

MSK PATHOLOGY REVIEW

4th Quarter 2019

Initiatives
Innovations
Accomplishments

A Journey of
***Technological
Evolution***
in Research
and Diagnostics



Memorial Sloan Ketterin
Cancer Center

With this issue of the MSK Pathology Review, we resume the publication of our departmental quarterly newsletter after a 6 month hiatus. The lack of intervening issues has a simple explanation. Our talented science writer, Hope Cristol, decided to move on to new opportunities, and it took us quite some time to find a replacement. Finally, we were fortunate to find Onward Publishing, Inc., a professional writing group that has assigned several different writers to assist us with our production. Meanwhile, Sarah Virgo has continued to collect material and ideas for stories. The current issue is among our most comprehensive to date, including updates on events over the past 6 months along with continuing our series on diagnostic teams, individual faculty investigators, and fellows' milestones. We introduce a "Case of the Quarter" feature and highlight the quality improvement efforts throughout the department. Clearly, the MSK Pathology Review is back on track, and the continuing accomplishments and innovations from our department ensure we will have plentiful material for many issues to come! I would like to take this opportunity to acknowledge those who have contributed so much to this project – Hope Cristol, Allix Mazzella, Jordana Shapiro, and of course Sarah Virgo, whose investment in this effort is absolutely key to its success. I hope you will all enjoy this new edition!

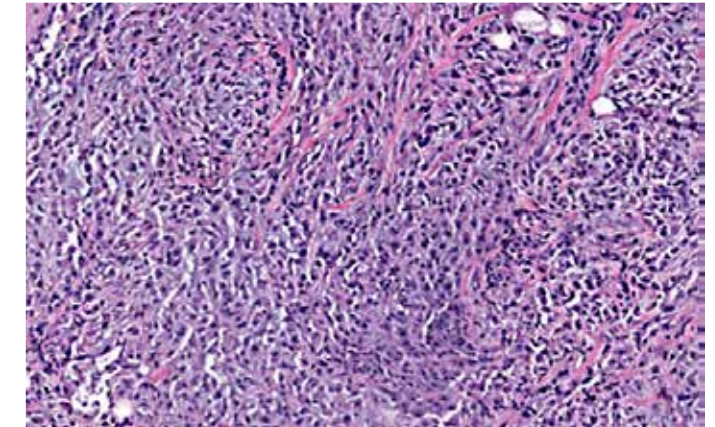
- David Klimstra, MD

CASE HISTORY

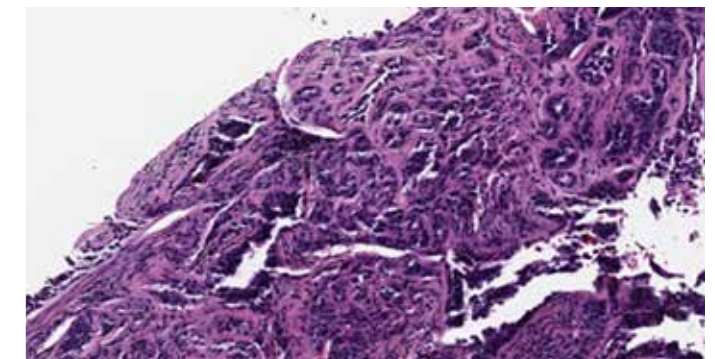
59 year old woman with palpable and tender 3.5 cm right lateral breast mass and weight loss and no axillary lymphadenopathy. Of note, she presented with a 1.6 cm right upper lobe lung mass. Both biopsies are shown here. The patient ultimately underwent mastectomy due to rapid growth of the breast mass.

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

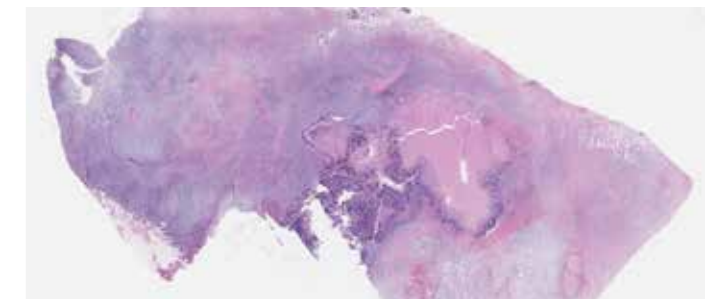
Scan the QR code to view digital slides available on mskcc.pathpresenter.com



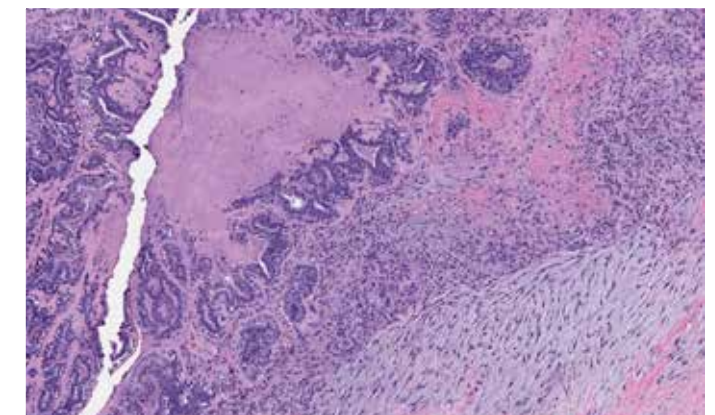
Breast, biopsy



Lung, biopsy



Breast, excision (10x)



Breast, excision (100x)

WENBIN XIAO, MD



For a relatively new hematopathologist, Dr. Xiao already has remarkable research experience.

By Hope Cristol

Some MSK pathologists prefer the clinical side of their responsibilities; others are primarily researchers. Hematopathologist Wenbin Xiao prefers both. Instead of splitting his time evenly between them, his career has focused primarily on either one or the other at different times.

After completing his MD/PhD training, Xiao spent six years doing bench work, first as a postdoc and then as a research scientist. “At that time, my research was mostly focused on signal transduction in leukemic cells,” Xiao says. “But I was trained as a physician, so I wanted to get involved in patient care as well.”

