to carry out groundbreaking research that will help other patients in the future."

12,000

Over the past five years, the Last Wish Program has conducted over 150 autopsies, which have yielded around 12,000 tissue samples. These samples have contributed to research that has received over $19 million in grant funding.

For more information on how to donate to the Last Wish Program please call 646-888-3253 or email us at pthLastWish@mskcc.org

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PLATFORMS

Agaram–International Society of Bone and Soft Tissue Pathology. *Soft Tissue Spindle Cell Neoplasms: Emerging Entities*

Agaram, Y. Zhang, Antonescu–Bone & Soft Tissue Pathology. *A Molecular Reappraisal of Glomus Tumors (GT. A Study of 93 Cases with a Focus on NOTCH Gene Fusions*

Basturk, Klimstra–*New Concepts and Controversies in the Diagnosis of Pancreatobiliary and Gastrointestinal Tract Neuroendocrine Neoplasms*

Benhamida, Basturk, Weigelt, Reis-Filho, Klimstra–Pancreas Pathology. *Pancreatoblastomas and Acinar Cell Carcinomas Share Epigenetic Signatures Distinct From Other Neoplasms of the Pancreas*

Brogi–*The Never-Ending Saga of Papillary Lesions of the Breast*

Chen–*Diagnostic Approach to Renal Tumors with Papillary Architecture: Updates Using 2016 WHO Classification*

Chen–Genitourinary Pathology Society. *Molecular Stratification of Kidney Cancer: Clinical Relevance of Molecular Types Emphasized*

Chiang–Gynecologic Pathology. *Recurrent Chromatin Remodeling Pathway Mutations Identified in Ovarian Juvenile Granulosa Cell Tumors*

Chiang–International Society of GynecologicalPathology.*S100and NTRK Staining to Report NTRK Fusion Sarcoma of the Cervix*

D'Alfonso, Hanna, Grabenstetter, Tan–Informatics.*Machine Learning as an Ancillary Tool in the Assessmentof Shaved Margins for Breast Carcinoma Excision Specimens*

Ferguson, Momeni-Boroujeni, Zheng, Ho, Arcila, Ross, S. Dogan–Head & Neck Pathology. *HER2 Gene Amplification and Protein Expression Assessment in 44 Salivary Duct Carcinomas*

Fine–*Large Gland Lesions of the Prostate on Needle Biopsy*

Fine, Magi-Galluzzi–*Dynamic Evolution in Prostate Cancer Diagnosis and Reporting: What the Pathologist Needs to Know*

Ghossein–North American Society of Head and Neck Pathology. *Latest Advances in the Diagnosis of NIFTP*

Gopalan–Genitourinary Pathology. *Reporting Trends, Practices, and Resource Utilization in Neuroendocrine Tumors of the Prostate Gland: A Survey of Genitourinary (GU) Pathologists*

Gopalan, Fine, Chen, Al-Ahmadie, Sarungbam, Tickoo, Reuter–Genitourinary Pathology. *Prostate Cancer with Germline DNA Damage Repair Gene Alterations: A Clinical and Pathologic Assessment*

Grabenstetter, D'Alfonso, Wen, Brogi, Tan–Breast Pathology *Morphologic and Immunohistochemical (IHC) Features of Carcinoma Involving Microglandular Adenosis (MGA) of the Breast Following Neoadjuvant Therapy*

Klimstra–Gastrointestinal Pathology.*Gastrointestinal Stromal Tumors Arising in Uncommon Locations: Clinico-Pathologic Features and Risk Assessment of Esophageal, Appendiceal, and Colonic Tumors*

Klimstra–Pancreatobiliary Pathology Society. *Mucinous Cystic & Intraductal Neoplasms of the Pancreatobiliary Tract*

Kuba, Xu, Antonescu–Breast Pathology. *The Impact of MYC Amplification on Clinico-Pathologic Features and Prognosis of Radiation-Associated Angiosarcomas of the Breast*

Lin, Pantanowitz–*Short Course #49: Telecytology for Rapid On-Site Evaluation: From Implementation to Clinical Challenges*

