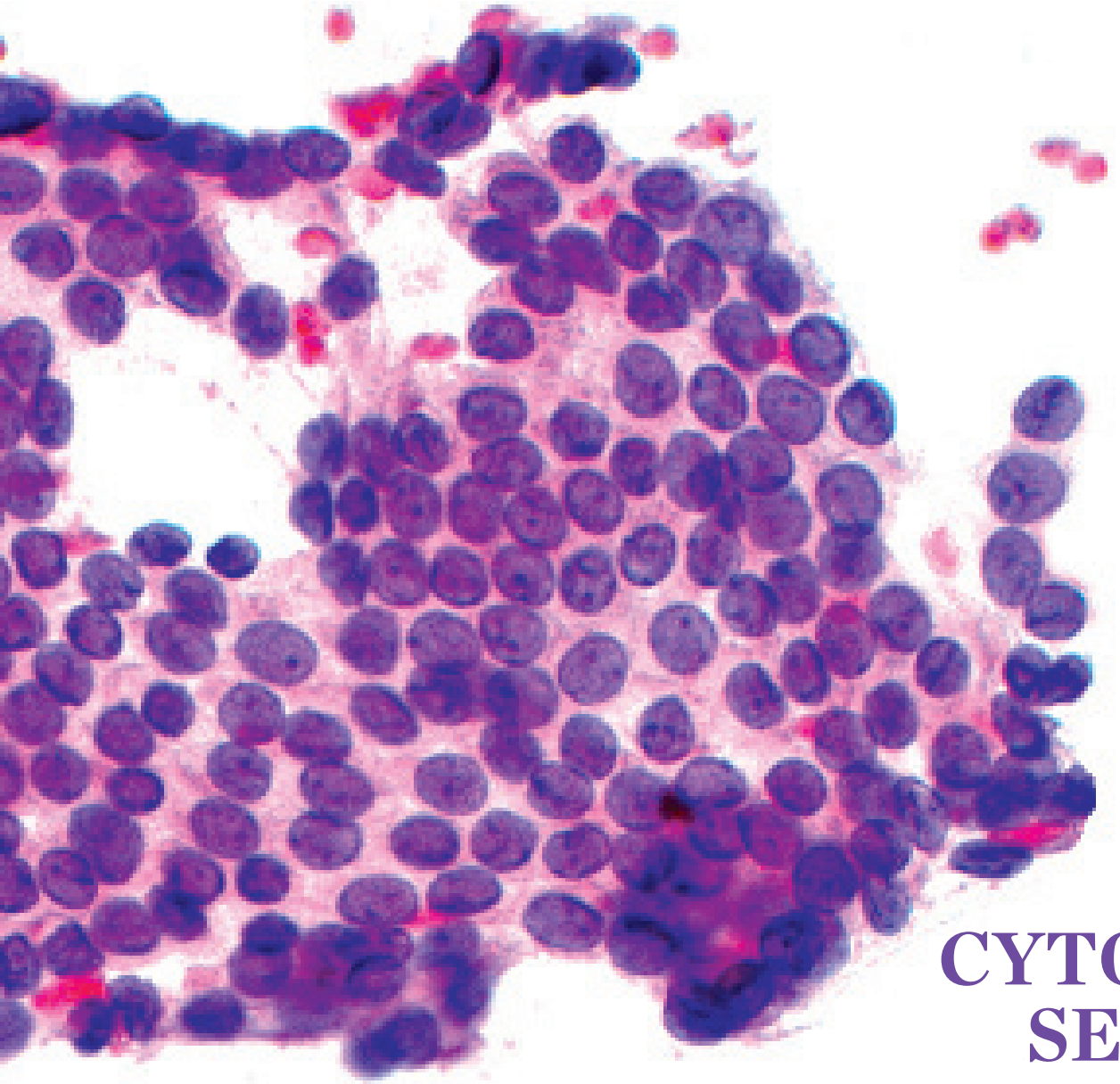
MSK PATHOLOGY REVIEW

INITIATIVES
INNOVATIONS
ACCOMPLISHMENTS



THE CYTOLOGY SERVICE AT MSK

Memorial Sloan Kettering Cancer Center

1ST QUARTER
2018

COMMENTARY

FROM THE DEPARTMENT CHAIRMAN

> The personal consult practice has evolved since the days of Stewart and Foote but it continues to represent a source of fertile teaching material for our fellows while offering our expert pathologists the opportunity to extend their contributions to patient care beyond the walls of MSK.

A major part of patient care in Pathology at MSK involves the review of slides from other institutions. Many pathology consultation cases are sent because patients being treated at MSK must submit outside pathology material for review. These "departmental consults" make up nearly 40% of our case volume in surgical pathology, cytology and hematopathology. Additionally, "personal consult" cases are sent to specific expert MSK pathologists when colleagues at other institutions need help with the interpretation, when patients would like an additional opinion, or when treating clinicians hope to benefit from our super-specialized oncologic pathology expertise.

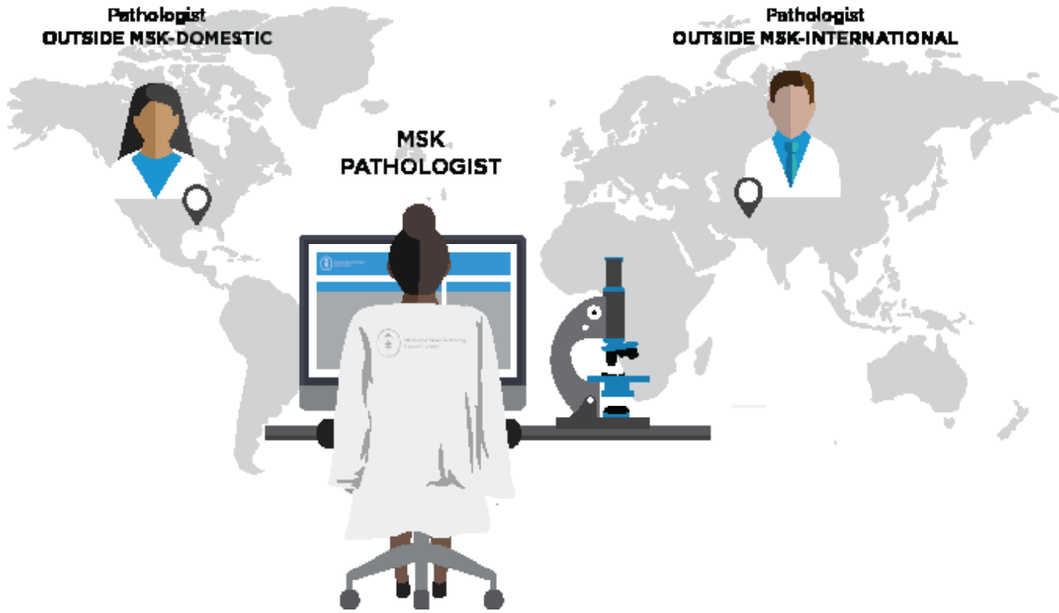
The review of personal consult cases has long been a part of our practice, and there are archives of these cases from the days of Stewart, Foote, Rosai and other senior pathologists. The Stewart and Foote material in particular has been collected into a teaching file, and their consult letters offer a glimpse into the state of knowledge available at the time before the heavy reliance on immunohistochemistry, molecular analysis, and other advanced diagnostic tools. Remarkably, some cases represent entities that had not yet been described at the time they were reviewed, yet the insights based on routine microscopy were often quite prescient. The consultative opinions were conveyed in letters rather than formal pathology reports, sometimes decorated with personal remarks and humor now regrettably considered inappropriate for medical documents. In his 1962 letter about a spindle cell thymoma, Dr. Foote wrote that he had shared the case as well with Dr. Stewart, who "immediately made a diagnosis of thymoma, accompanied by one of his quick little grunts, indicating diagnostic satisfaction. I wish I could break him of this trait of grunting since it is well-known that it is the quiet pig that gets the most swill." I dare say our current reports are a shade less colorful!

The personal consult practice has evolved since the days of Stewart and Foote but it continues to represent a source of fertile teaching material for our fellows while offering our expert pathologists the opportunity to extend their contributions to patient care beyond the walls of MSK. Patients are becoming aware of the importance of expert pathology review, and increasingly the consults are motivated by the patient's wish to ensure their diagnosis is as accurate as possible, using all available advanced techniques to derive the maximal information about prognosis and therapeutic options. At present, the majority of our consults are sent as they were 75 years ago, with glass slides, paper reports, and paraffin blocks packaged carefully (one hopes!) and shipped to Manhattan from far corners of the globe. Cases from the US can arrive the next day, but many overseas consults are delayed, especially when biological materials are held in Customs – a scenario that can add days or weeks to the transit time. The information accompanying the pathology material can also vary substantially, often requiring time-consuming efforts by our administrative staff to retrieve basic patient or insurance information. Efforts now underway seek to streamline these processes at MSK. A web-based consult interface has already been launched, which allows consulting physicians (or patients) to enter standard information via the internet, obviating the need to initiate outside contact once the slides are received, and also giving the consulting individuals the knowledge that their information has been received. This enhancement in communication does nothing to speed the receipt of the slides, however. To improve this aspect requires the use of digital pathology, such that scanned slides can be transmitted electronically, almost in real time. Under the leadership of Dr. S. Joseph Sirintrapun and the clinical informatics team (see separate article on p.24), we are making great strides towards a fully digital pathology consult portal.

In general, the comfort level of using digital slides for diagnosis has improved since the roll out of routine digital scanning for archiving purposes. Fellows and attendings now commonly review old material digitally. A survey of users conducted as part of a study on the operational aspects of digital pathology by Drs. Matthew Hanna, Joseph Sirintrapun, and others(which was presented recently at the 2018 USCAP meeting in Vancouver) found that the majority of MSK pathologists are comfortable using digital slides for diagnosis especially if the glass slides could be made available when needed. Thus, the department is primed to take the next step and receive digital consult cases in lieu of (or in advance of) receiving glass slides. Some simple means to review digital consult slides already exist; remote hosting sites at other institutions or in the cloud already provide access to digital cases, and many of us have been asked to provide opinions on these types of cases. However, this remote viewing option has a number of drawbacks: the connections can be slow, resulting in a poor browsing experience; the cases are not formally accessioned, creating a range of regulatory and billing problems; the digital slides are only hosted for a discrete interval and are no longer available once the consult review has been performed. In order to create a more formal digital consultation process, we have decided to create a user interface that will allow the consulting pathologists to upload digital slides and patient information through our consult portal, crossing the MSK firewall to be archived within our system along with all of the digital slides we are creating internally. The case will be accessioned as a digital case; additional glass slides or other materials can be added if received subsequently. This will allow continued access to the digital slides for research or subsequent review, which is especially helpful for the 11% of personal consult cases in which the patient later seeks care at MSK. Reports will be generated through CoPath as usual, and the current billing process for glass slide consults will apply.

The efforts to identify a consult portal vendor, establish the interfaces with CoPath and online systems, and vet the security issues have consumed nearly a year of work, but the plans are now taking shape. Once active, the digital consult portal will allow rapid access to expert MSK pathologists for colleagues and patients anywhere in the world. We will have the option to grow the consult practice, and for partner institutions with digital scanning capabilities, we could even consider allowing departmental consults to be sent digitally through the portal. For routine diagnoses, the benefits of time efficiency along with the elimination of costly glass slide shipping make this a very attractive option. And the ability to review outside slides and have an MSK Pathology diagnosis in the chart prior to a new patient's first visit will create enormous downstream value as well. We will provide updates on the status of the consult protocol in upcoming *MSK Pathology Review* issues.

- David Klimstra, MD



MARC ROSENBLUM, MD AND TEJUS BALE, MD, PHD

NEUROPATHOLOGY AT MSK

Beyond diagnostic excellence, you'll find optimism, enthusiasm and humanity

By Hope Cristol

Molecular diagnostics didn't exist when neuropathologist Marc Rosenblum, MD, first began practice some 35 years ago. Next-generation sequencing, methylation array analysis and other novel technologies have led to more precise diagnosis, targeted treatments and, in some cases, better outcomes. "Molecular diagnostics provides information of taxonomic, prognostic and predictive significance," Dr. Rosenblum says, echoing the chorus of veteran colleagues who marvel at what's become possible in the field.

He's also not shy about discussing the flipside: a recent past in which cancers were less precisely and accurately classified. Dr. Rosenblum, Chief of the Autopsy Service and Director of Neuropathology, has personally delivered a lot of bad news to oncology teams as well as distraught patients and families. Ironically, that's part of what makes him exceptional.

While pathologists are laboratory-based physicians, Dr. Rosenblum has made himself available to patients from his earliest days in practice. "Over the years, it hasn't gotten any easier to explain when I've made a life-threatening diagnosis, but I think this is a professional obligation," he says. "I never give treatment recommendations – I refer patients to bedside physicians for that – but I do try to explain just what is wrong."

GOING THE EXTRA MILE

There are some patients with whom Dr. Rosenblum has kept in contact for years. He cites one example of a pediatric patient he first diagnosed with Ewing sarcoma. That was before technology developed five years later that would enable Dr. Rosenblum to revisit the diagnosis. Ultimately, he discovered the boy had a rare cancer termed high-grade neuroepithelial tumor with BCOR alteration. "With technological advances delving into genomic abnormalities, we now realize that there are entities that we simply had no idea existed before," he says.

The boy's father was so grateful for Dr. Rosenblum's commitment to the case that he sent a note of thanks after his son passed away. It's one of countless examples of admiration – from patients and clinicians alike – for Dr. Rosenblum.

"I knew of him by legend before I knew him personally because everyone who meets him knows that he's an amazing clinician, an amazing diagnostician and an all-around great guy," says his neuropathology colleague Tejus Bale, MD, PhD.

BEYOND CLINICAL CASES

Dr. Bale is the only other member of the Neuropathology team. She joined MSK in October after completing a fellowship in neuropathology at Brigham and Women's Hospital, Boston Children's Hospital and Beth Israel Deaconess Hospital and a fellowship in molecular genetic pathology at Harvard Medical School.

Dr. Rosenblum says the small size of his team reflects cancer demographics. Compared with cancers of the lung, breast and colon, "brain tumors just don't come in those numbers, thank goodness," he says.

That leaves the neuropathologists time for their other clinical and research interests. Dr. Rosenblum is a member of the department's Cytology Service. Dr. Bale participates in the Molecular Diagnostic Service and spends time on collaborative research with the Brain Tumor Center.

In addition to the studies that both neuropathologists support at MSK, Dr. Rosenblum has an interest in defining new diagnostic entities in the spectrum of glial and glioneuronal tumors. Some of this work calls for collaboration with pathologists in other parts of the country and around the world. "These tumor types are rare, so you have to pool the resources of busy and frequently consulted neuropathologists to carry out larger-scale studies," Dr. Rosenblum says.

He notes that his research, while important, takes a backseat to primary patient care. However, he's effusive about the possibilities and progress of both at MSK.

"I may be accused of tribalism, but I've been here for 35 years and I've seen this remarkable institution transform from the day I set foot in it. What we do is even more extraordinary now," he says.

Dr. Bale, who hasn't witnessed the transformation, is nevertheless finding herself swept up by the enthusiasm at (and for) the Pathology Department. "There's so much going on here, so many great projects, ideas and people, the challenge is choosing the ones to prioritize," says Dr. Bale. "It's a good challenge to have."