He returned to medicine, completing his residency and fellowship and then joined the staff at MSK. For a while, much of his work was on the clinical side of pathology. But his

strong research interest kept tugging at him and soon he was back at the bench.

STUDIES ON AML

For the past three years, Xiao has been working to better classify hematological malignancies at the genetic level – especially secondary acute myeloid leukemia (AML). He cowrote a seminal review of the genetic basis of hematologic malignancies, published in *Blood*. The current World Health Organization (WHO) classification is “mostly based on morphology, history, and integrates some genetic data. For nearly half of the AML, the genetic information is still not utilized to classify disease”, Xiao says.

Several of his recently published studies explored the genetic underpinnings of rare

“The current World Health Organization (WHO) classification is ‘mostly based on morphology and history, and integrates some genetic data. For nearly half of the AML, the genetic information is still not utilized to classify disease.’”

subclasses of AML. Among the subclasses, core-binding factor AML tends to have a good prognosis. However, it can turn into aggressive disease if it gains genomic mutations over time. Xiao was the lead author of a 2017 study, published in *Blood Advances*, in which a patient with inv(16) AML achieved five complete remissions with various chemotherapies but ultimately died from this aggressive and highly invasive disease. Bone marrow biopsies performed at each relapse revealed a consistent gain in cytogenetic abnormalities and a KRASG12D mutation. Although unusual, this unique case highlights how acquired genomic alterations can quickly alter prognosis, even for a chemosensitive patient.

Another study, published in *Leukemia* in 2018, focused on an extremely rare and aggressive subclass: acute leukemia with megakaryocytic and erythroid differentiation (ALMED).

Previous research in mice suggested a cooperative role of JAK/MAP kinase pathway activation and TP53 mutations in the

pathogenesis of ALMED. Xiao and colleagues were the first to explore the disease’s mechanisms of pathogenesis in humans and concluded that the mechanism of pathogenesis in humans is similar to that in animals.

His recent work also identified PHF6 and DNMT3A mutations in mixed phenotype acute leukemia, a rare type of leukemia often challenging to diagnose. The findings, published in *Blood Advances* in 2019, showed a phenotype-genotype correlation between mutations and mixed phenotype, which can potentially facilitate the diagnosis.

More recently, Xiao reported at the ASH meeting a subset of AML patients showing RUNX1 mutations and plasmacytoid dendritic cell differentiation, a rare cell type normally responsible for host immunity against viral infection. Accurate diagnosis of this AML variant may benefit the patients from appropriate targeted therapies.

EVOLVING RESEARCH ROLE

Xiao continues to focus on secondary AML and is adding to the evidence on

mutations including PHF6 and RUNX1. “The mutations of these two molecules probably comprise about 60% of secondary AML cases,” he says.

Xiao’s studies have relied on clinical data. However, he has recently moved back to the bench, joining the lab of Ross Levine, MD, the Laurence Joseph Dineen Chair in Leukemia Research and Chief of Molecular Cancer Medicine with the Human Oncology and Pathogenesis Program (HOPP). “I will apply my findings from the clinical side and use this knowledge to make mouse models to learn about the mechanisms of the disease,” Xiao says.

Treatments for secondary AML are not adequate and disease prognosis is poor. This is partly because molecular targets have not yet been identified. Also, the disease usually strikes people later in life who “cannot tolerate regular cytotoxic chemotherapy. The patient could die from complications,” Xiao says. “So we need to find better targeted therapy, which means we need to find those targets.”

THE FOURTH ANNUAL SYMPOSIUM IN TRANSLATIONAL RESEARCH IN PATHOLOGY Honors William L. Gerard Award Winner and Highlights Cutting-Edge Pathology Research

By Julie Grisham

On March 28, Memorial Sloan Kettering's Department of Pathology hosted its Fourth Annual Symposium in Translational Research in Pathology. The event, which included the presentation of the William L. Gerard Award, was held in the Zuckerman Research Laboratory Auditorium.

The winner of this year's Gerald Award was Kojo Elenitoba-Johnson, the Peter C. Nowell MD Professor at the Perelman School of Medicine at University of Pennsylvania. Dr. Elenitoba-Johnson is an international leader in the fields of hematopathology, molecular and

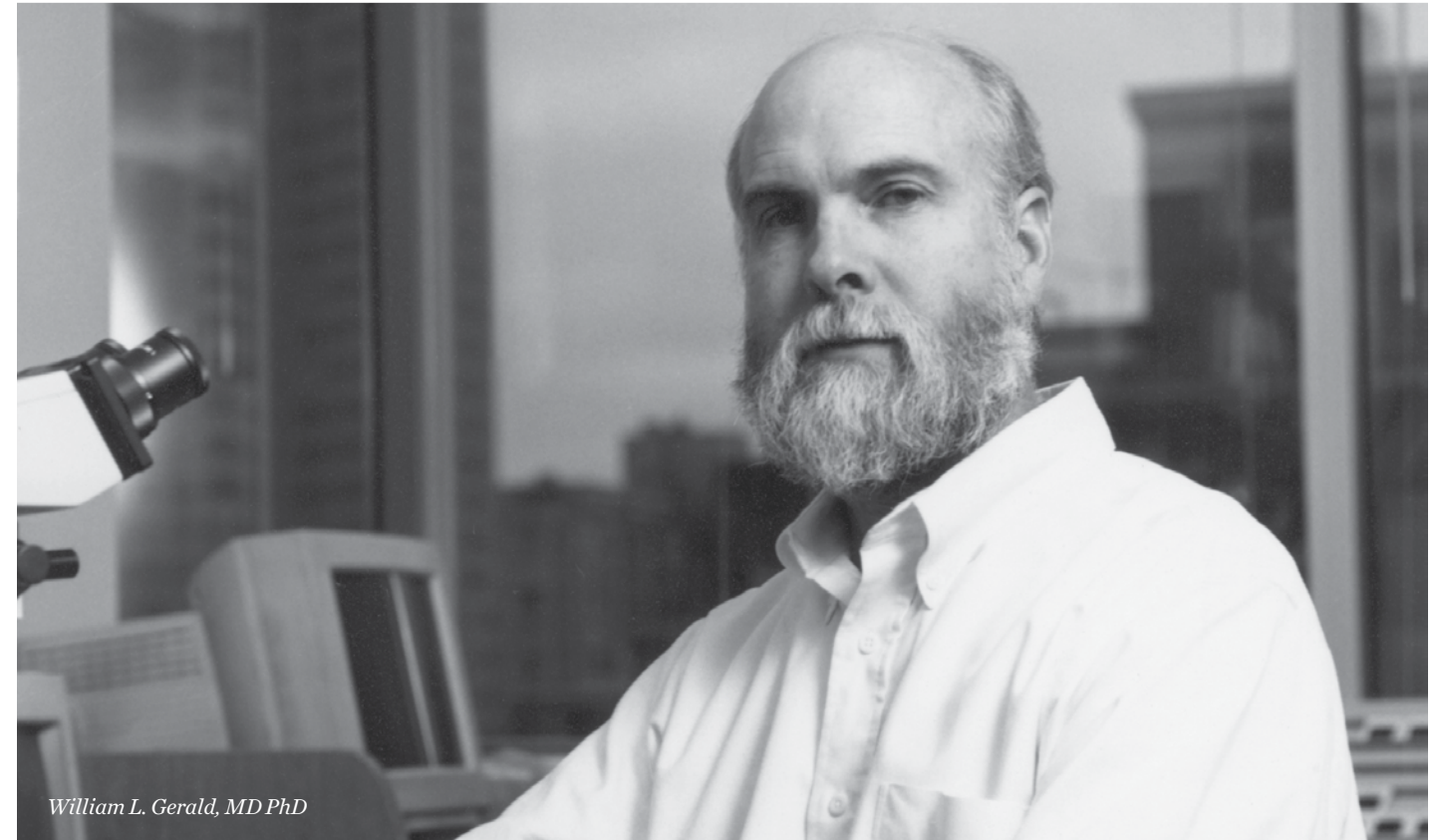
genomic pathology, and mass spectrometry-driven proteomics. He gave a lecture entitled "Mass Spectrometry as a Driver for Discovery in Lymphoma Pathogenesis."