Liu, Mata, Arcila, Y. Zhang, A. Dogan, Roshal, Xiao–Hematopathology. *Erythroid/Megakaryoblastic Leukemia with TP53 and RUNX1 Mutations Frequently Occurs in Blast Transformation of Philadelphia Chromosome-Negative Myeloproliferative Neoplasms: A Single-Institution Experience with 56 Cases*

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Momeni-Boroujeni, Vanderbilt, Murali–Gynecologic Pathology. *Alterations in Chromatin Remodeling Genes in Endometrial Epithelial Tumors are Associated with Prognosis*

Park, Soslow–Gynecologic Pathology. *International Endocervical Adenocarcinoma Criteria and Classification (IECC. An Independent Cohort with Clinical and Molecular Relevance*

Perron, Brogi, Murray–Breast Pathology. *Local Recurrence of Benign and Borderline Phyllodes Tumors: Analysis of Margin Status and Clinico-pathologic Features*

Perron, Wen, Hanna, Brogi, Ross–Breast Pathology. *HER2 Immunohistochemistry in Invasive Micropapillary Breast Carcinoma: Complete Assessment of an Incomplete Pattern*

Reis-Filho–International Society of Breast Pathology. *Rare Types of Breast Carcinomas*

Reis-Filho–*Problematic Breast Tumors Reassessed in Light of Novel Molecular Data*

Reuter–*Hot Topics in Pathology 01–GU Pathology–The Testis: From Grossing to Reporting*

Schwartz, Brogi, Pareja, Weigelt, Reis-Filho, Wen–Breast Pathology. *Adenoid Cystic Carcinoma of the Breast: A Single Institution Experience with Emphasis on Solid Variant with Basaloid Features*

Shia, Klimstra, Basturk– Pancreas Pathology. *Solitary Fibrous Tumor of the Pancreas*

Soslow, Park–Gynecologic Pathology. *Clinical and Pathological Determinants of Outcome in Invasive Stratified Mucinous Carcinoma (iSMILE) of the Cervix: An International Multicentric Study*

Tang–*Increasing Importance of HER2 Testing in the Context of an Expanding Targeted Therapies Landscape–Gastrointestinal Cancer: Latest Updates and Practical Guidelines for Pathologists*

Weigelt, Chiang–Gynecologic Pathology. Epigenetic Signatures of Synchronous and Metastatic Endometrioid Adenocarcinomas

Wen–*Uncommon Histologic Subtypes of Triple Negative Breast Cancer*

Xu–Endocrine Pathology Society. *Anaplastic Thyroid Carcinoma: Everything the Pathologist Needs to Know*

Xu, Antonescu–Head & Neck Pathology. *Head and Neck (H&N) Malignant Mesenchymal Neoplasms with GLI-1 Alterations: A Pathologic Entity with Distinct Histologic Features and Potential for Distant Metastasis*

Xu, S. Dogan, Katabi, Ghossein–Endocrine Pathology. *Dissecting Anaplastic Thyroid Carcinoma (ATC. Comprehensive Clinico-Pathologic, Immunophenotypic, and Molecular Studies of 357 Cases*

Yang, Chang, S. Dogan, Travis, Arcila, Ladanyi, Rekhtman–Pulmonary Pathology. *Multifocal Invasive Mucinous Adenocarcinomas Involving Different Lobes are Clonally Related and Represent Intrapulmonary Spread as Defined by Molecular Profiling*

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L. Zhang, Nafa, Hameed–Bone & Soft Tissue Pathology. *A Next Generation Sequencing Study of Seven Primary Central Chondrosarcomas in the Pediatric Population Showed Recurrent IDH Mutations and a Novel EWSR1-SMAD3 Fusion*

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Al-Ahmadie, Reuter–Genitourinary Pathology. *Urothelial Dysplasia: Diagnostic Value in Clinical Practice 20 Years Since the 1998 WHO/ISUP Consensus*

Baine, Buonocore, Chang, Rekhtman, Sauter, Travis–Pulmonary Pathology. *The Distinction Between Spread Thru Air Spaces (STAS) and Artifacts in Selected Images is Highly Reproducible*

Baine, Travis Buonocore, Chang, Rekhtman, Sauter–Pulmonary Pathology. *Histologic Patterns of Lung Adenocarcinoma Reported on Biopsy Accurately Predict Composition of Resected Tumor*