DESCRIBING CNS TUMORS

Numerous central nervous system (CNS) tumors are now known to have defining genetic abnormalities. Below are just some of the entities that Dr. Rosenblum was involved in describing and characterizing, as well as their associated genetic aberrations:

- Papillary glioneuronal tumor (*SLC44A1-PRKCA* fusion)
- Angiocentric glioma (*MYB* rearrangement/fusion)
- Embryonal tumor with multilayered rosettes (chromosome 19q13.42 amplification)
- Diffuse leptomeningeal glioneuronal tumor (*BRAF-KIAA* 1549 fusion and 1p deletion)
- Glioblastoma with primitive neuronal component
- Micronodular and vacuolating neuronal tumor (*MAP2K1,BRAF,FGFR* alterations)
- Chordoid glioma (*PRKCA* mutation)
- Polymorphous low-grade neuroepithelial tumor of the young (*FGFR* fusions, *BRAF* mutations)

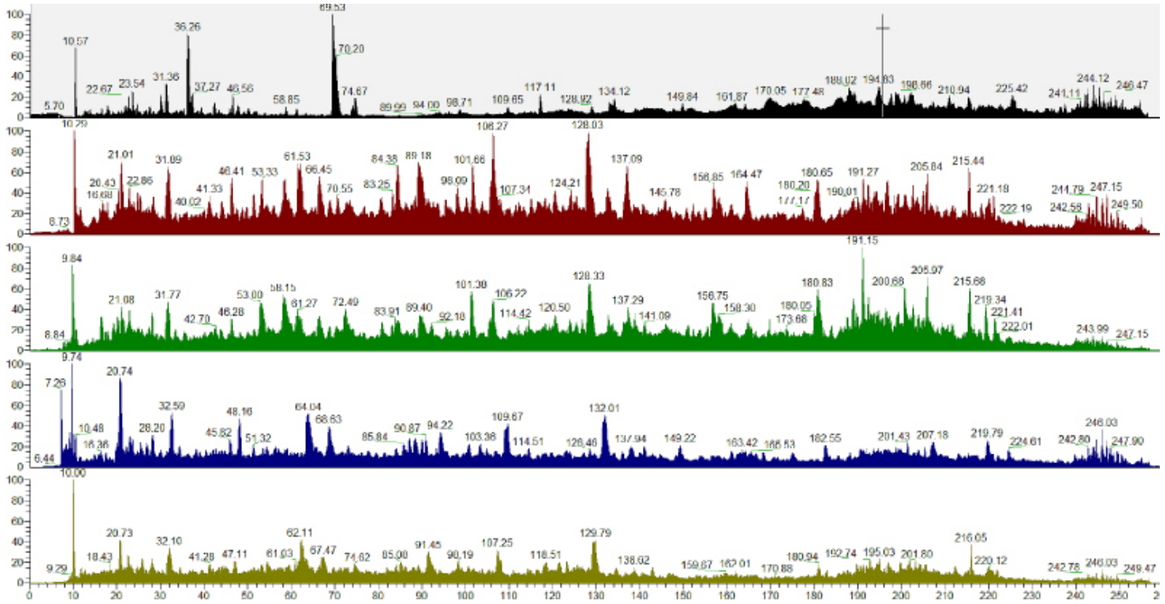
PERSPECTIVES ON MASS SPECTROMETRY-BASED PROTEOMICS

The technology is emerging as an important tool in pathology and precision diagnostics

By Hope Cristol

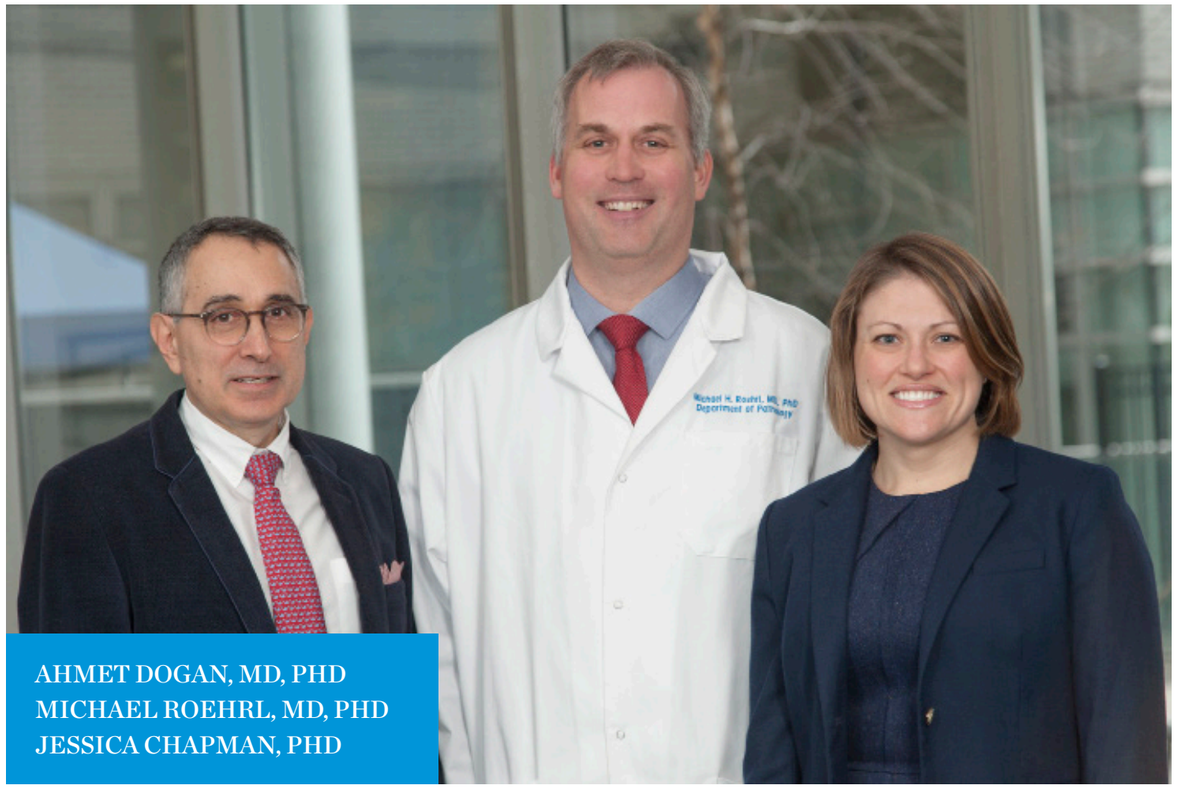
The Pathology Department physicians and scientists who focus on mass spectrometry diagnostics are highly enthusiastic about its current and potential roles in patient care. The technology is being used to identify virtually all proteins in a cancer cell as well as examine any snowball effects occurring from abnormally expressed proteins, explains Ahmet Dogan, MD, PhD, Chief of the Hematopathology Service. He and Jessica Chapman, PhD, Director of the Clinical Proteomics Laboratory within the Pathology Department, are working on clinical assays using mass spectrometry-based proteomics.

Another proponent of "mass spec" is Michael H. Roehrl, MD, PhD, GI Pathology faculty, principal investigator of a research laboratory, and Director of MSK's Precision Pathology Biobanking Center. Dr. Roehrl uses mass spectrometry in his lab to identify and characterize proteome-level alterations of various solid tumors.



Mass Spectrometric Ion Chromatograms of Pancreatic Cancer
Image: Roehrl Lab

HERE, ALL THREE EXPERTS OFFER SHORT TAKES ON THIS POWERFUL TOOL THAT'S PRODUCING VALUABLE PATHOLOGICAL INSIGHT



AHMET DOGAN, MD, PHD
MICHAEL ROEHRL, MD, PHD
JESSICA CHAPMAN, PHD

MASS SPECTROMETRY VS. ANTIBODY-BASED ASSAYS

Ahmet Dogan, MD, PhD

> "We have 20,000 proteins but only have maybe 30 or 40 well-developed reagents for each cancer type."

"To identify proteins that are abnormally expressed, historically we have used immunohistochemistry. The challenge is that you need a specific reagent for each protein. We have 20,000 proteins but only have maybe 30 or 40 well-developed reagents for each cancer type. Also, in many instances these reagents cannot detect normal versus abnormal proteins. Mass spectrometry-based proteomics can.

Another significant difference from other protein assays we have, like ELISA and immunofluorescence, is that mass spectrometry is unbiased. With antibodies, you have to decide which ones to use. You basically see what you are looking for. With mass spectrometry, we're not saying, 'Show me whether this is expressed or not'. We are saying, 'What's all in here?'

This is redefining aspects of the field. In the case of amyloidosis, mass spectrometry has dramatically increased diagnostic accuracy. It's also enabled us to identify things we didn't even know existed. For example, LECT2 amyloidosis is now the third most common type in the United States, and we didn't know it existed before mass spectrometry."

BIOLOGICAL QUESTIONS

Michael H. Roehrl, MD, PhD

> “Mass spectrometry is also well suited to proteomic response monitoring and resistance characterization.”

"One of the things my lab is interested in is how cancer interacts with the immune system. Using mass spectrometry, we can ask important biological questions such as, 'What portions of proteins in a patient's tumor are visible or invisible to the human immune system? Why is that? How does that change over time, and how does that inform how the patient might respond to immunotherapy?'

Mass spectrometry is also well suited to proteomic response monitoring and resistance characterization. In other words: how a patient's cancer responds under treatment, whether a targeted therapy is hitting the intended pathway, and how a tumor might escape from treatment.

Mass spectrometry enables us to ask functional questions that we otherwise cannot address. With genomics and other nucleic acid-based assays, it is simply impossible to study dynamic changes in a signaling pathway with and without a drug. You really need to measure the protein domain directly. There are multiple methods to do that, but I think one of the most powerful – because it doesn't rely on antibodies and it's very sensitive – is mass spectrometry-based proteomics."

HOW MASS SPECTROMETRY WORKS

Jessica Chapman, PhD

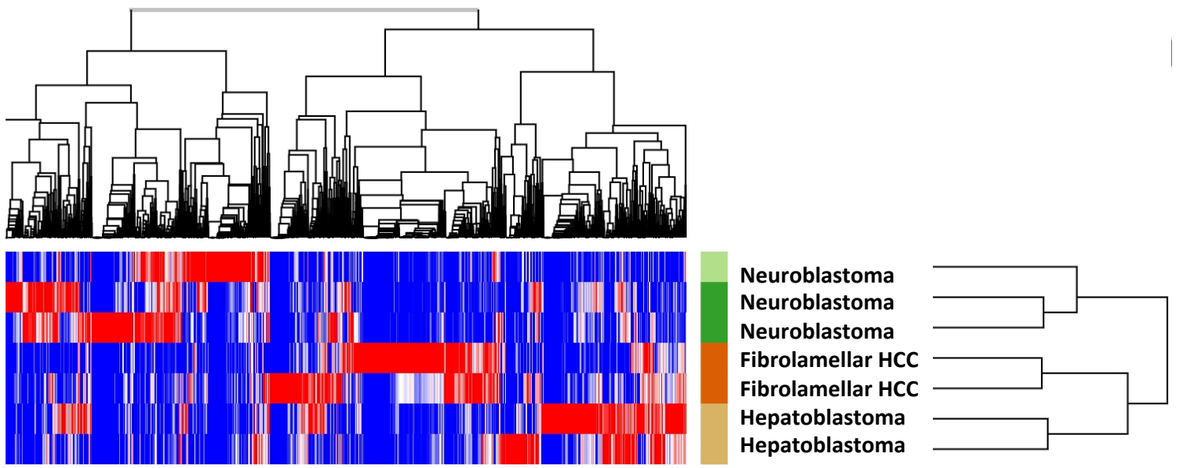
> “You get analytical information about proteins with incredible detail from this technology.”

"A general workflow would start with a biological sample, such as tissue, fluid or blood. We digest the proteins down into peptides using [enzymes called] endoproteinases.

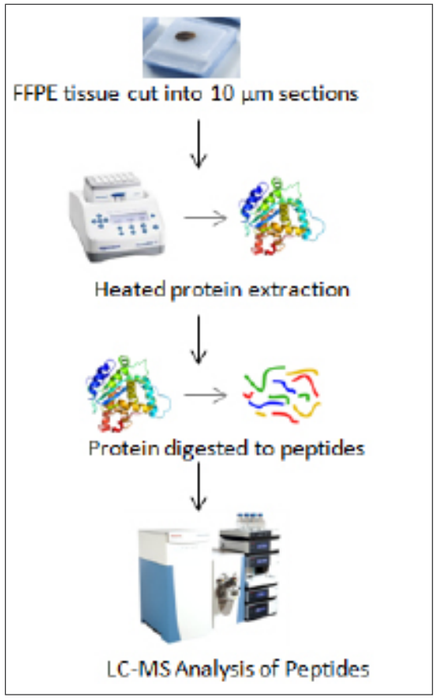
Ideally, the peptides have somewhere between five and 25 amino acids. We separate these using liquid chromatography. Then they are eluted off a column into a mass spectrometer.

With a mass spectrometer, we very accurately measure the mass of the peptides. Then we isolate peptides one at a time within the instrument and apply a little bit of energy so they bump into inert gas molecules, which results in fragmentation of the peptide backbone. Then we measure the fragment ions to determine the peptide sequence.

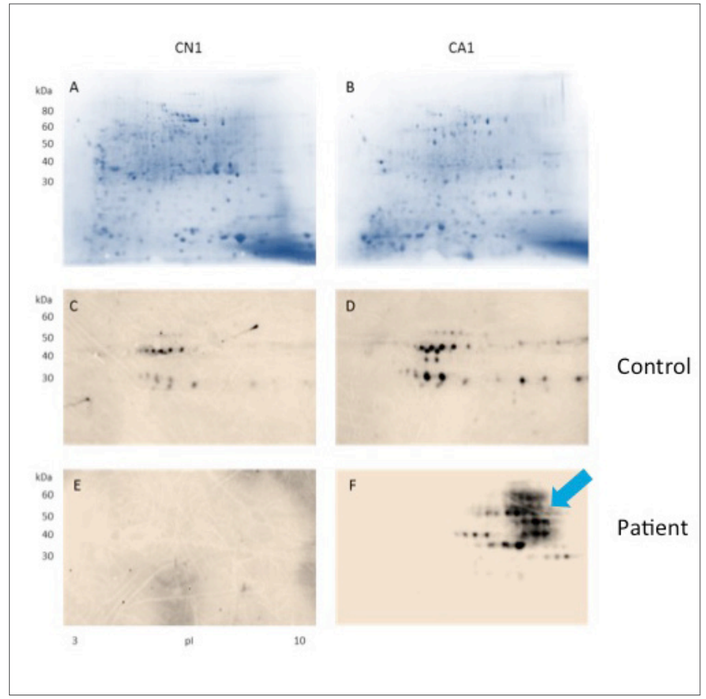
If you were to measure intact peptides, the mass could correspond to multiple sequences. But when you fragment the peptides, you can determine the combination of amino acids and their order. Using a protein database, you can identify which protein or group of proteins are the source of the peptide. You get analytical information about proteins with incredible detail from this technology. "