Dr. Elenitoba-Johnson is also the founding director of Penn Medicine's Center for Personalized Diagnostics and chief of the Division of Molecular and Genomic Pathology at Penn Medicine.

Attendees were welcomed to the symposium by Dr. David Klimstra, Chair of the Department of Pathology. Several other pathologists from the department gave presentations on a range of topics, including sample preparation, the role of fusion genes, and assessing minimal residual disease (see page 9 for a full lecture schedule).

The Gerald Award was created to recognize the contributions and values brought to MSK's Department of Pathology by William L. Gerald, who died in 2008. Dr. Gerald was a pioneer in the molecular characterization of cancer at a time when now-commonplace molecular techniques were still cutting-edge technology. Throughout his career, he provided mentorship and collaboration to numerous trainees and colleagues. The award is a tribute to his scientific contributions and personal attributes and to the legacy of his work in the department.

Past recipients of the Gerald Award include Drs. Arul Chinnaiyan of the University of Michigan Medical School, David Huntsman of the University of British Columbia, Adrienne Flanagan of the University College London Cancer Institute, and A. John Iafrate of Massachusetts General Hospital and Harvard Medical School.



William L. Gerald, MD PhD



KOJO ELENITOBA-JOHNSON, MD

Professor, Perelman School of Medicine at the University of Pennsylvania, Founding Director, Penn Medicine's Center for Personalized Diagnostics, Chief, Division of Molecular and Genomic Pathology, University of Pennsylvania, Penn Medicine's Center for Personalized Diagnostics

By Ahmet Dogan, MD, PhD

Kojo Elenitoba-Johnson is the inaugural Peter C. Nowell, MD Professor at the Perelman School of Medicine at University of Pennsylvania. He is also the founding director of Penn Medicine's Center for Personalized Diagnostics, as well as the chief of the division of molecular and genomic pathology. Dr. Elenitoba-Johnson is an international leader in the fields of hematopathology, molecular and genomic pathology, and mass spectrometry-driven proteomics.

Dr. Elenitoba-Johnson earned his medical degree from the College of Medicine at the University of Lagos. He completed his residency in anatomic and clinical pathology at the Brown University School of Medicine, where he served as Chief Resident. He then moved on to the National Cancer Institute to complete a fellowship in hematopathology, as well as to the Leadership Development for Physicians in Academic Health Centers program at the Harvard School of Public Health. Before arriving at Penn, Dr. Elenitoba-Johnson was the Henry Clay Bryant Professor at the University of Michigan and served as director of the Molecular Diagnostics Laboratory there.

His research focuses on the pathogenesis of human malignant lymphomas, biomarker discovery by genomic and proteomic profiling, and cancer. Dr. Elenitoba-Johnson has been recognized with numerous awards, including the American Society for Investigative Pathology Scholarship in 1993, the Outstanding Graduating Resident Award from Brown University in 1995, the Society for Hematopathology Pathologist-in-Training Award in 1998, Outstanding Teaching Awards in Anatomic Pathology from the University of Utah (1999 and 2003), and the Ramzi S. Cotran Young Investigator Award from the United States and Canadian Academy of Pathology

in 2006. He is an elected member of the American Society for Clinical Investigation and is the recipient of the 2012 Outstanding Investigator Award from the American Society for Investigative Pathology.

Dr. Elenitoba-Johnson is a member of the Board of Scientific Counselors for the National Cancer Institute in the National Institutes of Health. He is an associate editor for the *Journal of Hematopathology* and a member of numerous professional societies, including the American Society of Hematology, American Society for Investigative Pathology, United States and Canadian Academy of Pathologists, and Association for Molecular Pathology (AMP). He served as the Chair of the Hematopathology Division of the AMP from 2008 to 2009. He has authored or co-authored more than 170 peer-reviewed research publications and has contributed more than 40 chapters to professional textbooks on pathology.

The Fifth Annual Symposium in Translational Research in Pathology will take place on Thursday, March 26, 2020. Dr. Sunil Lakhani of the University of Queensland will receive the William L. Gerald Award.