Baine, Travis, Klimstra, Sauter–Pulmonary Pathology. *Histologic Features of Desmoplastic Mesothelioma (DMM)*

Baine, Travis, Sauter, Chang, Buonocore, Jungbluth, Rekhtman– Pulmonary Pathology. *Novel Biologic Subsets of Small Cell Lung Carcinoma Defined by ASCL1 and NeuroD1: Immunohistochemical and Histopathological Characterization*

Basturk–Pancreas Pathology. *Is It Justifiable to Move the Grade-1 Ki67 Index Cut-Off from 3% to 5% for Pancreatic Neuroendocrine Tumors as Has Been Proposed? The Cases that Fall to 3-5% Category Have Clinicopathologic Characteristics Closer to Those >5%*

Basturk–Pancreas Pathology. *Epithelial Inclusions in the Gallbladder: Cytoisospora belli Organisms or Degenerative Intracytoplasmic PAS-Positive Hyaline Globules*

Basturk–Pancreas Pathology. *Whipple-Ables: Clinico-Pathologic Comparison of 1032 Cancers Removed by Pancreatoduodenectomy Based on Pathologic Re-Review Using Refined Site-Specific Criteria*

Basturk–Pancreas Pathology. *A Proposal for Improved T-Staging of Pancreatic Ductal Adenocarcinoma by Using Microscopic Examination as the Basis for Determining Size and T-Stage*

Beech, Tang, Klimstra, Shia–Gastrointestinal Pathology. *Esophageal Adenocarcinoma Showing Extensive Neuroendocrine Differentiation after Induction Chemo-Radiation: The Molecular View of a Poorly Understood Phenomenon*

Caniello, Chan, Roshal, Lin–Cytopathology. *Role of Flow Cytometry Studies in the Diagnosis of Classical Hodgkin Lymphoma in Cytology Specimens*

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Chang, Sauter, Buonocore, Vanderbilt, Arcila, Travis, Ladanyi, Rekhtman–Pulmonary Pathology. *Histologic Challenges in Distinguishing Separate Primary Lung Carcinomas from Intrapulmonary Metastases Using Broad Next-Generation Sequencing as a Gold Standard for Determining Tumor Clonal Relationships*

Chapman-Lim, A. Dogan, D'Alfonso–Breast Pathology. *Mammary Amyloidosis: An Uncommon Entity that May Present as Mammographic Microcalcifications*

Chui, Soslow– Gynecologic Pathology. *TP53-Wildtype High-Grade Serous Tubo-Ovarian Carcinomas*

Dahoud, Imam, Tang–Gastrointestinal Pathology.*Heterogeneity of Signet Ring Cell Carcinoma at Different Primary Sites–Human Observation Precedes Artificial Intelligence*

Dahoud, Momeni-Boroujeni, Vanderbilt, Soslow–*Clinicopathologic and Genomic Analysis of Copy Number-High (CH-H) Endometrial Carcinoma*

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Pareja, Wen, Weigelt, Reis-Filho–Breast Pathology.*Genomic Analysis of Multifocal Ductal Carcinoma In Situ and Synchronous Invasive Ductal Carcinoma*

Park, Soslow–Gynecologic Pathology. *FIGO (2018) Stage 1B Endocervical Adenocarcinomas: A Detailed Study of Clinical Outcomes Informed by Clinico-pathological Parameters Including HPV Status*

Raza, Travis, Buonocore, Chang, Jungbluth, Rekhtman, Ladanyi, Sauter–Pulmonary Pathology. *Utility of Methylthioadenosine Phosphorylase (MTAP), 5-Hydroxymethyl cystosine (5-HMC) and BAP1 Immunocytochemistry (ICC) in Cytology Specimens for the Diagnosis of Malignant Mesothelioma*

Rekhtman, Travis, Yagi–Pulmonary Pathology. *The Roles of Whole Block Imaging with Micro-Computed Tomography in Lung Adenocarcinoma*

Reis-Filho, Weigelt–Gynecologic Pathology. *The Chronology of Development of Endometrioid Endometrial and Ovarian Tumors in Patients with Synchronous Disease*