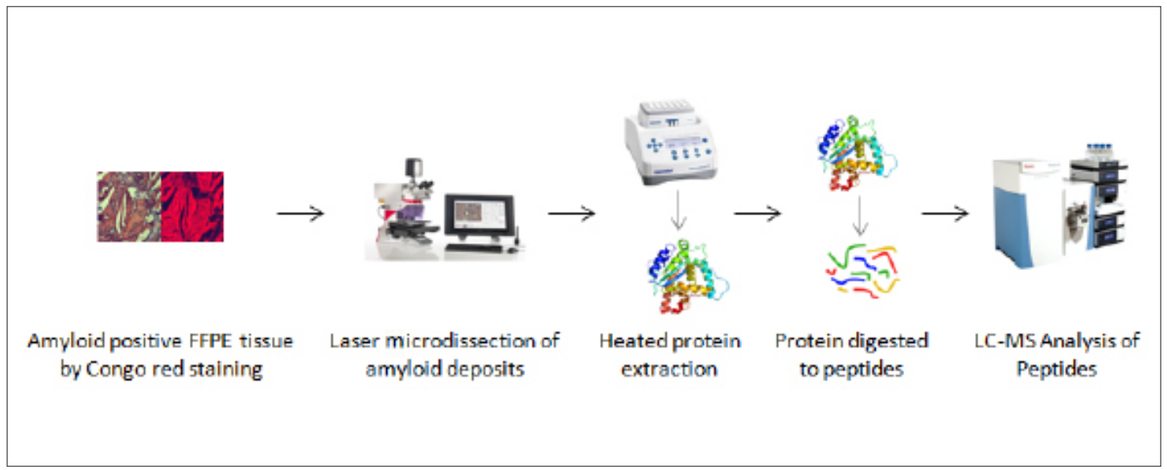
TUMOR PROFILING BY LC-MS IN A CLINICAL TRIAL
IMAGE: ROEHRL LAB



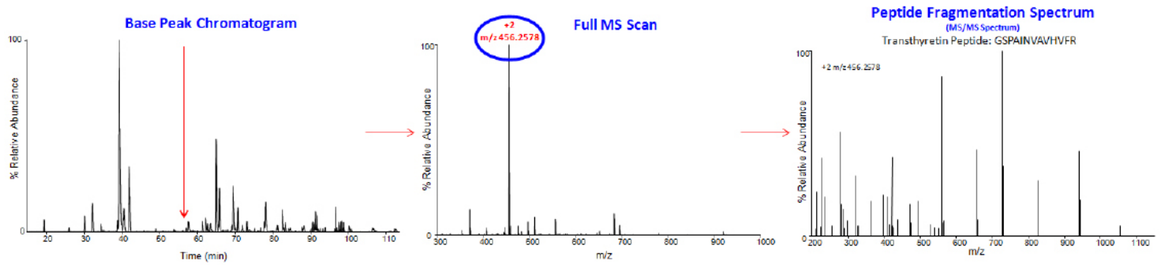
This is a general workflow for the preparation of FFPE tissue for LC-MS analysis. First 10µm sections are cut and left unstained. Protein is extracted using heat and sonication followed by digestion into peptides with an endoproteinase. The peptide mixture is then separated by LC and directly eluted into the MS.



Immuno-Proteomics of Colon Cancer
Image: Roehrl Lab



This workflow shows the sample prep protocol for the amyloidosis assay, but the general steps are similar for many sample types. First the tissue region of interest is isolated. Then protein is extracted using heat and sonication followed by digestion into peptides with an endoproteinase. The peptide mixture is then separated by liquid chromatography and directly eluted into the mass spectrometer.



A schematic of LC-MS/MS data, including a base peak chromatogram showing an overview of the sample, a full scan spectrum showing all peptides that are entering the MS at one time, and the MS/MS or fragmentation spectrum from which the sequence of the peptide is determined. Peptides are then assigned to proteins using protein databases and the proteomic profile can be determined. This is an example of an amyloidosis sample, and using mass spectrometry the sub-type of the disease is determined, which assists clinicians in providing the best patient treatment.

FUTURE CLINICAL ASSAYS

Drs. Chapman, Dogan and Roehrl are using mass spectrometry-based proteomics to develop clinical assays – one of which could be in routine clinical use soon.

NEAR TERM: An amyloidosis assay that Drs. Chapman and Dogan developed is almost ready to be implemented. "The disease can be quite subtle. You may not see the cancer, but with mass spectrometry you see this abnormal protein produced by the cancer," Dr. Dogan says.
Dr. Roehrl's lab has recently published methods for total humoral antigen-ome profiling that will become an assay for immune monitoring of solid tumors.

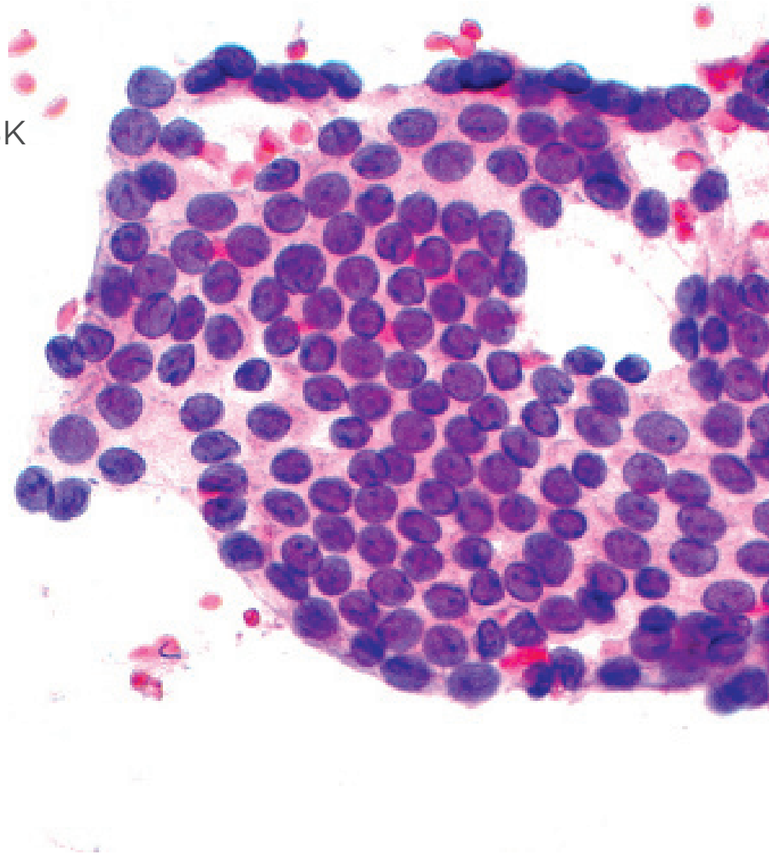
MEDIUM TERM: The doctors will be looking at downstream effects of abnormal proteins: components of their snowball effects that could be treated with drugs, particularly in lymphoma and leukemia, as well as solid tumors such as colorectal and pancreatic tumors.

LONG TERM: Global protein profiling is an ambitious project intended to identify new prognostic markers, diagnostic markers, therapeutic targets and drug targets.
In addition, Dr. Roehrl's lab is working on "deep proteome profiling," an assay in development that's akin to a broad, genome-wide panel. His team is also working on the characterization of tumor immunity. "This type of profiling is an assay for proteomic pathway changes," he says.

TELEPATHOLOGY, ROBOTIC MICROSCOPES AND MORE

The Cytology Service at MSK continues its tradition of collaborative innovation

By Hope Cristol



In the scheme of cancer care, pathologists are the physicians behind the scenes. But they, too, have teams of dedicated people behind them, enabling their important work to evolve, improve and ultimately serve more patients. Cytology Service Chief Oscar Lin, MD, PhD, is an example of a Pathology leader who credits his team and many other colleagues for the remarkable advances in cytology at MSK.

Dr. Lin, however, has been a driving force for positive change at MSK since he joined the staff in 1999. Prior to his arrival, the Pathology Department had not offered fine needle aspiration biopsies (FNAB) since the 1930s. In 2000, he re-established the FNA service, improving the care of patients by providing same day procedures and, in many instances, same day diagnosis.

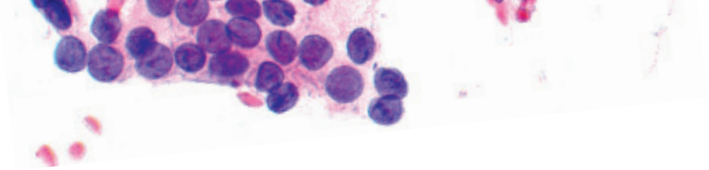
"The field of cytology has undergone many changes in the last few years. In the past, most cytology services would focus primarily in screening pap smears. Now, more and more cytology specimens are not pap smears and come from many other sites, which is a paradigm change for many other institutions," Dr. Lin says.

As FNAB became more popular in the evaluation of many types of tumors, particularly lesions of the thyroid and other superficial organs, Dr. Lin helped expand access to FNA biopsies for non-MSK patients. To establish the FNA Biopsy Clinic at the 60th Street Outpatient Center, he relied heavily on Administrative Manager Allix Mazella, who played a major role in the clinic's establishment and protocols. (Read more about Allix on page 22.) He also recruited Jean-Marc Cohen, MD, to be the clinic's director and enhance the service provided by offering ultrasound-guided FNAB.

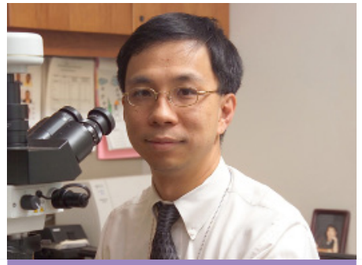
"Our motivation to offer this service to non-Memorial patients is that, in addition to having a biopsy done by highly trained experts, they also get the chance to be referred right away to an oncologist or surgeon at MSK. This saves valuable time in the management of these cancer patients."

Besides establishing the FNA service, Dr. Lin led the introduction of digital technologies – primarily telepathology – in the practice of cytology. The Cytology Service is advancing the field and improving cancer care in numerous other ways as well.

MEET THE TEAM



MSK's cytopathologists are actively involved in both clinical work and research, taking advantage of labs and resources for immunohistochemistry, flow cytometry, cytogenetics and molecular pathology. **THE CYTOLOGY SERVICE INCLUDES:**



OSCAR LIN, MD, PHD
Chief Attending

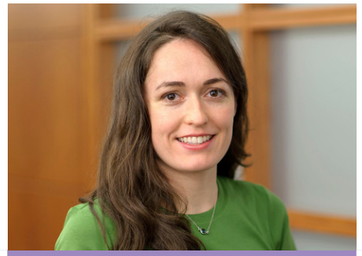
MARC ROSENBLUM, MD
Chief Attending (chief for Neuro)

CHRISTINA VALLEJO, MD
Attending

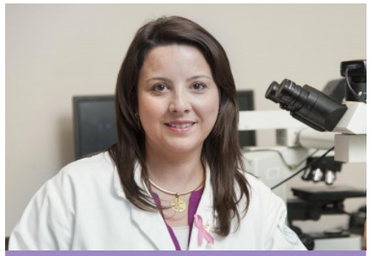
JEAN-MARC COHEN, MD, FCAP
Attending

NATASHA REKHTMAN MD, PHD
Associate Attending

NARASIMHAN AGARAM, MBBS
Associate Attending



CARLIE SIGEL, MD
Assistant Attending



MARCIA EDELWEISS, MD
Assistant Attending

RAJMOHAN MURALI, MBBS, MD
Assistant Attending

DARREN BUONOCORE, MD
Assistant Attending

JENNIFER SAUTER, MD
Assistant Attending

THE GROWING NEED FOR TELECYTOLOGY

Rapid on-site evaluation plays an important role during FNAB and core biopsies at MSK. It enables the pathologist and clinician to determine the adequacy of cellular material for initial diagnosis and whether additional samples are needed.

"Nowadays, oncologists need not only a pathological, morphology-based diagnosis, but also the molecular profile of the tumor. The molecular profile can help guide treatment in this era of personalized medicine," Dr. Lin says.

He notes that the primary purpose of an adequacy assessment is to see if the lesional material is represented in the biopsy obtained, thus eliminating or reducing the need for a repeat biopsy. However, he says, "We go beyond that at Memorial. We will assess what potential type of tumor it is and will triage the specimen obtained for the appropriate special studies required."

As the need for rapid on-site evaluation increased – corresponding with the evolution of molecular diagnostics as well as the rise of FNAB performed across MSK sites – Dr. Lin had several challenges to address. First, on the main campus, there aren't enough pathologists to perform initial adequacy assessments for all the cytological material collected. Second, there aren't enough FNAB or core biopsies performed at the regional sites to warrant hiring cytotechnologists there.

Dr. Lin has either resolved or is in the process of resolving these shortfalls, thanks to an early-adopter mindset and cutting-edge digital solutions developed and implemented with help from his Cytology Service team; Evangelos Stamelos, manager of Pathology Information Systems; Sahussapont Joseph Sirintrapun, MD, Director of Pathology Informatics; and others.

TELECYTOLOGY ON THE MAIN CAMPUS

Until a few years ago, pathologists were absent from many adequacy assessments. Instead, cytotechnologists would go to Interventional Radiology to prepare slides and determine whether the material was sufficient for pathological analysis, explains Cytology Lab Manager Dorota Rudomina.

It would be impossible for a pathologist to perform so many adequacies in multiple locations. Telecytology is changing that. The system comes from Remote Medical Technologies (RMT), and it's based on a camera, attached to a microscope, that live-streams specimen images to a pathologist using a secure server.

Rudomina, who played a central role in establishing telecytology systems at MSK, explains that the cytotechnologist is still required to be present in Interventional Radiology to prepare slides and show the cells of interest to the pathologist. Once a slide is on the microscope stage, the cytotechnologist calls a pathologist using the Vocera system: a secure, wireless, mobile communication platform, like a "mini walkie-talkie," she says. The pathologist then logs into the system and reviews high-resolution images of the slides from a laptop, desktop or mobile device.

The RMT system allowed the Cytology Service to dramatically reduce the number of pathologists required for the high volume of adequacy assessments. Physicians now perform an average of 30-35 adequacy assessments every day on the main campus using telecytology. Of course, having a pathologist's expertise also makes adequacy assessments more accurate, reducing the need for repeat biopsies.

INTRODUCING ROBOTIC MICROSCOPES

MSK's expansion to regional centers has brought the need for adequacy assessments to these locations. However, the estimated 1-2 daily biopsies performed by interventional radiologists at the regional centers doesn't justify staffing the sites with full-time cytotechnologists. Once again, telepathology offers an innovative solution.

The Sakura VisionTek system, which involves a robotic microscope, eliminates the need for cytotechnologists onsite. Instead, interventional radiologists at the regional centers have become certified to do some of the work previously performed by cytotechnologists. They now prepare slides, load them into a robotic microscope and call a cytotechnologist at the main campus, who then reviews live images of the slides. The remote cytotechnologist is the only one who can control the microscope (via arrow keys, for example).

Pathologists don't participate in these adequacy assessments, but they will in the future. Dr. Lin and colleagues are exploring systems that would enable the cytotechnologist to review the images, while also sharing the images with a cytopathologist.

There are several robotic microscope systems in use and more are being added at regional campuses. The first, in 2014, was deployed at MSK Westchester for Interventional Radiology and now includes ultrasound radiology. MSK Commack's is used for both interventional and ultrasound radiology. MSK Monmouth uses the Sakura system for interventional radiology and the thoracic service. In the near future these systems will be deployed at MSK Basking Ridge, MSK Bergen County and MSK Nassau.

OTHER CYTOLOGY SERVICE CONTRIBUTIONS

The Cytology Service has played a valuable role in the utilization of molecular studies when other types of biopsies don't yield enough material. For example, sometimes core biopsies procured from tumors in difficult-to-access areas (say, close to a vital organ or large vessel) do not provide enough cells for all the necessary studies. The next step would be to analyze the cytology material, but even that might prove to be insufficient.

What's a pathologist to do, then, if an additional biopsy is needed but ill-advised because of the tumor's location? Dr. Lin's team now has an enhanced protocol for just this dilemma.