For additional information or to register for the course, please visit: www.mskcc.org/trs2020

Research Presentations

*Selected Fellows and Faculty
Moderators: Drs. Hameed, Reis-Filho and A. Dogan*

Comprehensive Solid Tumor Microbiome Profiling Via Analysis of Unmapped Reads in Large Panel, Hybridization Capture-Based NGS Assay Data
Dr. Chad Vanderbilt

Developing a Robust Sample Preparation Procedure for Deep Fourier-Transform Mass Spectrometric Profiling of Formalin-Fixed Paraffin-Embedded Clinical Tissue Specimens
Dr. Michael Roehrl

Recurrent but Not Pathognomonic Fusion Genes in Mucinous Carcinomas of the Breast
Dr. Fresia Pareja

Genomic Profiling of Mucinous Adenocarcinoma Can Assist in Determination of Site of Origin
Dr. Amir Boroujeni

GLI1-Amplified Soft Tissue Neoplasm: A Novel Entity Showing Morphologic Overlap with Tumors with GLI1 Gene Fusions
Dr. Narsi Agaram

Detailed Morphologic and Genetic Features of Urothelial Carcinoma in Patients with Lynch Syndrome
Dr. Hikmat Al-Ahmadie

Evolving Landscape of Minimal Residual Disease Assessment in Hematological Malignancies
Dr. Mikhail Roshal

Modalities and Applications for Quantitative Multiplexed Immunostaining in Immuno-Oncology
Dr. Travis Hollmann

Introduction, Gerald Award Presentation & Special Lecture Mass Spectrometry as a Driver for Discovery in Lymphoma Pathogenesis
Dr. Kojo Elenitoba-Johnson



MICHAEL BERGER, PHD



Michael Berger, PhD, Makes an IMPACT

By Kayt Sukel

When Michael Berger, PhD, now Associate Director of the Marie-Josée and Henry R. Kravis Center for Molecular Oncology at Memorial Sloan Kettering Cancer Center, joined MSK in 2010 he had never worked directly with pathologists. That said, he hoped to find new ways to apply his training in genomics and computational biology to improve diagnosis and treatment selection at one of the nation's foremost cancer centers. At the time, work in cancer genomics was still largely confined to the research lab and it wasn't fully clear how it might move from the bench to the bedside.

"In hindsight, it was fortunate timing," he says. "Leading cancer centers like MSK were trying to determine how best to incorporate genomic technologies and analysis into clinical care, which was exactly what I was excited to do. I've come to realize that pathology really is at the center of our clinical genomics efforts, offering new ways to diagnose different cancers as well as help

guide treatment decisions by identifying the genetic pathways that may be dysregulated in individual patients' tumors."

HONING GENOME SEQUENCING

In the years since, Dr. Berger has worked closely with his colleagues in the Department of Pathology's Molecular Diagnostics Service to develop a groundbreaking genome-sequencing test called MSK-IMPACT™, which stands for Integrated Mutation Profiling of Actionable Cancer Targets. This unique, comprehensive test can detect specific mutations in hundreds of genes, as well as alterations in genetic pathways in both rare and common forms of solid cancer tumors. With the MSK-IMPACT™ results in hand, clinicians have targeted information to guide them as they match patients to a specific therapy or to a clinical trial that may benefit them.

"Typically, pathologists render a diagnosis based on looking at tissue under

a microscope," says Dr. Berger. "But the genetic analysis that we perform can tell us about certain genomic alterations that are characteristic of certain tumor types, as well as which mutations, amplifications, or rearrangements might be targetable by available drugs. This provides complementary biological and clinical information that can give a pathologist a better idea of what type of cancer is there and how a particular patient might respond to a particular therapy."

Dr. Berger and his team spent years developing, refining, and clinically validating MSK-IMPACT™, carefully selecting what genes to include in the test panel, coming up with effective strategies to deal with lower-quality tumor specimens, and creating a bioinformatics platform to provide doctors with meaningful, actionable results. "The test reaffirms the importance of pathology not only to correctly diagnose a patient's cancer but to provide as much information as possible to oncologists so they can improve the quality of care they are giving each patient," says Dr. Berger.

EXPANDING IMPACT

One of the most valuable aspects of the MSK-IMPACT™ program is the size of the dataset the pathology department has now accumulated. At last count, more than 200 scientific papers have been published incorporating MSK-IMPACT™ data. "We are sharing this dataset in real time with all of the investigators at MSK," says Dr. Berger. "It opens up a whole new set of research opportunities, both within pathology and in other departments. It is remarkable how these data continue to provide new insights into how cancer can and will be treated in the future."

In addition, Dr. Berger's laboratory is working to expand pathology's genomic

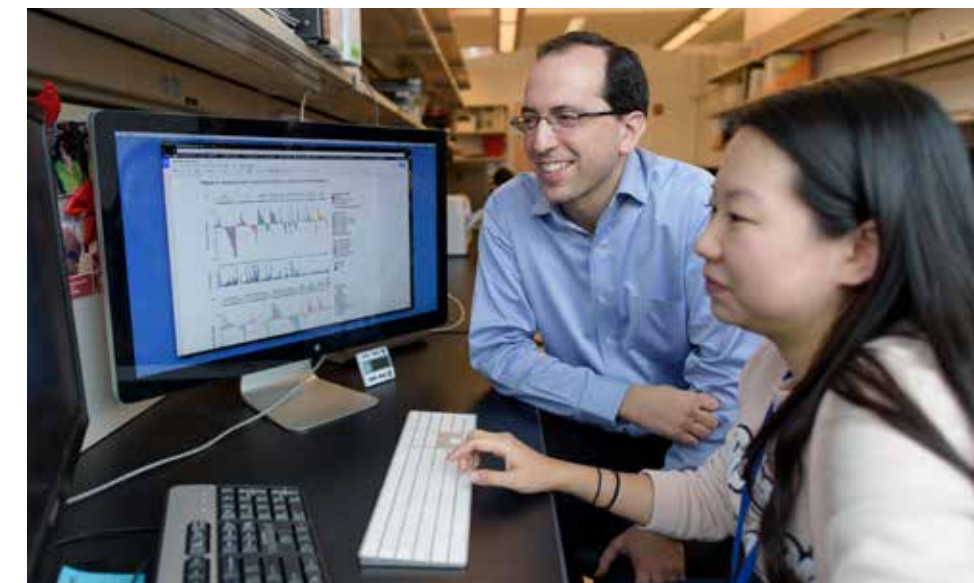
offerings. Since receiving New York State Department of Health approval to use MSK-IMPACT™ as a clinical test in 2014, Dr. Berger has made continual improvements, adding additional analyses and the ability to sequence new types of biological specimens in order to expand the test's clinical utility and its suitability for additional populations of patients.