Ross, Zehir, Wen, Brogi, Weigelt, Reis-Filho, Pareja–Breast Pathology. *Genetic Alterations Targeting KIT in Breast Cancer*

Salama, Momeni-Boroujeni, Vanderbilt, Soslow–Gynecologic Pathology. *Molecular Landscape of HPV Negative Vulvar Squamous Cell Carcinoma Including NOTCH Alterations*

Shia–Gastrointestinal Pathology. *Clinicopathologic Feature of Varicella Zoster Virus Infection of the Upper Gastrointestinal Tract*

Shia–Gastrointestinal Pathology. *Metastases to the Stomach: Frequent Fliers and Unexpected Guests*

Soslow, Murali–Gynecologic Patholog. *Cytologic Features of Undifferentiated and Dedifferentiated Carcinomas of the Endometrium*

Soslow, Park, Chiang, Reis-Filho, Zehir, Mandelker, Murali, Weigelt–Gynecologic Pathology. *Concordance between Immunohistochemistry for DNA Mismatch Repair Proteins and Next Generation Sequencing for the Identification of Microsatellite Instability in Endometrial Cancer*

Soslow–Gynecologic Pathology. *Evaluation of HPV RNA In-Situ Hybridization (ISH) and p16 Immunohistochemistry (IHC) Concordance in Endocervical Adenocarcinomas*

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Vakiani, Shia–Gastrointestinal Pathology. *Processing Rectal Cancer Resection Specimens: A Comparative Evaluation of a Cross Sectioning Approach with Wholemount Blocks and Slides Versus the Regular Approach*

Weigelt, Park, Murali–Gynecologic Pathology *Massively Parallel Sequencing Analysis of Gastric-Type Cervical Adenocarcinomas Reveals Mutations in Cell Cycle-Regulation Genes and Rare Potentially Targetable ERBB2 Mutations*

Wong, Brogi, Wen–Breast Pathology. *Poor Response to Neoadjuvant Chemotherapy in Metaplastic Breast Carcinoma*

Wong, Hanna, Edelweiss, Brogi, Hameed, Ross, Yagi–Breast Pathology.*A Feasibility Study in the Automated Quantification of HER2 Gene Amplification in Breast Cancer Using Chromogenic In Situ Hybridization Whole Slide Images*

X.Wu,Momeni-Boroujeni,Soslow, Weigelt–Gynecologic Pathology. *Genetic Alterations in Mullerian Adenosarcoma with High-Grade Sarcoma Components*

Umphress, Tang–Gastrointestinal Pathology. *Is Histologic Grade Prognostically Important Among Goblet Cell Neoplasms Confined to the Appendix*

Xu, Katabi, S. Dogan, Ghossein–Endocrine Pathology. *Should Medullary Thyroid Carcinomas Be Graded?*

Xu, Katabi, Hameed, Ghossein, Yagi–Endocrine Pathology. *Defining Crucial Pathologic Parameters in Thyroid Neoplasm Using 3D Whole Block Imaging (WBI) with Micro-resolution CT Scanner (MicroCT. A Proof of Concept*

Xu, Sethi, S. Dogan, Ghossein, Katabi–Head & Neck Pathology. *Clinicopathologic Characteristics of Young Patients with Oral Squamous Cell Carcinoma (OSCC)*

Yagi–Gastrointestinal Pathology. *Application of Whole Block Imaging (WBI) by Micro-Computed Tomography for the Evaluation of Endoscopic Submucosal Dissection Specimens*

Yagi–Informatics. *Mitosis Detection with Tiny-YOLO*

C Yang, Ladanyi, Travis, Busam, Rekhtman–Pulmonary Pathology. *UV Genomic Signature Classifies Lung Melanomas of Unknown Primary as Metastases from Occult Cutaneous Melanomas*

S-R Yang, Mata, Benayed, Rekhtman, Ladanyi, Jungbluth, Hechtman–Pathobiology & Techniques. *Detection of RET Kinase Fusions Using DNA, RNA, and Protein-Based Methods*

L. Zhang, Klimstra, Hameed, Roehrl–Bone and Soft Tissue Pathology. *Towards Biomarkers and Therapeutic Targets for Dedifferentiated Chondrosarcoma Discovered by Fourier Transform Mass Spectrometry Proteomics*

Zhu, Ho, Petrova-Drus, Nafa, Quesada, A. Dogan, Arcila–Pathobiology & Techniques. *Evaluation of T-Cell Receptor (TCR) Repertoire by Next-Generation Sequencing (NGS) Based TCR Gamma Chain Clonality Testing*

JESSICA CHAPMAN, PHD

Director of Clinical Proteomics

By Kayt Sukel

Q What are you responsible for in your current role?