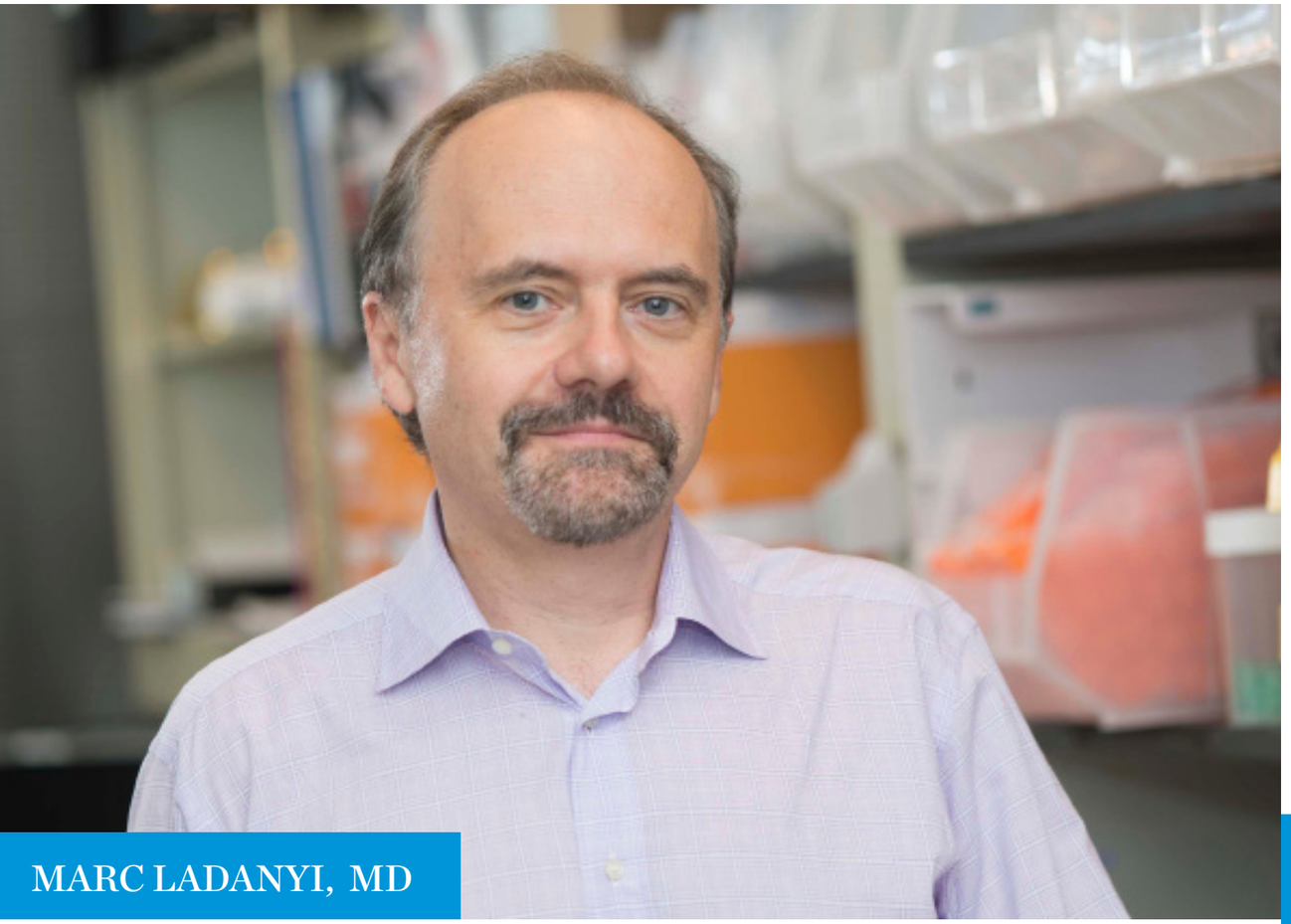
"We developed a method to use cytology material that used to be discarded after processing. This is the so-called 'residual material,' which includes supernatant obtained after the cells are separated for analysis," Dr. Lin says.

His team, in collaboration with the Molecular Diagnostics Service, have assessed over 80 cases to date using this method. "We are now able to save certain patients from another procedure that could put them at risk for serious complications."

INSIGHTS FROM THE RESEARCH LAB OF
MARC LADANYI

The veteran pathologist talks about his lab's focus on therapeutic strategies – and why he doesn't own a Bentley

By Hope Cristol



MARC LADANYI, MD

Marc Ladanyi, MD, is one of the most recognizable names in pathology at MSK. That's because in this era of molecular diagnostics, the Chief of the Molecular Diagnostics Service is central to many of the department's major initiatives, including MSK-IMPACT.

Dr. Ladanyi holds the endowed William J. Ruane Chair in Molecular Oncology and his name has been on over 400 research papers published during his three decades of service to the Department. (He is the third most senior attending, with only Drs. Victor Reuter and Marc Rosenblum having been here longer.)

In addition to his clinical duties overseeing Molecular Diagnostics, Dr. Ladanyi also has a research lab that works in the areas of sarcomas and thoracic malignancies.

"What's maybe unexpected is that so much of the work in my research lab is focused on novel therapeutic strategies," Dr. Ladanyi says. "The cliché would be that a pathologist doesn't work on therapies, but that in fact is what we're most interested in. Perhaps significantly, the only award I got in medical school was for the top grade in pharmacology, which made the choice of going into pathology seem paradoxical but now maybe it makes more sense!"

In a recent conversation with *MSK Pathology Review*, he spoke about some of the latest work from his lab, as well as how he stays on top of the ever-evolving field.

DRAWING FROM MSK-IMPACT

Dr. Ladanyi's research team fluctuates between 8-10 people. The work is largely driven by observations from human cancer genomic studies, more recently including MSK-IMPACT.

In lung cancer, the researchers have done functional studies of cell lines harboring mutations of both *NF1* and *RASA1*. In a paper published in 2017 in *Clinical Cancer Research,* they reported that concurrent *RASA1* and *NF1* loss-of-function mutations function as lung cancer drivers. The mutations also define a genetic subset of non-small cell lung cancer that may respond to a MEK inhibitor such as trametinib.

His team is also looking at novel resistance mechanisms to different kinase inhibitors in lung cancer. Many of these resistance mechanisms are first observed through MSK-IMPACT testing in patients with recurrence of disease while on kinase inhibitor treatment.

The sarcoma work largely focuses on Ewing sarcoma, synovial sarcoma and desmoplastic small round cell tumor (DSRCT). The team has been researching these sarcomas for some time. (Dr. Ladanyi's lab, together with that of the late William Gerald, originally identified the *EWSR1-WT1* fusion in DSRCT). Now, the researchers hope to use new insight about the genomics of these tumors to develop better treatment approaches.

EXPLORING THERAPEUTIC NUCLEIC ACIDS

Speaking of applying genomics to treatment approaches, the team has explored modified oligonucleotides as drugs to inhibit certain genes, particularly fusion genes and others that may be of therapeutic interest.

"I think it's a promising area," Dr. Ladanyi says. "There are already a handful of oligonucleotide-based drugs for some non-cancer conditions, so we're looking to generate preclinical data to show that this could be an attractive therapeutic option for further development in sarcomas that otherwise lack good drug targets."

SARCOMA DRUG SCREENS

Dr. Ladanyi has worked with MSK's core facilities and other teams to do large drug screens in several sarcomas. A few years ago, they screened a library of more than 300,000 chemical compounds for growth inhibition of Ewing sarcoma cells. The researchers identified a novel type of proteasome inhibitor that did the job, selectively inhibiting Ewing sarcoma cells by inducing apoptosis.

"The running joke in the lab at the time was that the patent on this novel proteasome inhibitor was going to pay for my first Bentley," Dr. Ladanyi says. "Then we got scooped by a group at the Karolinska, so no Bentley for me."

Dr. Ladanyi adds that his research team has collaborated on similar screens for other sarcomas, including malignant rhabdoid tumor, and they're pursuing several interesting leads. Much of this work has been done with MSK pediatric oncologist Neal Shukla, MD.

KEEPING UP WITH ADVANCES

Dr. Ladanyi joined MSK in 1987 as a fellow, obviously well before molecular pathology transformed the field. How has he stayed on top of it all, and for so long?

"One thing you realize when you've been around for a while is that you're like a witness to history. The way you keep up with advances is that you're there when the advances are made," he says.

He adds that he and other pathologists at MSK have kept up with the field in a general sense by collectively being ahead of the curve in different ways. "It helps to be at an institution where every day you are having scientific conversations that will take place at most other institutions only several years later. And this ties in with what might be the best scientific career advice I ever read: always seek out and talk to people who are smarter than you are."

RESEARCH ROUNDUP

These are just a few of Dr. Ladanyi's notable research papers published in 2017 and 2018:

- *New England Journal of Medicine*: "Efficacy of Larotrectinib in TRK Fusion-Positive Cancers in Adults and Children."
- *Nature Medicine*: "Mutational landscape of metastatic cancer revealed from prospective clinical sequencing of 10,000 patients."
- *Precision Oncology*: "Plasma DNA-Based Molecular Diagnosis, Prognostication, and Monitoring of Patients With EWSR1 Fusion-Positive Sarcomas."
- *Clinical Cancer Research*: "RASA1 and NF1 are Preferentially Co-Mutated and Define A Distinct Genetic Subset of Smoking-Associated Non-Small Cell Lung Carcinomas Sensitive to MEK Inhibition."
- *Cell*: "Comprehensive and Integrated Genomic Characterization of Adult Soft Tissue Sarcomas."

A LEADER IN SARCOMA RESEARCH

Cristina Antonescu, MD, talks about the discoveries from her lab and the people who help make them possible

By Hope Cristol

CRISTINA ANTONESCU, MD

Cristina Antonescu, MD, Director of Bone and Soft Tissue Pathology, is one of several veterans of the Pathology Department: She joined the faculty in 1999 after completing her fellowships in oncologic pathology and sarcoma research at MSK. As a clinician, her role is to establish accurate pathologic diagnosis, grading and staging. But she is just as passionate about and dedicated to her role as a scientist.

Since 1999, Dr. Antonescu has served as the Director of the Pathology Core for the Sarcoma Program Project. She started her own lab in 2004. Key areas of her research are KIT oncogenic signaling in the pathogenesis of gastrointestinal stromal tumors (GISTs) and molecular characterization of novel fusion genes, activating mutations or gene copy number changes.

The sarcoma research program at MSK, to which she has contributed greatly, has made numerous important discoveries. It's also been recognized as a leader in sarcoma research by the National Cancer Institute (NCI), which has supported MSK with Soft Tissue Sarcoma Program Project Grants for nearly 30 years.

Dr. Antonescu's expertise runs deep and her list of research achievements is lengthy. However, she shares these recent highlights from her lab – and expresses gratitude for the people and groups behind her success.

KEY DISCOVERIES

One major focus of Dr. Antonescu's lab is the discovery of new genetic abnormalities in sarcomas for improved classification and diagnosis. Before the era of next-generation sequencing, she used standard molecular techniques, such as RACE (Rapid Amplification of cDNA Ends) and FISH (fluorescence in situ hybridization) for positional cloning. Some of her earlier discoveries include the *EWSR1-CREB1* fusion in gastrointestinal clear cell sarcoma, *EWSR1-POU5F1* in soft tissue myoepithelial tumors, and *WWTR1-CAMTA1* in epithelioid hemangioendothelioma.

More recently, her team established a highly efficient pipeline for novel gene fusion discovery that includes whole transcriptome RNA sequencing and FusionSeq bioinformatic algorithms. Using this method, the researchers described more than 20 novel translocations in the past eight years, such as:

- *NAB2-STAT6* in solitary fibrous tumors
- *MIR43-NOTCH* in malignant glomus tumors
- *VGGL2*-related fusions in congenital spindle cell rhabdomyosarcoma
- *FOS* and *FOSB*-related fusions in epithelioid hemangioma

After thorough validation, these new genetic alterations have now been incorporated as routine molecular diagnostic markers at MSK and beyond. In addition, they pave the way for additional research on potential therapeutic targets.

SUPPORTING ROLES

Dr. Antonescu takes great pride in her research lab team. Lei Zhang, involved in running the fluorescence in situ hybridization, has worked in the lab for more than 12 years and developed hundreds of novel probes to validate and screen the new fusions. Yun Shao (Peter) Sung is the group bioinformatician. A team member for many years, Peter has established a reliable RNA sequencing data analysis pipeline for novel fusion gene discovery. Dr. Antonescu is also pleased to have new team member Yumi Fujisawa, who is focusing on cell culture and genotyping.

Over the years, Dr. Antonescu has mentored international investigators with a special interest in sarcoma pathology and molecular biology, such as Antoine Italiano and Francois Le Loarer (Bordeaux, France), Costantino Errani (Bologna, Italy), John Huang and Karen Kao from Taiwan.

"Additionally, my lab serves as a valuable resource for mentoring and assisting some of the junior members of our department, such as Narasimhan Agaram, MBBS, with various sarcoma subtypes, Sarah Chiang, MD, with characterization of new gene fusions in endometrial stromal sarcomas, Nora Katabi, MD, in the molecular characterization of salivary gland tumors, and Natasha Rekhtman, MD, PhD, in undifferentiated thoracic tumors with *SMARCA4* abnormalities," Dr. Antonescu says.

FUNDING THE LAB

Dr. Antonescu's first American Cancer Society research grant in 2004 enabled her to start her lab. Subsequent government funding through either sarcoma-related Program Project or SPORE mechanisms have been instrumental for her work. However, she is especially grateful for the extramural funding she receives. Dr. Antonescu says it has been essential to keep the lab growing. Specifically, she mentions contributions from The GIST Cancer Research Fund, Angiosarcoma Awareness, Team Luke, Shuman Fund, Cycle for Survival (an MSK fundraiser for rare cancers, in partnership with Equinox), and others.

"As the research lab is expanding, taking on new endeavors and methodologies, one consistent task for the near and long term future is to ensure a constant flow of grants and funding to support these activities," Dr. Antonescu says.

SPORE RESEARCH HIGHLIGHT

Dr. Antonescu is Director of the Pathology Core for the National Cancer Institute's SPORE in soft tissue sarcoma. She also serves as the clinical co-leader of a project exploring the mechanisms of KIT signaling and imatinib resistance in GIST.

About half the GIST patients who benefit from imatinib will eventually become resistant to it, and few other treatments are available. Dr. Antonescu and colleagues are exploring the pathways involved in imatinib-resistant GIST and conducting preclinical investigations in hopes of finding new options for these patients.

COMING SOON
INTEGRATED REPORTS

By next year, the multitude of reports for a given patient could be synthesized into a single, searchable file

By Hope Cristol

There's a basic workflow for clinical pathology at MSK: A patient comes in for surgery or a biopsy, the sample goes to pathologists, tests are performed, reports are written. There might be four reports for a patient. There might eventually be 94.

The treating physician must go through the pathology reports whenever there's a new addition, extract the most salient information and make proper treatment decisions. It's an increasingly big lift given the rise in available genomic information.

Ahmet Zehir, PhD, Director of Clinical Bioinformatics, is leading an effort to integrate the pathology reports for each patient. "This way the treating physician only looks at one report with pertinent results instead of going through multiple reports and trying to summarize the information in their minds," Dr. Zehir says.

More than merely merging pathology reports, the integrated reports will also synthesize critical values and provide pathologists' interpretation of genomic and clinical data.