"Originally, the test was used on patients with advanced cancer who are treated by medical oncologists and are candidates for clinical trials," he says. "But we want to expand our program to also test patients with earlier stage disease who are typically treated by surgeons. In doing so, we may be able to identify prognostic biomarkers that could affect how aggressively patients should be treated or monitored for disease recurrence."

He and his team have also developed a complementary sequencing test called MSK-ACCESS, or Analysis of Circulating Cell Free DNA to Evaluate Somatic Status. Sometimes referred to as a "liquid biopsy," this offers clinicians a way to screen for cancer or metastasis from a simple blood sample without the need for an invasive tumor biopsy. It was approved for clinical use by the New York State Department of Health in the summer of 2019.

"The opportunity to sequence DNA from a blood sample to detect mutations is very exciting," says Dr. Berger. "It allows us the ability to profile tumor DNA levels longitudinally throughout a patient's treatment course, even in patients from whom we cannot obtain tumor tissue. It's exciting and continues to show how genomics can help inform clinical treatment decisions to provide better outcomes for our patients. At the end of the day, that's what everyone here at MSK wants."

“The test reaffirms the importance of pathology not only to correctly diagnose a patient’s cancer but to provide as much information as possible to oncologists so they can improve the quality of care they are giving each patient.”





A Journey of *Technological Evolution* in Research and Diagnostics

MSK Pathology Chairman David Klimstra, MD, shares his vision for the future in his prestigious Maude Abbott Lecture at the 2019 USCAP annual meeting

By Kayt Sukel

When David Klimstra, MD, Memorial Sloan Kettering Cancer Center's Pathology Chairman and James Ewing Alumni Chair, received word that he had been selected to give the 2019 Maude Abbott Lecture at the annual United States and Canadian Academy of Pathology (USCAP) meeting, his first reaction was disbelief.

Since 1980, the Maude Abbott Lecture, named for the pioneering Canadian pathologist who co-founded the International Association

of Medical Museums (later known as the International Academy of Pathology), has been one of the greatest honors that can be conferred by the USCAP. Each year, USCAP's executive committee puts forth for consideration three candidates, "revered authorities" who have contributed and continue to contribute to the advancement of pathology. Dr. Klimstra says his selection came out of the "clear blue sky."

His next reaction was anxiety at the prospect of delivering the meeting's highly anticipated keynote lecture. "I had no inkling I had even been nominated. And then to be asked to give what is supposed to be the key lecture of my career — well, it was a little nerve-racking. This isn't your standard talk where you report on specific research findings or give some type of didactic lecture," says Dr. Klimstra. "In this lecture, you need to reflect on where pathology's been and then offer more philosophical thoughts on where it is heading in the future — and you give it in front of thousands of your peers. I was very honored. But I also knew I had a lot of work to do to get that type of talk ready."

A LONG AND PRESTIGIOUS CAREER

Of course, Dr. Klimstra is no stranger to hard work. Twenty-eight years ago, after completing his anatomic pathology residency at Yale University, he followed his mentor, Juan Rosai, MD, to MSKCC to complete an oncologic surgical pathology fellowship. He's been with the department ever since.

"At the time, there were about 18 pathologists on the faculty, and now we are one of the largest cancer pathology departments in the world," he says. "Back then, almost all of those faculty were diagnostic pathologists who practiced general cancer pathology. The same pathologists were signing out the skin biopsies, the bone marrow biopsies, the breast biopsies, the colon resections — you name it. It was a broad general practice. But now we have become very subspecialized with most of our now 100 faculty members focused on a specific niche, which gives us world-renowned diagnostic expertise in literally every different area of cancer pathology."

Dr. Klimstra first became interested in pathology while studying at Yale. Like most who pursue a career in medicine, he was driven largely by a desire to help people. But when his pathology courses first placed him in front of a microscope, he was immediately hooked.

"I've always loved science," he says. "But, in medical school, I became really interested in understanding disease at the morphologic level. If I can see it under a microscope, it somehow just makes more sense to me. I really appreciate the more mechanistic aspects of how a cancer develops and progresses and the ability to put all those pieces together in a logical pattern to understand a disease."

Over the course of his career, Dr. Klimstra has put his microscope to good use by working to better understand the pathology of tumors of the digestive system, pancreas, liver, and neuroendocrine system. Today, he is an internationally recognized expert on the correlations between the clinical, morphological, immunohistochemical, and molecular features of both common and rare tumors that develop in those areas.

When asked why he gravitated toward these forms of cancers even as early as his residency, he recounts an interesting case he encountered as a resident. That case, a pancreatic acinar cell carcinoma, led to his first major publication. He realized that very few American pathologists were studying pancreatic neoplasia at that time, and upon moving to MSKCC in 1991, it was clear there was a tremendous opportunity in pancreatic pathology. It was a challenging topic, given the aggressive behavior of most pancreas cancers, but it was also one with the potential to make a major difference in cancer care. Even now, he notes, few pathologists have established themselves in this discipline.

A WAY FORWARD FOR PANCREATIC CANCER

Pancreatic ductal adenocarcinoma, the most common type of pancreatic cancer, is an insidious and particularly lethal form of the disease, explains Dr. Klimstra. “Its five-year survival rates are in the single digits for the average patient. So, anything we can do to detect it earlier, even before it is radiographically evident, creates a greater opportunity to cure it. One of my interests has been in characterizing the precursors of pancreatic cancer so we can intervene before invasive cancer develops.”

And based on our current knowledge, pancreatic cancer is proving to be more heterogeneous than we first believed, which is another reason Dr. Klimstra feels it’s so important that more people investigate how it develops and progresses. “There are probably fifteen different kinds of pancreatic cancer and each has very specific attributes,” he said. “But if we can understand how the distinctive clinical, histological, and molecular features fit together to result in disease, we have the best chance to define treatments to help our patients.”