A I came to Memorial Sloan Kettering Cancer Center (MSK) in 2017 with the goal of taking mass spectrometry–based proteomics and moving it into a clinical setting. Proteomics, in general, is the study of proteins. It is understood that certain proteins are expressed differently in healthy tissues as opposed to tumors. Researchers can use mass spectrometry to study the differences in proteomic profiles of malignant tissues and try to determine how they might influence the development and growth of those tumors. However, the next step is to translate this wealth of information into clinically applicable tests. My role involves identifying unmet needs in diagnostic, prognostic or disease tracking testing. Then developing, validating, and implementing those kinds of clinical assays that can be used by pathologists and clinicians. In the bigger picture, those tests could help doctors choose more precisely targeted treatments for their patients.

We already have one NYS DOH approved clinical test. This test uses FFPE biopsy tissue to determine the causative protein. Amyloidosis is a disease caused by the deposition of a misfolded protein that displaces healthy tissue and can lead to organ failure and even death. Determining the causative protein is essential for proper treatment. My first major task as Director of clinical proteomics was to get the test validated. Now, we have a streamlined process that includes coordination of the hematopathology office coordinators, histotechnologists, myself, and the clinical technologists in the proteomics laboratory. In addition, I put a lot of effort into ensuring the instrumentation is kept in optimal condition which includes hands-on training of the technologists. This is not instrumentation or techniques that are common in clinical laboratories so it is an opportunity to teach someone something new.

Q What brought you to MSK?

A I did my post-doctoral work at the FBI laboratory in Quantico, Virginia. Then I went to work in the proteomics laboratory at NYU Medical Center. While I enjoyed that work and learned a lot about building and running a laboratory over my six years there, I was ready to try something new. When I learned about this job, I was intrigued by the prospect of using mass spectrometry-based proteomics in a clinical setting. In clinical settings, mass spectrometers are usually used for small molecule or single protein target analysis. I wanted to be more directly involved in the clinical community and hopefully play a role in establishing how these new assays and tests could be effectively used in patient care.

Q What are some of the favorite parts of your day-to-day work?

A I'm always learning! When I came to MSK, I only knew the basics about pathology. I really enjoy interacting with the different people in the department. I get to learn what everyone does, from the pathologist to the histotechnologist preparing the samples, and what goes into their jobs. I've also learned quite a bit on the administrative side—all the moving parts that go into running a lab and the greater pathology department here. It helps me do my own job better.

Another large part of my role is research. I have developed wonderful collaborations with pathologists, laboratory medicine faculty, and SKI researchers. These connections are very important in doing truly translational science.

Q From your perspective, what sets MSK apart from other cancer centers?

A There's a real sense of community here. I've gotten to know people across the institution such as members of the security department, environmental services, shipping and receiving, and others. Since my desk and laboratory spaces are quite spread out I have a lot of opportunities to interact with members of the MSK community outside of Pathology as I walk between buildings. It feels like family. I'm happy that I'm able to do truly interesting work but also that, when I walk down the halls, everyone says hello and smiles. It really is a great place to work.