BENEFITS FOR PATHOLOGISTS

Victor Reuter, MD, Vice Chair of Pathology, is a key collaborator in this initiative, but he modestly describes his role as representing the department and its pathologists. "My number one goal is making sure that this tool is user friendly," he says.

Automation will be essential, of course, to ensure the new reports are a boon and not a burden to pathologists. The good news on that front is that Dr. Zehir and his team are making automation a priority. As an example: Today, pathologists type sentences to describe the results of immunohistochemistry assays for specific biomarkers. "We can automate this by forming the sentence for them, and they can just enter positive or negative findings," Dr. Zehir says.

Another advantage for pathologists is that the data for the integrated reports will be searchable. For the first time, it will be a simple task to identify a cohort of patients who are positive for a certain biomarker.

AHMET ZEHIR, PHD AND VICTOR REUTER, MD

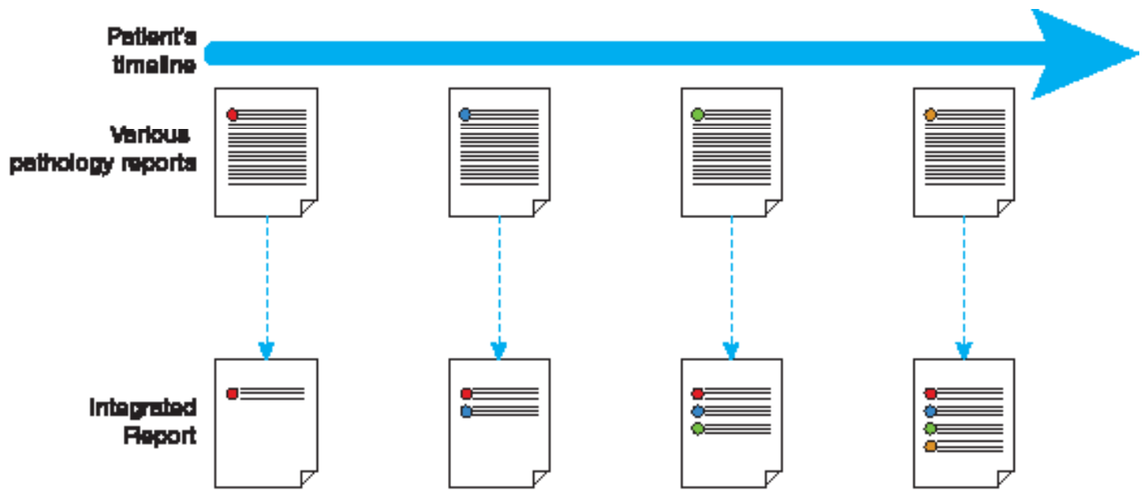
A HYPOTHETICAL CASE

Dr. Reuter offers a hypothetical example of integrated reports in action. "Let's say that I have looked at a renal tumor that is extremely aggressive. I have performed a lot of ancillary studies, but at the end of the day I really cannot classify it, beyond calling it renal cell carcinoma, type unclassified, a term which exists in the WHO classification of tumors," Dr. Reuter says.

He sends the tumor for molecular analysis and a week later finds out it has a mutation of the fumarate hydratase (FH) gene.

Dr. Reuter continues, "Wouldn't it be logical for me to integrate into the pathology report that this renal cell carcinoma, unclassified type, we now know has a mutation in the FH gene, which has been associated with familial diseases?"

The renal cell carcinoma is still morphologically unclassifiable, but with genomic information, there's more to the story. That mutation that might be clinically relevant not only to the patient, but also the patient's family, starting a chain of events that may lead to genetic counseling. With an integrated report, all this information would be at physicians' fingertips in a single document.



ROLLING OUT THE REPORTS

Dr. Zehir hopes to roll out integrated reports to the Hematopathology Service team later this year. The team currently has a version of an integrated report, but it lacks the automation and searchability of the model Dr. Zehir's team is developing.

"They add results and add their interpretive commentary, but it's all plain text. If you want to search for a specific patient later, it's kind of impossible," Dr. Zehir says.

Dr. Reuter agrees that it's smart to start with Hematopathology. "If you think about it, the overwhelming majority of hematopathology [biospecimens] are triaged to different laboratories: immunohistochemistry, flow cytometry, if there's bone marrow that will be read, and also the bone marrow aspirate," he says. "Those are all different reports being done on the same patient at pretty much the same time, and [an integrated report] brings those together and provides interpretation."

If the tool works as well as expected, it will be implemented across Pathology – hopefully by next year. But Dr. Reuter sees no reason why such a powerful tool couldn't be exported to other departments across the institution.

Dr. Zehir, too, envisions the project having broad reach. "I look at the integrated reporting project as a stepping stone to better prospectively collect clinical data and to share it with the institition with a more structured way," Dr. Zehir says.

JORGE REIS-FILHO, MD, PHD

THE DIRECTOR OF EXPERIMENTAL PATHOLOGY HIGHLIGHTS SOME OF HIS LAB'S LATEST DISCOVERIES

By Hope Cristol

Jorge Reis-Filho, MD, PhD, Director of Experimental Pathology, is one of the few members of the Pathology Department who is exclusively dedicated to research. His work focuses on two areas: the molecular underpinning of rare cancers, particularly breast cancers, and characterization of intratumor genetic heterogeneity in breast cancers.

"By combining traditional pathology with cutting edge genomics, we can not only push the boundaries of what we know, but also change patients' lives," Dr. Reis-Filho says. Here, he offers a snapshot of recent projects from his lab.

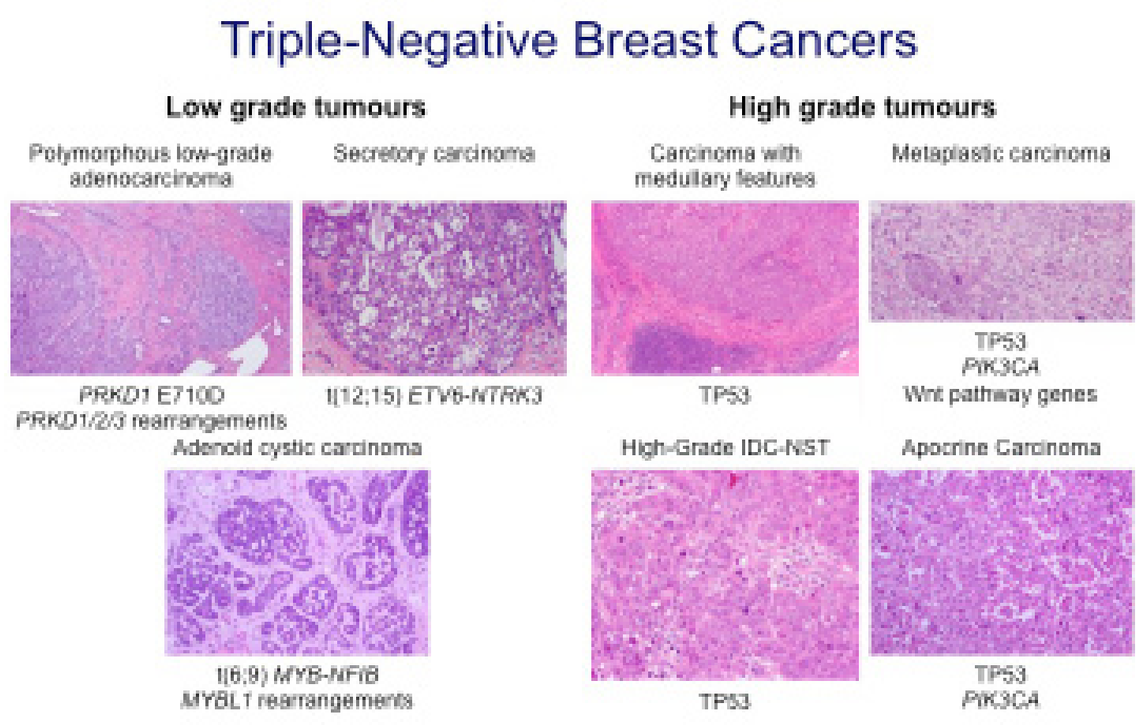
DISCOVERING NEW DRIVERS

Genetic analysis of tumors is a lynchpin of cancer research as well as of precision medicine. Given the unprecedented technological developments in the last decade, researchers can now decode the entire genome of a tumor quickly and inexpensively, searching for molecular alterations that cause normal cells to become cancerous.

Distinguishing between driver genetic changes and passenger genetic changes is by no means trivial. Through large-scale studies of common types of cancer, including the analysis of over 20,000 patients using MSK-IMPACT, most of the driver mutations have been identified. These driver genetic alterations in common cancer types can be used to subclassify the tumors into distinct biological and clinical subtypes.

Dr. Reis-Filho's team focuses on the analysis of the genetic features of rare cancer types. "Tumors from each of the rare cancer types, unlike common malignancies, are much more homogeneous, have simpler genomes, and are often driven by a single highly recurrent driver alteration," says Dr. Reis-Filho. "It is as if these are biological outliers."

His group has reasoned that if these tumors are homogeneous in their genetic make-up, then by sequencing a handful of tumors from each rare cancer type, their driver genetic alterations can be identified. By using this approach, Dr. Reis-Filho and colleagues have identified:



OTHER RESEARCH HIGHLIGHTS

There's always something coming out of Dr. Reis-Filho's lab, which has 11 team members. Stay tuned for publications on:

- New driver genetic alterations in rare cancer types
- Liquid biopsy-based monitoring of breast cancers.
- Intratumor genetic heterogeneity and single cell sequencing analysis of breast cancer precursors

A **NEW MUTATION** affecting the gene *PRKD1* that defines polymorphous low-grade adenocarcinomas of the salivary glands

The **COMBINATION OF MUTATIONS** affecting *IDH2* and PI3K-pathway genes that defines a vanishingly rare form of breast cancer called solid papillary carcinoma with reverse polarity

A **SUBTYPE OF TRIPLE-NEGATIVE BREAST TUMOR**, adenomyoepithelioma, that has recurrent driver alterations of the oncogene *HRAS*

In addition, Dr. Reis-Filho's work on rare forms of triple-negative breast cancers has resulted in the identification of a subset of these tumors that are low-grade, have an indolent clinical behavior, and are driven by specific driver genetic alterations that render them different from most triple-negative cancers. These tumors have rather esoteric names, such as adenoid cystic carcinomas, secretory carcinomas, mucoepidermoid carcinomas and polymorphous low-grade adenocarcinomas. However, their identification is more than a mere academic exercise.

"Our work has actually brought histology back to the forefront of the analysis of triple-negative cancers. Identifying these subtypes now has clinical implications," Dr. Reis-Filho says.

RESEARCH ON DCIS

In the area of intratumor genetic heterogeneity, Dr. Reis-Filho emphasizes his team's research on ductal carcinoma in situ (DCIS), specifically its progression to invasive breast cancer.

The researchers developed single cell sequencing methods that can be applied to samples of formalin fixed, paraffin embedded DCIS tissue. They observed that intratumor genetic heterogeneity can be present as early as DCIS. This is contrary to the previous belief that tumors acquire heterogeneity later in their evolution.

"In some cases, indeed there is a selection of specific subclones from DCIS to invasive breast cancer," Dr. Reis-Filho says. "In other tumors, multiple clones within a DCIS can become invasive."

This has several implications. First, the research suggests DCIS is already a genetically advanced disease – that there are already many genetic alterations to begin with. Second, this heterogeneity may cause important challenges in identifying biomarkers that predict tumor behavior. Third, DCIS will progress differently among different patients.

"We need to understand the biology of each DCIS if we are to be able to manage these patients optimally," he says.

Q & A

WITH ALLIX MAZZELLA

ADMINISTRATIVE MANAGER

Q: What brought you to Memorial Sloan Kettering four years ago?

While earning my MPH in Healthcare Management, I knew I wanted to go into hospital administration because it would afford me the opportunity to manage operations and improve processes to directly benefit patient care. I also have a personal connection to Memorial Sloan Kettering as several relatives have been treated here. Of note, my grandmother was diagnosed with stage IV breast cancer in the '80s. She went on to live another 35 years and always maintained that this hospital saved her life. When the opportunity to apply for an administrative fellowship at MSK presented itself during grad school, I was overjoyed by the prospect of fulfilling my professional aspirations and working for an organization that meant so much to my family and me.

Q: You've moved through the ranks at MSK from Administrative Fellow in Hospital Administration to Administrative Coordinator in Pathology to Administrative Manager in Pathology. What accomplishments are you especially proud of?

Prior to working in Pathology, I created a tool to collect and analyze data from both MSK and the Hartford HealthCare Cancer Institute. These findings were ultimately used to identify both gaps and similarities in the way both institutions practice cancer care as part of the MSK Cancer Alliance initiative. I also worked with the Integrative Medicine Service to develop a mechanism to collect and evaluate patient-reported outcomes. This helped the service establish baselines and improve effectiveness of their therapies and treatment modalities.

When I started in the Cytology Service within Pathology, I helped to create and manage our Fine Needle Aspiration Biopsy Clinic. This service improves access to non-MSK patients who seek convenient appointments with an MSK pathologist.

I also standardized the process for the transportation of specimens from satellite locations. Before I revamped this workflow, each site followed its own process for sending samples to us. Now, all facilities use the same Pathology transport log and leak-proof tote bag for forwarding samples to the Main Campus. These samples are then reconciled against the transport log once they are received in central accessioning.

Q: What are you responsible for in your current role?

I manage non-technical operations for the Surgical Pathology and Cytology services. I ensure that accessioning, transcription and other administrative support roles are adequately staffed. I'm also responsible for making sure that my staff follow established protocols and are trained on new processes.

Together with pathologists and other managers, I identify areas of improvement within our operations and will create and implement new workflows to improve efficiency. For example, I am now in the process of looking for an IT solution so that we can use technology to better track samples sent to the Main Campus before they are entered in our Laboratory Information System. Process improvement projects often affect other departments, and I therefore collaborate closely with other services if Pathology plans to roll out a new workflow that will involve their staff.

Q: What do you find most gratifying about working in Pathology?

Although I don't always interact with patients, I am fortunate to be able to connect my day-to-day projects and performance improvement initiatives to their experience here. I find it very rewarding knowing that an effort to reduce the time it takes to deliver a specimen from the OR to Pathology, for example, can directly impact and enhance their care. I am also grateful to work with such a wonderful and supportive team of pathologists, fellow managers and staff. Everyone in our department is truly dedicated to MSK's mission, and I feel inspired to be surrounded by such enthusiasm.

Q: What might your colleagues be surprised to learn about you?

I think many of my colleagues already know this, but I love to write (and eat!). When I first finished college, I toyed with the idea of going to journalism school or becoming a food critic. Years ago, I wrote freelance restaurant reviews for New York Magazine, Not For Tourists and a book that features restaurants with local and sustainable menu options called Clean Plates. I don't write reviews any more, but I still do a whole lot of eating!

6 KEY BENEFITS
OF THE PATHOLOGY CONSULT PORTAL

The groundbreaking initiative will expand and improve access to MSK pathologists

By Hope Cristol

S. JOSEPH SIRINTRAPUN, MD

S. Joseph Sirintrapun, MD, the affable Director of Pathology Informatics, is leading MSK's future Pathology Consult Portal (PCP) – what he calls a moonshot. When the PCP goes live, “it will be a marvel of technical and human factors engineering,” he says.

On the back-end, the PCP is a complex integration of teams, tools and technology. On the front end, Dr. Sirintrapun says he “aspires for pathologists to discover and embrace a simple, intuitive engine that enables digital slide-based consults to flow in from anywhere.”