To date, Dr. Klimstra has published more than 400 peer-reviewed articles on tumors of the pancreas, and other organs, and co-authored four Armed Forces Institute of Pathology books, two editions each of *Tumors of the Pancreas* and *Tumors of the Gallbladder, Extrahepatic Bile Ducts and Ampulla of Vater*. He has also worked closely with the World Health Organization (WHO) and American Joint Commission on Cancer (AJCC) to develop appropriate classification and staging systems for tumors of the digestive system and endocrine organs to aid in detection and treatment of these conditions.

In his Maude Abbott lecture, Dr. Klimstra discussed the breadth of his research, starting in residency and continuing even now into his chairmanship, including his work to better understand less common forms of pancreatic cancer, acinar cell carcinoma (ACC) and pancreatic neuroendocrine tumor (PanNET). ACC makes up only about two percent of tumors that develop in the organ, but Dr. Klimstra says that even work on a rare disease like ACC highlights how pathology investigations have evolved over the last few decades and provides valuable insights that can be generalized to more common cancer types.

The theme of the lecture was the evolution of technology available to pathologists to study neoplastic disease. “We started by studying the conventional pathology. How do you make the diagnosis? How do the tumors stain using immunohistochemistry? What happens to the patients over time?” he explains. “But, over the years, with the availability of conventional and then next-generation genomic sequencing, we’ve discovered more and more molecular events that contribute to the development of ACC, including some potentially targetable molecular alternations that may allow us to treat patients specifically for this disease. We can learn a lot from unraveling the biology of tumors like this.” Data from newer technologies have enabled us to paint a much more complete picture of this and other rare neoplasms.

Dr. Klimstra’s lecture also touched on his work investigating PanNETs. Though not as rare as ACCs, PanNETs have a compelling biology of their own. “Pancreatic neuroendocrine tumors tend to

progress rather slowly as compared to conventional pancreatic cancer, sometimes evolving over years or even decades,” he says. “It’s a different type of tumor system and has different types of genetic aberrations that require a different kind of medical management. So, we’ve been working hard to characterize what features will predict the biology of these tumors. How can you tell whether they will be more or less aggressive? How do we identify which patients need immediate treatment as opposed to those who just need to be observed?”

That work, he says, has led to a new way of thinking about not only pancreatic neuroendocrine tumors, but neuroendocrine tumors that arise in other parts of the body.

“Ultimately, the goal of pathology isn’t just to understand the disease process, but to use those insights to make sure our patients are getting the best possible treatments.”

TOWARD THE FUTURE OF PATHOLOGY

Dr. Klimstra says that advances in genomic techniques and other technologies are now providing pathologists with a remarkable amount of new information. “Ten years ago, the primary role of the pathologist was to make the diagnosis and then provide any additional information that might help with prognosis,” he explains. “By and large,



David S. Klimstra, MD and Wendy L. Frankel, MD



“Here at MSK, we are sitting at the cutting edge of cancer pathology. What we are learning is not only shaping our own discipline but also cancer care at a global level. Working in this field has been and continues to be an enormous privilege. I’m really very lucky.”



From left to right: Drs. Marcia Edelweiss, Gloria Young, Laura Tang, David S. Klimstra, MD, Olca Basturk and Hui Chen

that was done using traditional morphologic techniques. But as genetic sequencing technology has evolved and become more affordable, we are now generating enormous amounts of information about mutations and other genetic alterations that may provide additional insights into how to best diagnose and treat these cancers.”

In addition to generating data on the alterations in tumor DNA, we are now analyzing gene expression, epigenetic alterations such as methylation, and protein profiles using mass spectrometry. These studies are generating an unprecedented amount of data that can help us better understand cancer biology. But only if they can make sense of all that data. That’s why, as Dr. Klimstra noted in his Maude Abbott lecture, one of the greatest challenges facing pathology in the future is how to integrate and interpret these vast amounts of complex data.

“To a certain extent, we are starting to do this today,” he says. “But we aren’t integrating all this information as well as we could be. The future will require us to develop better methods for data integration, including the possibility of using machine learning and artificial intelligence to augment our abilities. We also need to consider ways to potentially automate some of that integration as well so we can make our practice more efficient.”

He adds that, with big data analytics on the horizon, it will be more important for pathologists to become comfortable with computational methods as well as a wide variety of “-omic” data.

“We have a major program here at MSKCC where we can use digital representations of a microscopic slide or three-dimensional images of tissue and then use machine learning to do mathematical calculations on the images,” he says. “These tools can help us more easily recognize features we currently use for diagnosis today. But the real excitement is that the data embedded in these morphologic representations can be integrated with data from molecular and protein-based assays so we can understand a lot more about cancers than we do today. These new technologies hold enormous promise for the impact pathology can have on the rest of cancer medicine.”

As Dr. Klimstra reflects on his long career and his ongoing research program, he hopes that more medical students will consider pathology, particularly oncologic pathology, as a specialty. All successful cancer treatments, he says, spring from a foundation of accurate pathologic diagnosis.

“As pathologists, we not only recognize what the disease is and predict how it’s likely to behave, but we also provide information about what drugs are best to treat it,” he notes. “Unfortunately, the pathology that medical students experience is not really related to the daily practice of pathology. They don’t see how truly multidisciplinary the field is, how closely you work with the rest of the clinical team, and the kind of impact you can actually have on an individual patient’s care.”

Despite his love for his microscope, Dr. Klimstra said that he hopes future practitioners understand that cancer pathologists don’t just sit in a laboratory all day; they work closely with the rest of the clinical care team and play a pivotal role in diagnosis, treatment selection, and overall patient outcomes. When he looks at both his own work and that of his colleagues, he has found this line of work to be incredibly rewarding. “The opportunity that I have being chairman of this department and working with such an extraordinary group of faculty, trainees, technologists, and others, has been remarkable,” he says. “Here at MSKCC, we are sitting at the cutting edge of cancer pathology. What we are learning is not only shaping our own discipline but also cancer care at a global level. Working in this field has been and continues to be an enormous privilege. I’m really very lucky.”