CYCLE FOR SURVIVAL

MEMORIAL SLOAN KETTERING | EQUINOX

Pathology Teams

Accesioning Gatekeepers — **Team Captain:** Jigar Patel

Artificial Spintelligence — **Team Captain:** Christina Virgo

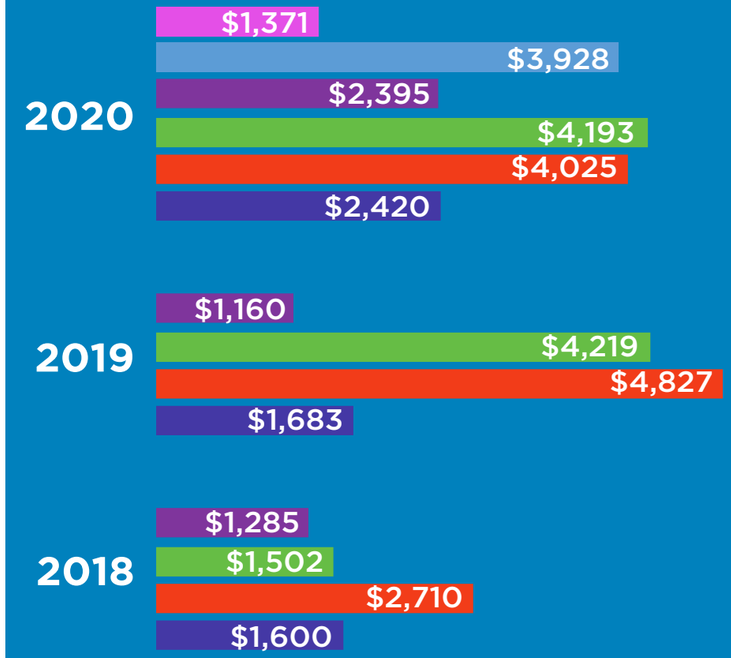
Pathology Warriors — **Team Captain:** Fernando Garcia

Pathology Pedals — **Team Captain:** Sarah Virgo

Bank This — **Team Captain:** Emily Lin

Rob Loves Lax (In Loving Memory of Rob Paterson) — **Team Captain:** Lorraine Corsale

$ Raised



Total Raised (2016–2020)

$45,110

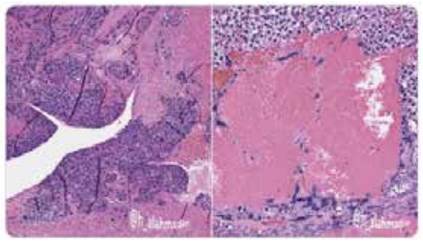
Social Media

Pathology@MSK
@MSKPathology

Our #PathIT Team addresses all of our information technology, LIS and digital technology needs. We're thankful for them and they're thankful for our laboratory professionals! Happy Lab Week!#PeopleofPathology

Hikmat Al Ahmadie
@h_alahmadie

These cells just love blood and blood vessels! Can you tell the two scenarios/settings? #GUPath #GCT #testiscancer



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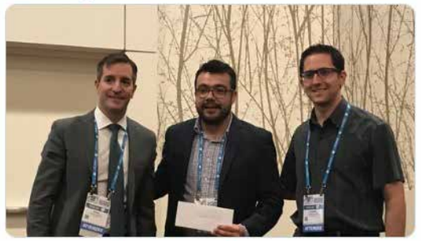
Our prep techs and file clerks are an integral part of the Cytology Service @MSKPathology. Thank you for all that you do! #PeopleinPathology #LabWeek2020

Leonel Maldonado
@LayonelMG

It was very humbling and an honor to have received the Mario Luna awward from the Latin American Pathology Foundation @LatinAmericanPF, for my project on fusions in uterine mesenchymal tumors @SarahCiang1 @AmirMom32351131 @KAyPArkMD @ RymaBenayed @MLadanyi @ MSKPathology @ USCAP2020



Pathology@MSK
@MSKPathology

We appreciate our #Molecular Diagnostics team and so does @cabotcheese! Thank you PeopleinPathology #Covid19

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As #LabWeek2020 begins, @MSKPathology would like to thank all our dedicated laboratory professionals working around the clock for our patients. You're all an integral part of the exemplary care provided by @sloan_kettering and we appreciate all that you do! #PeopleinPathology

Pathology@MSK
@MSKPathology

You're welcome.
#FeelGoodFriday #FanMail #HealthCareHeroes #MSKPathology

Pathology@MSK
@MSKPathology

For today's #PeopleinPathology appreciation tweet, we'd like to highlight our dedictaed team of Pathologist's Assistants. These #HealthCareHeroes are an integral part of the @MSKPathology team @ sloan_kettering and we appreicate all that you do! #PathAssist #MSKPathology