SIX MAJOR BENEFITS OF THE PCP,
WHICH MAY BE AVAILABLE AS A PILOT BY THE END OF THIS YEAR

1 IT BUILDS A BETTER PATHWAY FOR SECOND OPINIONS.
Dr. Sirintrapun's concept behind the PCP is to create an infrastructure so that outside institutions, patients, or anyone else who wants a second opinion can scan glass slides and upload them securely. This will eliminate potential problems of physically transporting slides, such as loss, delay, and damage. Another key is for the PCP to deeply integrate with the anatomic pathology laboratory information system (AP-LIS). Dr. Sirintrapun's vision is for the PCP to emerge as the primary pathway for rendering all opinions on outside pathology cases.

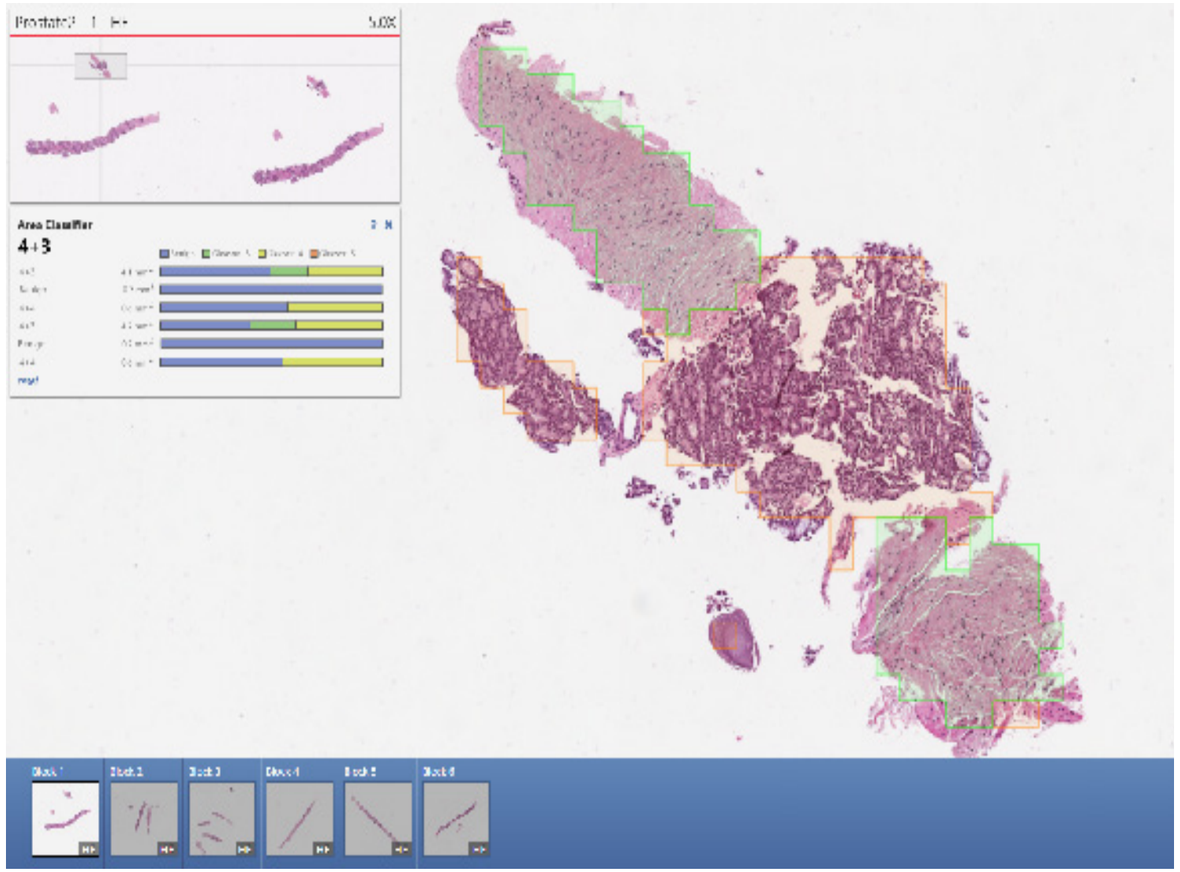
2 IT STREAMLINES BECOMING AN MSK PATIENT.
If you are interested in a second opinion and your case is uploaded for review, you officially become an MSK patient. Through the PCP, this simplification for patients proves a significant advance by leveraging automated mechanisms for patient registration.

3 IT BOLSTERS BONDS WITH MSK CANCER ALLIANCE MEMBERS.
MSK is committed to strengthening relationships with the three members of the MSK Cancer Alliance: Hartford HealthCare Cancer Institute, Lehigh Valley Health Network and the Miami Cancer Institute at Baptist Health South Florida. Already positioned to streamline patient registration, the PCP can offer customized "expedited lanes" for Alliance Member patients.

4 IT CREATES A GLOBAL PRESENCE.
Once operating at full scale, the PCP expands Pathology's reach not only domestically but also internationally. “There's an unlimited need for expert opinion outside the U.S.," Dr. Sirintrapun says, emphasizing the profound shortage of pathologists in Asia, Africa, South America and even Europe.

5 IT ESTABLISHES THE BENCHMARK FOR DIGITAL PATHOLOGY CONSULTATION.
Dr. Sirintrapun notes that a few other institutions have implemented pathology consultation portals with digital slide scanning technology. None thus far is built for large-scale adoption and utilization. “To further clarify, none eases the burden for patients in registration, none deeply integrates with the AP-LIS, and none is built to handle more than a few cases per week,” Dr. Sirintrapun says. The PCP at MSK will be built to handle thousands of uploads per week and feature tools that make the notificatio“n, reporting and communication between parties simple.

6 IT SHINES A SPOTLIGHT ON PATHOLOGISTS.
Patients often choose an oncologist, a surgeon or a hospital based on reputation. Selecting a pathologist? That's uncommon – but perhaps not for much longer. "What this portal has an opportunity to do is make pathologists the driver of patients coming to MSK," Dr. Sirintrapun says. "If you're a patient somewhere else and have concerns about your diagnosis, you can ask your doctor to upload a consultation to our portal. It changes the paradigm for how pathology is regarded across hospitals and institutions."



Screenshot of the PCP digital Viewer

MAJOR COLLABORATION

Like any important project at MSK, the Pathology Consult Portal involves multiple teams and players, including Pathology Senior Project Manager Jennifer Samboy, as well as:

PATHOLOGY LEADERSHIP

Victor Reuter, MD, Vice Chair
Pathology Department

Meera Hameed, MD, Service Chief
Surgical Pathology

David Klimstra, MD, Chairman
Pathology Department

PATHOLOGY IT

Evan Stamelos, Pathology Systems Manager

Vincent Lu, Administrative Coordinator

DATACENTER

Miroslav Trunec, Manager,
Server Technologies

HOSPITAL IS

John Philip, Senior Project Manager
Precision Oncology

Janet Mak, Vice President,
Applications

Janice Schacter, IS Manager

SECURITY

Mike Piscitelli, Security Analyst

MSKCC@USCAP 2018

PLATFORMS:

***Alex*, Nafa, Zehir, Arcila, Lin** – Cytopathology. *Residual Cytology Material for the Detection of Targetable Genetic Alterations by Next Generation Sequencing: An Institutional Experience* ***

***Alex*, Zehir, L. Wang, Nafa, Hameed, Ladanyi** – Bone and Soft Tissue Pathology. *Clinical Genomic Sequencing of 72 Pediatric and Adult Osteosarcomas Reveals Distinct Molecular Subsets with Potentially Targetable Alterations* ***

Antonescu – Gynecologic Pathology. *Clinicopathologic, Immunohistochemical, and Molecular Characterization of 30 Uterine Perivascular Epithelioid Neoplasms*

Basturk, Klimstra – Pancreas Pathology. *Pancreatobiliary Maljunction-Associated Gallbladder Cancer is as Common in the West as in the East, Shows Distinct Clinicopathologic Characteristics and Offers an Invaluable Model for Reflux-Associated Physio-Chemical Carcinogenesis*

Chen, Gopalan, Fine, Tickoo, Sirintrapun, Berger, Reuter, Al-Ahmadie – Genitourinary Pathology. *Molecular Profiling of Urothelial Papilloma and Inverted Papilloma of the Bladder*

Cotzia, Benayed, Soslow, Antonescu, Ladanyi, Chiang – Gynecologic Pathology. *Undifferentiated Uterine Sarcomas Represent Underrecognized High Grade Endometrial Stromal Sarcoma*

Cotzia, Berger, Ladanyi, Ghossein, Antonescu, S. Dogan – Head and Neck Pathology. *Genetic and Histologic Spectrum of SMARCB1-Deficient Carcinomas of the Head and Neck Including Sinonasal Tract, Thyroid and Skin*

***Favazza*, Soslow, Delair** – Gynecologic Pathology. *Clinical Outcomes of Patients with Tumor Displacement into Fallopian Tubes in Patients Treated by Robotically-Assisted Hysterectomy for Newly Diagnosed Endometrial Cancer* ***

Giri, Weigelt, Reis-Filho – Breast Pathology. *Lobular Carcinoma In Situ Displays Intra-Lesion Genetic Heterogeneity and Clonal Evolution in the Progression to Invasive Disease*

Gopalan, Al-Ahmadie, Chen, Sirintrapun, Tickoo, Reuter, Fine – Genitourinary Pathology. *Neuroendocrine Differentiation in the Setting of Prostate Cancer: Contemporary Assessment of 76 Consecutive Cases from a Single Institution*

Gupta, Benayed, Arcila, Zehir, Berger, Ladanyi, S. Dogan – Pathobiology. *TERT Promoter Mutation and Amplification: A Pan-Cancer Study on 20,184 Tumors Profiled by Clinical Genomic Sequencing* ***

***Hanna*, Reuter, Fine, Agaram, Hameed, Klimstra, Sirintrapun** – Informatics. *Implementation of Digital Pathology Offers Clinical and Operational Increase in Efficiency and Cost Savings* ***

Hechtman, Vakiani, Klimstra, Shia – Gastrointestinal Pathology. *Pathologic Patterns of Anti-PD-1 Induced Colitis*

***J. Chang*, Arcila, Montecalvo, Benayed, Borsu, Travis, Ladanyi, Rekhtman** – Pulmonary Pathology. *Next Generation Sequencing and Clinicopathologic Analysis of 101 Pulmonary Invasive Mucinous Adenocarcinomas Focusing on Comparison Among Molecular Subtypes* ***

***Jia*, Al-Ahmadie, Fine, Gopalan, Sirintrapun, Tickoo, Reuter, Chen** – Genitourinary Pathology. *Morphologic and Molecular Characterization of Renal Medullary Carcinoma: A Study of 18 Cases* ***

***Jia*, Al-Ahmadie, Fine, Gopalan, Sirintrapun, Tickoo, Reuter, Chen** – Genitourinary Pathology. *Clear Cell Renal Cell Carcinoma with Prominent Papillary Architecture: A Rare Morphologic Variant Supported by Molecular Evidence* ***

***Jelloul*, Khattar, Jungbluth, Lu Wang, Y. Zhang, A. Dogan** – Hematopathology. *MHC Class II Transactivator (CIITA) Abnormalities Are Frequent in B-cell Lineage Lymphomas and Are Associated with Loss of MHC Class II (MHCII) Expression* ***

Katabi, Ghossein – Endocrine Pathology. *Outcome of Non-Invasive Follicular Variant of Papillary Thyroid Carcinoma [NI-EFVPTC] with Oncocytic Features*

***Lewis*, *Kumar*, Arcila, Roshal, Xiao** – Hematopathology. *PHF6 Mutations Define A Subgroup of Mixed Phenotype Acute Leukemia with Aberrant T-cell Differentiation* ***

***Lewis*, Soslow, Delair, K. Park, Murali, Hollmann, *Arias-Stella*, Hameed, Benayed, Ladanyi, Jungbluth, Antonescu, Chiang** – Gynecologic Pathology. *ZC3H7B-BCOR High Grade Endometrial Stromal Sarcoma: A Report of 17 Cases of a Newly Defined Entity*

Montecalvo, *Alex*, Sauter, J. Chang, Jungbluth, Ladanyi, Antonescu, Travis, Rekhtman – Pulmonary Pathology. *Pulmonary BRG1 (SMARCA4)-Deficient Undifferentiated Neoplasms Represent An Exceptionally Aggressive Type of Sarcomatoid Carcinoma: Clinicopathologic and Genomic Evidence Supports A Link to Non-Small Cell Carcinoma* ***

***Muller*, Jungbluth, Ladanyi, Sauter** – Pulmonary Pathology. *Prominent Expression of Negative Immune Checkpoint Regulator VISTA in Malignant Pleural Mesothelioma (MPM)* ***

***Peng*, Delair, Sirintrapun, Chen, Chen, Al-Ahmadie, Fine, Tickoo, Reuter, Gopalan** – Genitourinary Pathology. *Pathologic Characterization of Speckle-Type POZ Protein (SPOP)-Mutated Prostate Carcinoma* ***

Reis, Gopalan, Chen, Fine, Tickoo, Sirintrapun, Reuter, Al-Ahmadie – Genitourinary Pathology. *PD-L1 Expression in Urothelial Carcinoma with Divergent Differentiation, Concordance Among Three Antibodies*

Rekhtman, Travis – Pulmonary Pathology. *Spread Through Air Spaces (STAS) Correlates with Prognosis in Lung Neuroendocrine Tumors (LNET)*

Roehrl – Informatics. *Computer Science Approaches to Extract Immunohistochemistry (IHC) Results from Surgical Pathology Full Text Reports Using Machine Learning and Natural Language Processing (NLP) Techniques*

Rosenblum, Antonescu – Bone and Soft Tissue Pathology. *NUT Carcinoma: A Midline Shift-Identification of a Subset of Undifferentiated Soft Tissue and Visceral Tumors Defined by NUTM1 Gene Fusions*

***Shahi*, Travis, Jungbluth, Ladanyi, Sauter** – Pulmonary Pathology. *Comparison of MTAP Immunohistochemistry (IHC) with p16/CDKN2A Deletions/Loss and Utility of MTAP and BAP1 IHC in the Diagnosis of Malignant Pleural Mesothelioma (MPM)* ***

Soslow – Gynecologic Pathology. *Clinicopathologic Characterization of Endometrial Carcinomas with More Than One Molecular Classifying Feature*

***T. Wang*, Askan, Zehir, Bhanot, Klimstra, Basturk** – Pancreas Pathology. *Mass-Forming Intraductal Neoplasms of the Biliary Tract Comprise Morphologically and Genetically Distinct Entities* ***

***Turashvili*, Soslow, Chiang** – Gynecologic Pathology. *Whole Genome DNA Methylation Profiling Distinguishes High Grade Endometrial Carcinomas* ***

***Zeng*, Brogi, *Turashvili*, Ross, Berger, Weigelt, Reis-Filho, Wen** – Breast Pathology. *Assessing Tumor Infiltrating Lymphocytes and Genomic Alterations n Pre-Treatment Core Biopsy and Correlation with Response to Neoadjuvant Chemotherapy* ***

POSTERS:

***Alex*, Travis, Rekhtman, Buonocore, Sauter** – Pulmonary Pathology. *Histologic Features Predictive of Response to PD-1 Blockade in Patients with Non-small Cell Lung Carcinoma* ***

Antonescu – Head and Neck Pathology. *Adamantinoma-Like Ewing Sarcoma of Salivary Glands*

Antonescu – Pediatric Pathology. *Specificity of BCOR Immunohistochemistry in Pediatric Renal Neoplasia*