Warren Alpert Center for Digital and Computational Pathology

Highlights Research Advances in Digital and Computational Pathology

By Julie Grisham

In May 2019, Memorial Sloan Kettering's Warren Alpert Center for Digital and Computational Pathology welcomed speakers and attendees to the Zuckerman Research Center Auditorium for its Second Annual Digital and Computational Pathology Spring Symposium. The meeting featured talks from faculty, research fellows and staff on the latest research initiatives at MSK in digital and computational pathology.

"Over the last 5 years, MSK has embraced new technologies that enable a truly digital workflow. The benefits of this investment have come to fruition in that we now have unparalleled resources for the integration of machine learning technologies in the review, diagnosis, and prognostic assessment of digital whole slide and tissue images. The work highlighted in the symposium showcases just that," says Dr. Yukako Yagi, Director of Digital Pathology at MSK.

The symposium was created to feature research that is ongoing and to highlight the collaborations between pathologists and the digital and computational laboratories that have the potential to positively and substantively impact clinical cancer care. Attendees have the opportunity to ask questions, meet with research staff and learn about the latest digital and computational advances within the department.

Presentations focused on topics ranging from the use of artificial intelligence in histopathology to the latest methods in microscopy and other imaging techniques. These new enhancements to cancer diagnoses offer a more in-depth analysis than is currently available.

"Pathology is in the midst of a revolution, from a qualitative to a fundamentally quantitative discipline. This transformation will be driven by the next generation of scientific leaders who will be able to combine a deep understanding of machine learning, histology and oncology to impact patient care," says Dr. Thomas Fuchs, Director of Computational Pathology.

The Warren Alpert Center for Digital and Computational Pathology was established in 2017 as an innovation center to facilitate novel research and development in digital pathology and algorithmic computational pathology for clinical cancer care and research. It also serves as a hub for existing digital pathology efforts to establish a fully digital workflow in MSK's Department of Pathology. Please see page 18-19 for a full list of lectures and posters from the 2019 Second Annual Warren Alpert Center For Digital And Computational Pathology Spring Symposium.



Research Presentations

Selected Fellows, Students & Faculty
Moderators: Drs. Yukako Yagi and Thomas J. Fuchs

Introduction to Digital Pathology Imaging

Dr. Yukako Yagi

Learning Histopathology Patterns Using Spatial Point Process

Chao Feng, PhD Candidate

Correlating Micro-Computed Tomography (Micro-CT) of Endoscopic Resected Gastrointestinal Specimens with Histopathology

Dr. Makoto Nishimura

Lung Immuno-Oncology

Dr. Chad Vanderbilt

Assessment of HER2 Amplification Status in Invasive Breast Cancer Using Bright-Field In Situ Hybridization and Digital Pathology

Dr. Dara S. Ross

Automated Cancer Segmentation of Histopathology Images Using Convolutional Neural Networks

Dr. David J. Ho

Precise Detection of PDL1 and PDL2 Amplification in Classical Hodgkin's Lymphoma Using a Confocal Microscope and the Simultaneous Visualization of Immunophenotypes and FISH Signals

Dr. Yanming Zhang

Towards Unsupervised Cancer Subtyping: Predicting Prognosis Using a Histopathology Visual Dictionary

Hassan Muhammad, PhD Candidate

Closing Remarks on the Future of Pathology

Dr. Thomas J. Fuchs
Director, Medical Machine Learning & Computational Pathology

FELLOWSHIP GRADUATION Class of 2018-2019

DAVID KLIMSTRA, MD

*Chair, Department of Pathology;
James Ewing Alumni Chair of Pathology*

It has been a privilege for us to work with all of you this past year. Teaching fellows is certainly part of the core mission of our department, and it is very rewarding to work with bright pathologists who challenge our concepts and keep us sharp every day. We also understand that training here as a fellow involves a lot of hard work! You have shown outstanding dedication and professionalism - it is no understatement that our jobs and your jobs have been so intertwined, it is hard to conceive of them separately - it has been a true partnership. I hope that the experience you have gained - both from the unusual cases you encountered here and from the more routine case material - will help you transition from trainee to attending and develop the confidence you will need as you go out into the "real world" of independent practice. Wherever you go, you will carry this fellowship experience with you. Don't be surprised if, in your first few weeks of practice, your new senior colleagues seek your opinion about challenging cases. You have trained at Memorial, and everyone knows that you now bring a higher level of expertise to the diagnosis of cancer. So, with thanks, I bid you best wishes for your future, and I hope we will see all of again at our alumni reunions and other professional events.

VICTOR REUTER, MD

*Vice Chair, Department of Pathology; Director,
Genitourinary Pathology; Director, Genitourinary
Pathology Fellowship; Director, Pathology Core Facility*

Dear fellows, you worked hard on behalf of our patients, Department and Center. Without your efforts it would be impossible to fulfill our mission. I am certain your hard work and dedication will serve you well as you continue in your journey. We are proud to have had you among us and wish you success. You are now part of our family and we are here to help you in any way we can. Don't forget to come back and visit.

MEERA HAMEED, MD

Chief, Surgical Pathology Service

Congratulations to all!



Where are they now?

ONCOLOGIC PATHOLOGY

Laurence Briski - Pulmonary Pathology Fellowship-*Univ of Michigan, MI*

Su Roychoudhury - Women's Health Pathology Fellowship-*NYU Langone, NY*

Rami Alhassan - Cytology Fellowship-*Univ of Utah, UT*

M. Rizwan Haroon Al-Rasheed - Renal/GU Fellowship-*Mt. Sinai, NY*

Nicholas Bercovici
Breast/GYN Fellowship-*Univ of Mass, MA*

Angel de Dios Quintero
Asst Pathologist - *Morristown Pathology Associates, NJ*

Mohsin Jamal
Molecular Fellowship-*Univ of Pittsburgh, PA*

Pallavi Khattar
Asst. Professor, Hematopathology-*Icahn School of Med at Mount Sinai, NY*

Pavel Kopach
Genitourinary Fellowship-*MSK*

Nicolas Lopez-Hisijos
Hematopathology Fellowship-*Loyola Univ Med Ctr, IL*

Christopher Metter
Renal/Solid Organ Transplant Fellowship-*Univ of Texas Southwestern Dallas, TX*