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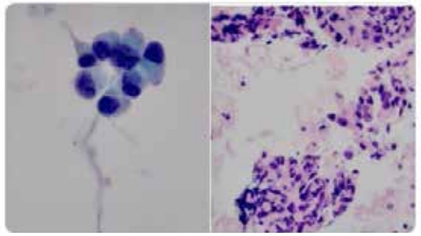
Jennifer Sauter, MD
@JL_Sauter

Bread and butter pathology from @MSKPathology 69 y/o F, axillary LN FNA #cyto #cytology @cytopathology



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2nd Quarter 2020

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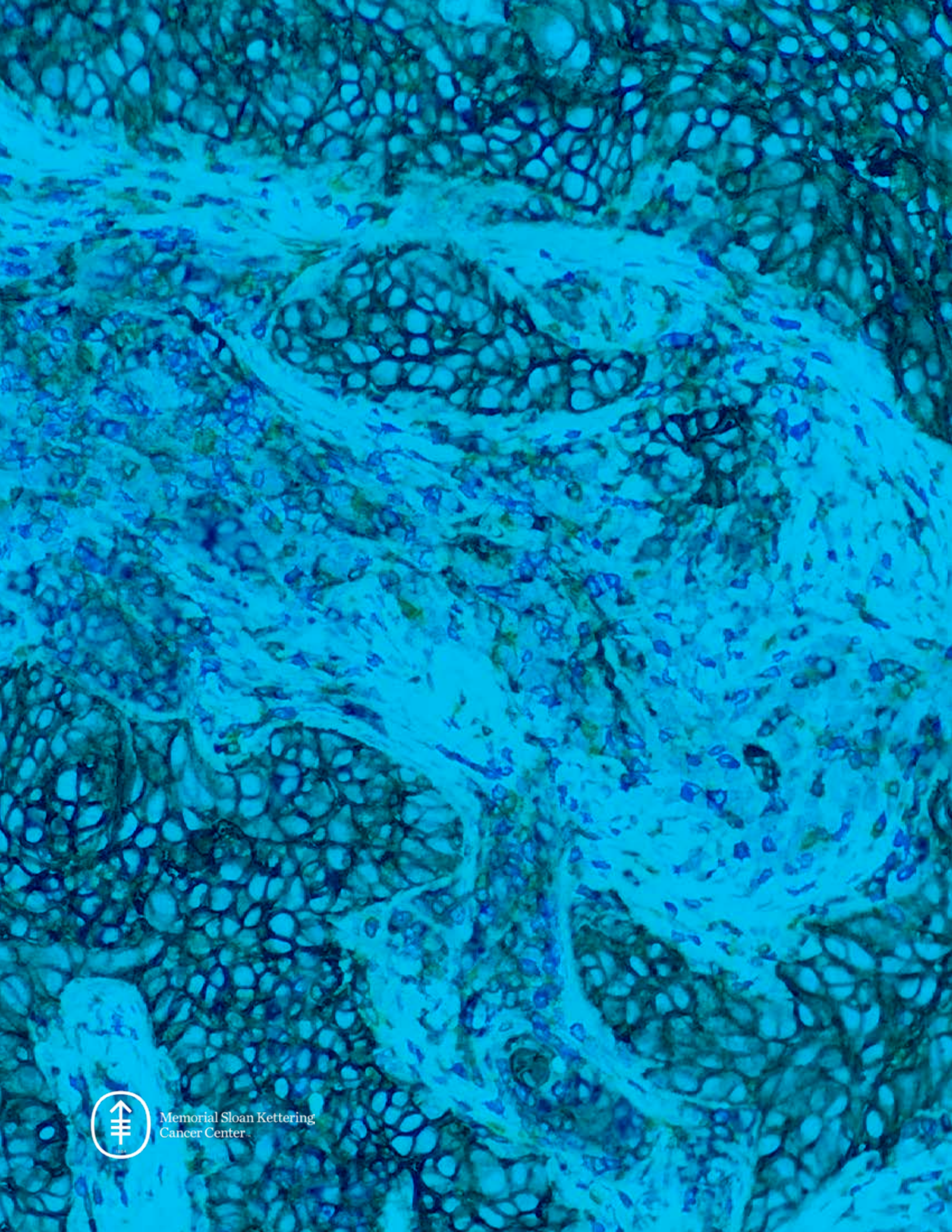

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