***Arias-Stella*, Ladanyi, S. Dogan** – Head and Neck Pathology. *Pathogenic SMARCA4 Mutations in Head and Neck and Thyroid Carcinomas are Rare* ***

***Arias-Stella, Lewis,* Benayed, Soslow, Antonescu, Ladanyi,**

Chiang, Jungbluth – Gynecologic Pathology. *Novel PLAG1 Gene Rearrangement Distinguishes Uterine Myxoid Leiomyosarcoma from Other Uterine Myxoid Mesenchymal Tumors* ***

Askan, Shia, Basturk – Pancreas Pathology. *Expression of Calretinin, Marker of Mesothelial Differentiation, in Pancreatic Ductal Adenocarcinoma: A Potential Diagnostic Pitfall*

Basturk, Weigelt, Askan, Lu Wang, Arcila, Pareja, Reis-Filho, Klimstra – Pancreas Pathology. *Sclerosing Epithelioid Mesenchymal Neoplasms of the Pancreas*

Benayed, Ho, Ladanyi, Hameed – Bone and Soft Tissue Pathology. *Comprehensive Detection of Known Fusion Genes in Sarcomas and Discovery of Novel Fusion Partners by a Clinical Targeted RNA Sequencing Assay*

Bhanot, Roehrl – Quality Assurance. *The Precision Pathology Biobanking Center (PPBC) Experience at International IBBL Biobank Proficiency Testing*

Bhanot, Roehrl – Quality Assurance. *The Rapidly Growing Role of Pathology in Clinical Trials at a Major Cancer Center*

Buonocore, Lin, Cohen – Cytopathology. *Misleading Clinical Significance of Bethesda Category IV for Thyroid Nodules*

Busam – Dermatopathology. *Genetic Overlap Between Primary Dermal Melanoma and Cutaneous Melanoma Metastases*

Chiang, *Cotzia*, Hechtman, Jungbluth, Murali, Soslow, Benayed, Ladanyi, Antonescu – Gynecologic Pathology. *NTRK Fusions Define a Novel Uterine Sarcoma Subtype with Features of Fibrosarcoma* ***

***Cotzia,* Al-Ahmadie, Chen, Gopalan, Sirintrapun, Tickoo, Reuter, Fine** – Genitourinary Pathology. *Grade Group 2 Prostate Cancer with Poorly Formed Glands Alone on Needle Biopsy: Histologic Features and Pathologic Outcomes at Radical Prostatectomy* ***

Delair, Soslow, Chiang, K. Park, Murali, Weigelt – Gynecologic Pathology. *Integration of Massively Parallel Sequencing and Immunohistochemistry for the Classification of Prospectively Collected Endometrial Cancers into Prognostically Relevant Subgroups*

Delair, Weigelt – Gynecologic Pathology. *Hotspot TERT Promoter Mutations in Adult-Type Granulosa Cell Tumors of the Ovary as Potential Drivers of Progression*

Fine, Al-Ahmadie, Chen, Gopalan, Sirintrapun, Tickoo, Reuter – Genitourinary Pathology. *Impact of Zone of Origin in Anterior-Dominant Prostatic Tumors: Long-Term Biochemical Recurrence-Free Survival in an Anatomically Well-Annotated Series*

Grabenstetter, Brogi, Wen – Breast Pathology. *Oncotype DX Recurrence Score in Multifocal/ Multicentric Ipsilateral Invasive Breast Carcinomas*

***Guo, Alex*, Lin** – Cytopathology. *Impact of the Paris System for Reporting Urinary Cytology Atypical Urothelial Cells Category at a Major Cancer Center* ***

***Gupta*, Aron, Cheville, Hansel, Lowenthal** – Genitourinary Pathology. *Female Urethral Carcinoma: Analysis of 29 Cases and Proposal for a New Staging System.* ***

***Gupta*, Chen, Al-Ahmadie, Sirintrapun, Fine, Berger, Tickoo, S. Dogan, Reuter, Gopalan** – Genitourinary Pathology. *TERT Copy Number Alterations, Promoter Mutations and Rearrangements in Adrenocortical Carcinomas: Clinicopathologic and Molecular Analysis of 62 Cases* ***

***Gupta*, Zarei, Sukov** – Genitourinary Pathology. *Clear Cell Renal Cell Carcinomas with PDGFRA/ KIT (4q12) Co-amplification and PDGFRB (5q32) Amplification.* ***

H. Zhang – Breast Pathology. *FOXK2 is A Novel Oncogene in Breast Cancer*

***Hajiyeva*, Edelweiss** – Breast Pathology. *Frozen Section of Sentinel Lymph Nodes in 702 Breast Cancer Patients Treated with Neoadjuvant Chemotherapy* ***

***Hanna*, Grabenstetter, Ross, Tan** – Breast Pathology. *Invasive Lobular Carcinoma with an Unusual Immunophenotypic Profile* ***

Jameel, Brogi, Ross, Weigelt, Reis-Filho, Wen – Breast Pathology. *Targeted Next Generation Sequencing Analysis of Metaplastic Breast Carcinoma* ***

***Jelloul*, Yabe, Y. Zhang, A. Dogan, Xiao** – Hematopathology. *Extramedullary Plasmablastic Transformation of Plasma Cell Myeloma: Clinicopathologic Study of 10 Cases* ***

Jungbluth, A. Dogan – Hematopathology. *In Situ Protein Expression Analysis of B-cell Maturation Antigen (BCMA)*

Jungbluth, Ghossein, Katabi – Head and Neck Pathology. *Expression of Cancer Testis Antigen PRAME, PD-L1 and PD-1 in Salivary Duct Carcinoma*

Jungbluth, Ladanyi – Bone and Soft Tissue Pathology. *SETD2 Mutation is a Recurrent Secondary Alteration in Synovial Sarcoma Associated with Loss of the H3K36ME3 Histone Mark*

Jungbluth, Lezcano, Busam – Pathobiology. *Cancer Testis Antigen PRAME is Abundantly Expressed in Metastatic Melanoma and Other Malignancies*

Jungbluth, Roehrl – Quality Assurance. *Carrier-Based Multi-Tissue Block (CBMTB) of Normal Tissues as On-Slide Quality Control for Automated Immunohistochemical Staining Procedures*

K. Park, Soslow – Gynecologic Pathology. *Clinical Outcomes of HPV-Associated and Unassociated Endocervical Adenocarcinomas (ECAs) Support the IECC Classification*

K. Park, Soslow – Gynecologic Pathology. *International Endocervical Adenocarcinoma Criteria & Classification: Validation and Interobserver Reproducibility*

K. Park, Soslow – Gynecologic Pathology. *Silva-type Patterns of Invasion and Correlates [Tumor Size, Lymph-vascular Invasion, and Lymph Node Metastasis] in HPV-Unassociated Endocervical Adenocarcinomas*

K. Park, *Turashvili* – Gynecologic Pathology. *Morphologic Patterns of Secondary Involvement of the Uterine Cervix by Non-Gynecologic Neoplasms* ***

***Khattar*, Jelloul, Y. Zhang, Arcila, Lu Wang, A. Dogan** – Hematopathology. *t(14;18) Negative Inguinal Follicular Lymphoma is Characterized by Genetic Abnormalities of 1p36/ TNFRSF14 and 16p/CREBBP Regions* ***

Klimstra – Pancreas Pathology. *Histopathology of Pancreatic Cancer in Patients with Germline Mutations in Ataxia-Telangiectasia Mutated (ATM) Gene*

Klimstra, Ghossein, Katabi – Head and Neck Pathology. *Misdiagnosed Myoepithelial Carcinoma of Salivary Gland: A Challenging and Potentially Significant Pitfall*

***Kumar*, Lewis, Roshal, A. Dogan** – Hematopathology. *Hairy Cell Leukemia Expresses Programmed Death 1 (PD-1): A New Diagnostic Marker* ***

Ladanyi – Techniques. *Determination of MLH1 and MGMT Promoter Methylation Status Using the Illumina High-Throughput Methylation EPIC (850k) Platform*

Lewis, Yao, Y, Zhang, Roshal, Xiao – Hematopathology. *Myeloid Neoplasms with Features of Both Myelodysplastic/ Myeloproliferative Neoplasm with Ring Sideroblasts and Thrombocytosis and Myelodysplastic Syndrome with Del (5q)*

Lu, Hameed – Bone and Soft Tissue Pathology. *Histone H3K36M Mutation and Trimethylation Patterns in Chondroblastoma*

***Matsuda, Hanna,* Grabenstetter, Brogi** – Techniques. *Developing an Efficient Approach for the Assessment of Tumor Extension by Ex Vivo Imaging of Breast Specimens: A Pilot Study Using X-Ray Tomosynthesis with Histopathologic Correlation* ***

***Mirsadraei*, Chen, Reuter, Lin** – Cytopathology. *Cytological Characteristics of Hereditary Leiomyomatosis and Renal Cell Carcinoma (HLRCC)-Associated Renal Cell Carcinomas* ***

Montecalvo, *Alex,* Sauter, *J. Chang,* Ladanyi, Antonescu, Travis, Rekhtman – Pulmonary Pathology. *SMARCA4 (BRG1) Deficiency in Lung Carcinomas Correlates with Poor Differentiation and Aggressive Clinical Behavior* ***

Montecalvo, Rekhtman, Katabi, Ghossein, Antonescu, Travis – Pulmonary Pathology. *Thoracic Hyalinizing Clear Cell Carcinoma: A Series of 3 Cases*

Montecalvo, Rekhtman, Travis – Pulmonary Pathology. *Clinical Significance of Morphological Patterns of Micropapillary Lung Adenocarcinoma: Classical and Filigree Patterns*

Montecalvo, Rekhtman, Travis – Pulmonary Pathology. *Micropapillary and Solid But Not Lepidic Components Correlate with Worse Prognosis in 1522 Invasive Predominant Nonmucinous Lung Adenocarcinoma (LADC)*

Murali, Chiang, Delair, Soslow, K. Park – Gynecologic Pathology. *Gastric-type Cervical Adenocarcinoma in Small Biopsy and Cytology Specimens*

***Muthukumarana*, K. Park, Soslow, Chiang** – Gynecologic Pathology. *BCOR Expression in Mullerian Adenosarcoma: A Potential Diagnostic Pitfall* ***

Pareja, Brogi, Weigelt, Reis-Filho – Breast Pathology. *Solid Papillary Carcinomas with Reverse Polarity (Solid Papillary Breast Carcinomas Resembling the Tall Cell Variant of Papillary Thyroid Neoplasms) Harbor Recurrent Mutations Affecting IDH2: A Validation Study*

Pareja, Edelweiss, Wen, Jungbluth, Weigelt, Reis-Filho – Breast Pathology. *HMGA2 Rearrangement in Breast Adenomyoepitheliomas Lacking HRAS and PI3K Pathway-Related Gene Mutations*

Pareja, Wen, Katabi, Brogi, Weigelt, Reis-Filho – Breast Pathology. *Pleomorphic Adenoma and Mucoepidermoid Carcinoma of the Breast are Underpinned by Gene Fusions*

Roehrl – Informatics. *The Big Data Opportunity in Research Biobanking: Design and Development of a Web-Based Application to Unify and Connect Biospecimen Information and to Overcome Data Silo Challenges*

Roehrl, Hameed, *Matsuda*, Murray, Brogi – Informatics. *The Roles of Micro-Computed Tomography (CT) in Breast Pathology* ***

Rosenblum – Neuropathology. *Clinicopathologic Features of Anaplastic Myxopapillary Ependymomas*

S. Dogan, Zehir, Ladanyi – Endocrine Pathology. *NKX2-1 Amplification is Associated with Aggressive Features in a Subset of Differentiated Thyroid Carcinomas of Follicular Cell Origin*

Shia – Gastrointestinal Pathology. *Are Enterocolic Mucosal Mast Cell Aggregates Clinically Relevant in Patients Without Suspected Systemic Mastocytosis?*

Sigel, *Werneck Krauss Silva*, Basturk, Klimstra, Tang – Cytopathology. *Cytologic Features of Well-Differentiated G3 Pancreatic Neuroendocrine Tumors* ***

Sirintrapun, Fuchs – Informatics. *Generation of Realistic (in silico) Histopathologic Images Using Generative Models Based on Deep Neural Networks*

Sirintrapun, Gopalan, Al-Ahmadie, Chen, Fine, Tickoo, Reuter, Yagi – Informatics. *Three-Dimensional Morphology of the Prostate by MicroCT*

Soslow – Gynecologic Pathology. *SWI/SNF-Deficient Undifferentiated Endometrial Carcinomas are Highly Aggressive and Resistant to Conventional Chemotherapy*

Soslow- Gynecologic Pathology. *Loss of Claudin-4 Expression is Common in Undifferentiated/ Dedifferentiated Endometrial Carcinomas*

***T. Wang*, Vakiani, Hechtman, Sigel** – Gastrointestinal Pathology. *Histoarchitectural Pattern Does Not Distinguish IDH1 Mutant Intrahepatic Cholangiocarcinomas from Non-IDH1 Mutant Controls* ***

Tickoo – Genitourinary Pathology. *Acquired Cystic Disease-Associated Renal Cell Carcinoma (ACKD-RCC)-Like Cysts*

Tickoo, Chen, Reuter – Genitourinary Pathology. *Challenges in Pathologic Staging of Renal Cell Carcinoma: An Interobserver Variability Study of Urologic Pathologists*

***Turashvili,* Chiang, Delair, K. Park, Soslow, Murali** – Gynecologic Pathology. *BRAF Mutations and Expression of Anti-BRAF-V600E (VE1) in Low-Grade Serous Tumors of the Ovary* ***

***Turashvili,* Murali, Soslow** – Gynecologic Pathology. *Prognostic Value of Clinicopathologic Variables in Synchronous Endometrial and Ovarian Carcinomas: Metastases or Independent Primary Tumors?* ***

***Vanderbilt*, Zehir, Arcila, S. Dogan, Ladanyi** – Techniques. *Mining Large Panel Hybrid Capture-Based Clinical Next Generation Sequencing Data for Novel Virus Pathogen-tumor Associations Based on Mapping of Off-Target Reads to Viral Genomics* ***

***Vyas*, Basturk, Jungbluth, Askan, Klimstra, Shia** – Gastrointestinal Pathology. *Immunohistochemical (IHC) and In-Situ Hybridization (ISH) Analysis of Common Hepatocellular Markers in Gastrointestinal Adenocarcinomas with Hepatoid Differentiation* ***

***Vyas*, Hechtman, Vakiani, Klimstra, Shia** – Gastrointestinal Pathology. *In Colorectal Carcinoma (CRC), True Tumor Cell Staining for PD-L1 is Uncommon and Occurs in Sporadic Microsatellite-Instable Tumors with Loss of MHC-I* ***

Wen, Weigelt, Reis-Filho – Breast Pathology. *Clonal Evolution in the Progression from Ductal Carcinoma in Situ to Invasive Ductal Carcinoma*

***Werneck Krauss Silva*, Al-Ahmadie, Chen, Gopalan, Sirintrapun, Tickoo, Reuter, Fine** – Genitourinary Pathology. *Microscopic Bladder Neck Invasion Re-Visited: Correlation with Tumor Topography, Staging and Grading* ***

Yagi, Hameed – Bone and Soft Tissue Pathology. *Whole Block Imaging in Bone Tumors*

LECTURES:

Basturk, Olca (Pancreatobiliary Pathology Society): *Genomic Profiling of Intraductal Pancreatobiliary Neoplasms*

Brogi, Edi: (Evening Specialty Conference – Breast Pathology): *Case 4*

Chen, Ying-Bei: Diagnostic Approach to Renal Tumors with Papillary Architecture: Updates Using 2016 WHO Classification

DeLair, Deborah (International Society of Gynecological Pathology): *The IMPACT of Next Gen Sequencing Panels in Gynecological Cancer*

Ghossein, Ronald (Endocrine Pathology Society): *New TNM Staging in Thyroid Cancer*

Hechtman, Jaclyn: Identifying the Rare: Evolving Diagnostics Standards in Characterizing Cancer

Hechtman, Jaclyn: Peculiar Polyps: Diagnostics of Less Common Colorectal Lesions and Awareness of Their Clinical Associations

Katabi, Nora: Hot Topics in Pathology 01 – Head & Neck Pathology – Head & Neck Pathology-New and Improved

Rekhtman, Natasha (American Society for Cytopathology): *Current Concepts in Lung Cancer*

Shia, Jinru: (Evening Specialty Conference – GI Pathology): *Case 3*

Soslow, Robert (Evening Specialty Conference – GYN Pathology): *Case 4*

Tang, Laura: Hot Topics in Pathology 01 - GI Pathology – TNM in 2018: Problems in Daily Practice

COURSES:

Practical Molecular Diagnostics for the Practicing Surgical Pathologist- **Maria Arcila**

Surgical Pathology and Cytopathology of the Pancreas and Ampulla - **Olca Basturk**

Molecular Advances in Gynecologic Pathology: An Update for the Anatomic Pathologist - **Britta Weigelt**

MODERATORS:

(Pancreatobiliary Pathology Society): **Olca Basturk**, Co-Moderator

(Platform Presentations – Breast Pathology): **Timothy D'Alfonso**, Co-Moderator

(Platform Presentations – Pathobiology): **Snjezana Dogan**, Co-Moderator

(Platform Presentations – Cytopathology): **Oscar Lin**, Co-Moderator

*** *Denotes fellow contribution.*

Italics indicate MSK fellow.

QIFXIV

QUALITY **IMPROVEMENT** FAIR

The QUALITY IMPROVEMENT FAIR at MSKCC is an annual institution-wide event hosted by the Division of Quality and Safety showcasing various improvement efforts and initiatives across the institution.

THE PURPOSE OF THE FAIR IS TO:

- Create awareness of various projects and initiatives occurring across the Center
- Improve collaboration among colleagues
- Educate staff on quality and safety principles and guidelines
- Emphasize patient safety and quality of care as top priorities among senior leadership and across the Center
- Celebrate the hard work of our staff in their continual efforts in maintaining a safe environment for our patients

The Department of Pathology was featured with three projects under the leadership of Sarah Cook Virgo, Brian Murphy and Tessara Baldi.

"PATHOLOGY CONSULTATIONS: EMPOWERING USERS, IMPROVING TURN AROUND TIME AND EMBRACING THE DIGITAL AGE"

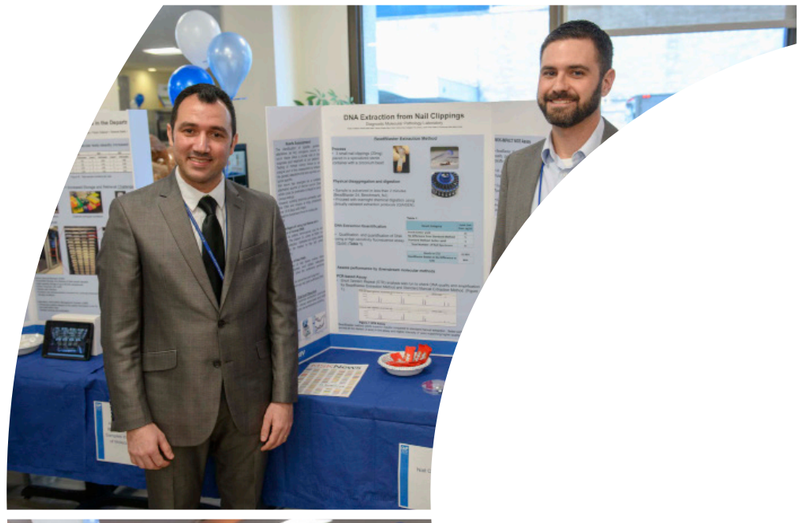
Sarah Cook Virgo

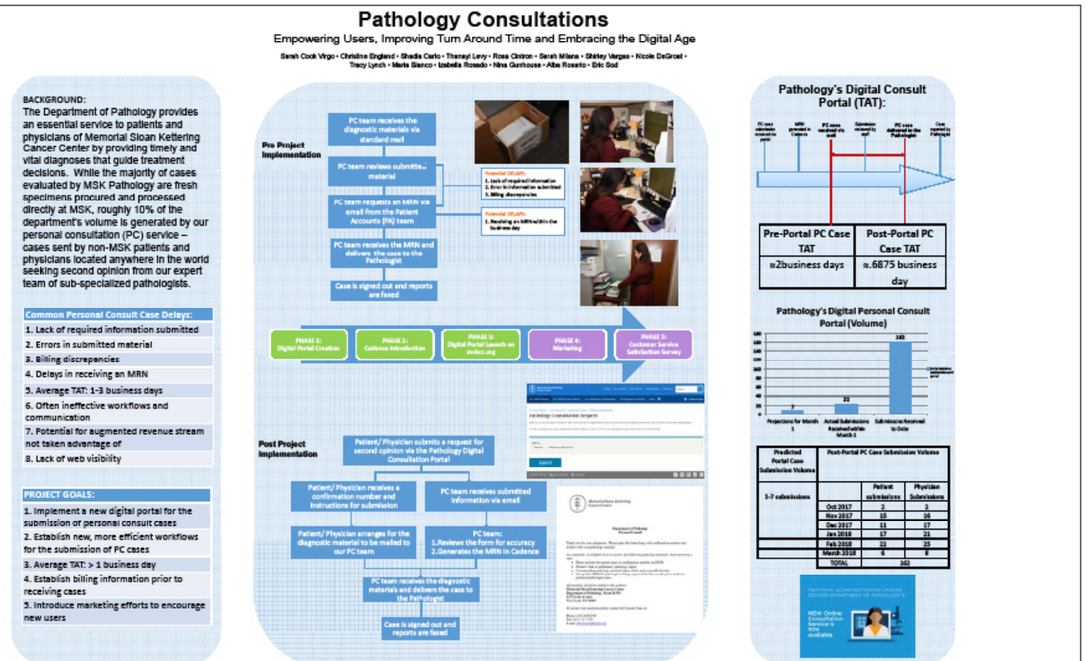
"DNA EXTRACTION FROM NAIL CLIPPINGS: DIAGNOSTIC MOLECULAR PATHOLOGY LABORATORY"

Tessara Baldi

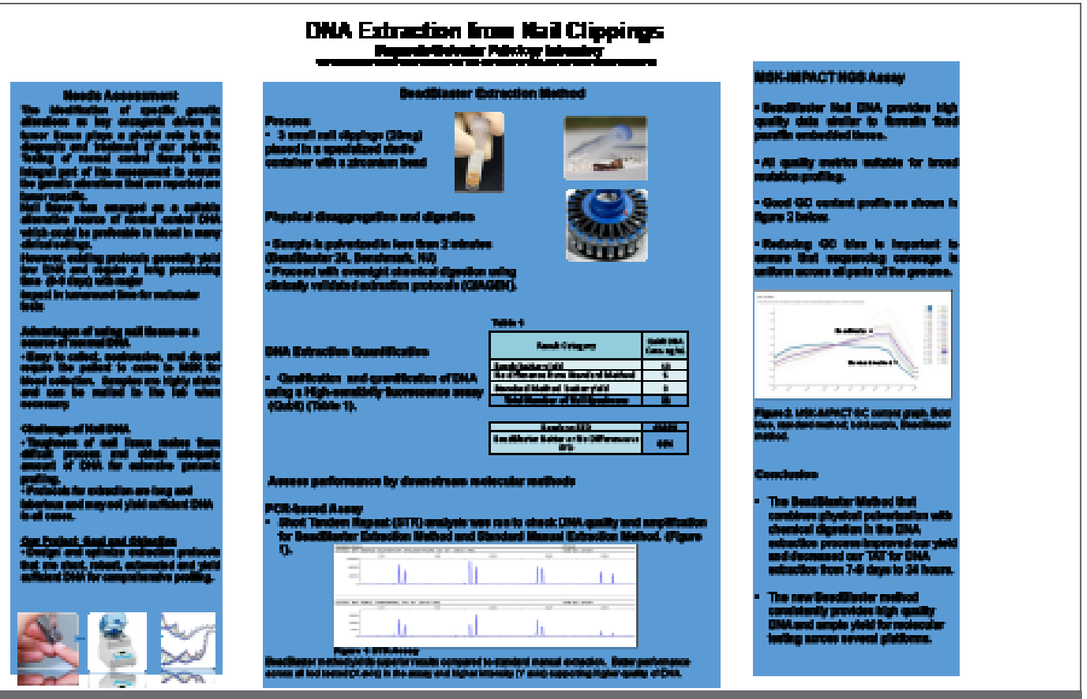
"AUTOMATED STORAGE AND RETRIEVAL OF CLINICAL DNA SAMPLES IN THE DEPARTMENT OF MOLECULAR PATHOLOGY"

Brian Murphy

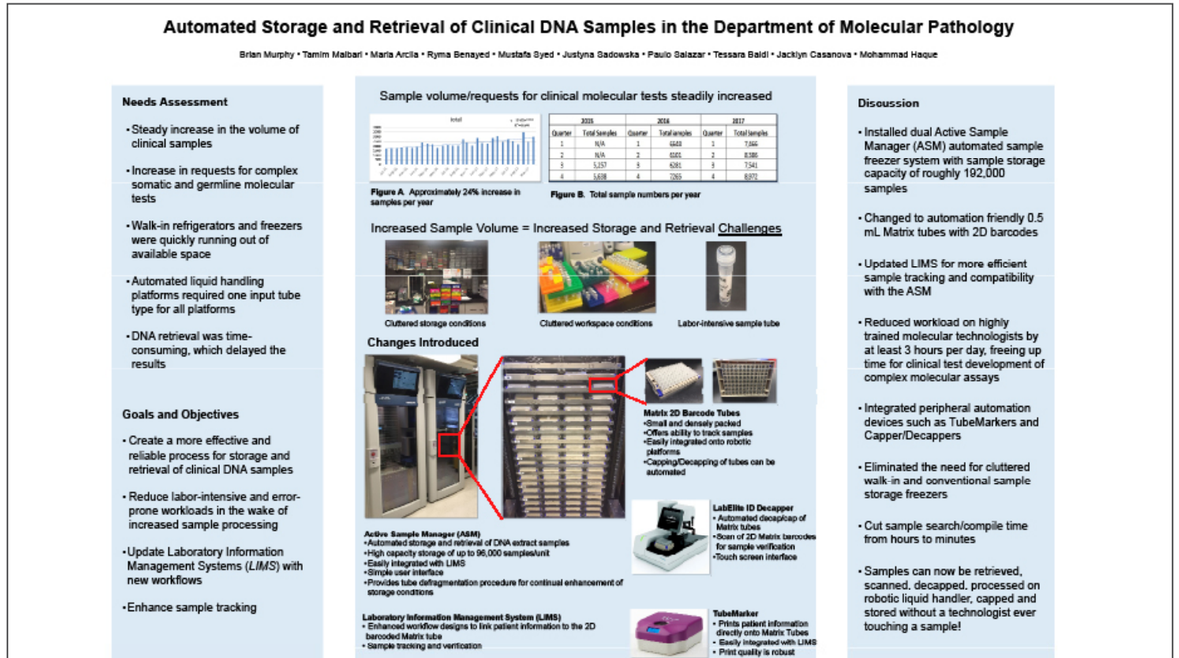




"PATHOLOGY CONSULTATIONS: EMPOWERING USERS, IMPROVING TURN AROUND TIME AND EMBRACING THE DIGITAL AGE"
Sarah Cook Virgo



"DNA EXTRACTION FROM NAIL CLIPPINGS: DIAGNOSTIC MOLECULAR PATHOLOGY LABORATORY"
Tessara Baldi



"AUTOMATED STORAGE AND RETRIEVAL OF CLINICAL DNA SAMPLES IN THE DEPARTMENT OF MOLECULAR PATHOLOGY"
Brian Murphy

FACULTY PUBLICATIONS

Andry C, Duffy E, Moskaluk CA, McCall S, **Roehrl MHA**, Remick D. Biobanking – Budget and the role of pathology biobanks in precision medicine. *Acad Pathol* 2017; 8: 4.

Askan G, Bagcı P, **Hameed M**, **Basturk O**. Dedifferentiated liposarcoma of the gastroesophageal junction. *Turk J Pathol* 2018; 34: 104-107.

Begg CB, Ostrovnaya I, Geyer FC, Papanastasiou AD, Ng CKY, Sakr RA, Bernstein JL, Burke KA, King TA, Piscuoglio S, Mauguen A, Orlow I, **Weigelt B**, Seshan VE, Morrow M, **Reis-Filho JS**. Contralateral breast cancers: Independent cancers or metastases? *Int J Cancer* 2018; 142: 347-356.

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Hoang L, **Chiang S**, Lee C. Endometrial stromal sarcomas and related neoplasms: New developments and diagnostic considerations. *Pathology* 2018; 50: 162-177

Hu ZI, **Shia J**, Stadler ZK, Varghese AM, Capanu M, Salo-Mullen E, Lowery MA, Diaz LA, **Mandelker D**, Yu KH, Zervoudakis A, Kelsen DP, **Iacobuzio-Donahue CA, Klimstra DS**, Saltz LB, Sahin IH, and O'Reilly EM. Evaluating mismatch repair deficiency in pancreatic adenocarcinoma: Challenges and recommendations. *Clin Cancer Res* 2018; 24: 11326-1336.

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Gao J, Heins ZJ, Gross BE, Kelsen DP, **Zhang L**, Strong VE, Schattner M, Gerdes H, Coit DG, Bains M, Stadler ZK, Rusch VW, Jones DR, Molena D, **Shia J**, Robson ME, Capanu M, Middha S, **Zehir A**, Hyman DM, Scaltriti M, **Ladanyi M**, Rosen N, Ilson DH, **Berger MF**, **Tang L**, Taylor BS, Solit DB, Schultz N. Genetic predictors of response to systemic therapy in esophagogastric cancer. *Cancer Disc* 2018; 8: 49-58.

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1ST QUARTER 2018 PROMOTIONS

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Associate Attending

TRAVIS HOLLMANN, MD, PHD
Associate Attending

AHMET ZEHIR, PHD
Assistant Attending

EFSEVIA VAKIANI, MD PHD
Associate Attending

MIKHAIL ROSHAL, MD
Associate Attending

CYCLE FOR SURVIVAL

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This year, there were at least FOUR teams representing the Department of Pathology for Cycle for Survival. 100% of your donations will fund pioneering research led by Memorial Sloan Kettering to benefit people worldwide, who are facing rare cancers. Thank you for your continued support! For those interested in joining or donating, please contact our team captains:

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UPCOMING COURSES

http://mskcc.org/neoplasticdiseases.com

2ND QUARTER 2018

THE HISTORY OF PATHOLOGY AT MEMORIAL SLOAN KETTERING CANCER CENTER

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GENITOURINARY PATHOLOGY TEAM

RESEARCH PROFILE: NORA KATABI, MD

CYTOGENETICS TEAM

RESEARCH PROFILE: JACKIE HECHTMAN, MD