Reza Setoodeh
Instructor-*Cedar Sinai, CA*

Alpa Shah
Breast Pathologist-*Aurora Diagnostics, Las Vegas, NV*

Wenjing Shi
Cytology Fellowship-*Univ of Southern California, CA*

James Van Gorp
Hematopathology Fellowship-*MSK*

Hai Wang
Cytology Fellowship-*Baystate Health/Univ of Mass, MA*

Lisi Yuan
Cytology Fellowship-*Cleveland Clinic, OH*

BREAST PATHOLOGY

Elena Salagean
Sabbatical

Jennifer Zeng
Asst Attending Pathologist-*Montefiore Med Ctr, NY*

Jin Xu
Asst Professor-*UW Madison Sch of Med and Public Health, WI*

CYTOPATHOLOGY

Brie Kezlarian
Asst Attending Pathologist (Cytology)-*MSK*

Stephanie Muller
Pathologist-*Private Hospital, CA*

Daniel Lubin
Pathologist (H/N & Cytopathology)-*Emory University, GA*

DERMATOPATHOLOGY

Amin Hedayat
Dermatopathology-*Private Practice*

Jad Saab
Pathologist (SurgPath, Derm, Molecular)-*Canada*

GASTROINTESTINAL PATHOLOGY

Monika Vyas
Attending Pathologist-*Beth Israel Deaconess Med Ctr/Harvard Med Sch, MA*

GENITOURINARY PATHOLOGY

Sounak Gupta
Faculty Position-*Mayo Clinic, MN*

Liwei Jia
Asst Professor-*Univ of Texas Southwestern Med Ctr, TX*

GYNECOLOGIC PATHOLOGY

Sheila Segura
Surgical Pathologist-*Indiana Univ, IN*

HEMATOPATHOLOGY

Alexander Chan
Asst Attending Pathologist (Hematopathology)-*MSK*

Ramya Gadde
Cytopathology Fellowship-*Dartmouth-Hitchcock Med Ctr, NH*

Priyadarshini Kumar

*Attending Hematopathologist-
St. Jude Children's Research Hospital, TN*

Ying Liu
Molecular Genetic Pathology Fellowship-*MSK*

Hammad Tashkandi
Molecular Genetic Pathology Fellowship-*Univ of Pittsburgh, PA*

MOLECULAR PATHOLOGY

Amir Momeni Boroujeni
Gynecologic Pathology Fellowship-*MSK*

Edwin Gandia
United States Army-*Walter Reed Med Ctr, MD*

James Solomon
Asst. Director of the Clinical Genomics Laboratory-*Weill Cornell Med Ctr, NY*

Efsevia Vakiani
Associate Attending Pathologist
(GI & Molecular Pathology)-*MSK*

Menglei Zhu
Hematopathology Fellowship-*MSK*

THORACIC PATHOLOGY

Andrew Golden
Pathologist-*Kaiser Permanente, MD*



New Mentoring Program HIGHLIGHTS CAREERS IN LABORATORY SCIENCE

By Julie Grisham

The Memorial Sloan Kettering Department of Pathology has announced the launch of mScope (Mentoring Scientific Careers with Opportunities in Pathology Excellence) — a new program that pairs students with laboratory specialists. Its goal is to educate high school and undergraduate students about careers in the laboratory sciences.

Under the direction of Sarah Virgo and Christina White, the mScope program seeks to encourage the next generation of laboratory professionals by bringing them into the lab environment and educating them about educational and career opportunities. It was designed to enable participating students to share connections with laboratory scientists while fostering tomorrow's laboratory workforce.

"We've had so much success with bringing students from STEM [science, technology, engineering, and math]-focused high schools into the lab for field trips that we decided to increase

the opportunities for them to learn about careers in laboratory science," says Christina White. "The truth is that there is a lack of exposure to opportunities that exist in the lab. By connecting students who may have an interest in science but haven't officially decided on a career with our laboratory staff, we have a real opportunity to address the critical staff shortages that exist not only in our labs, but across the US." adds Sarah Virgo.

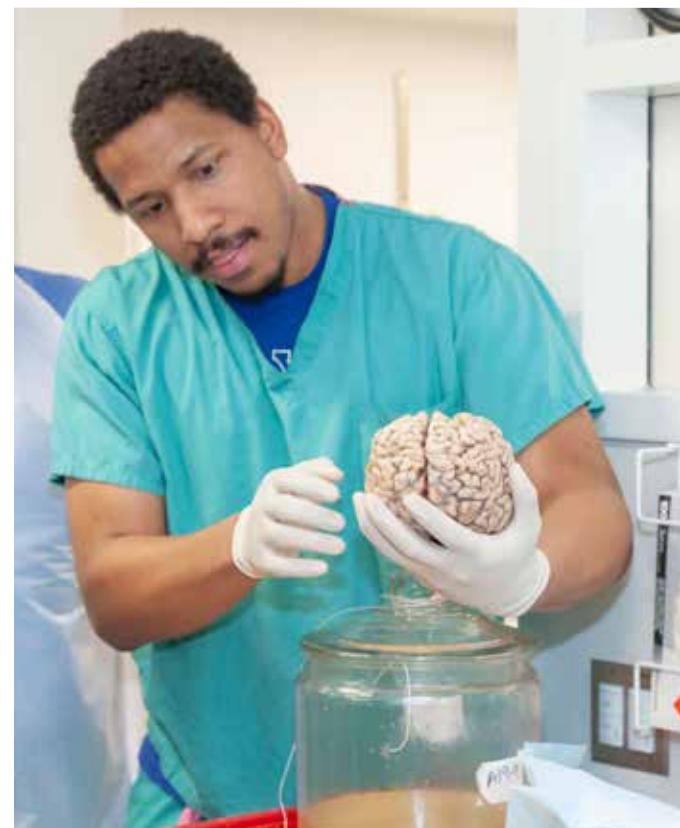
The program is designed to provide students with exposure to a full range of pathology specialties including histology, surgical pathology, cytology, hematopathology, and molecular pathology. Participants will gain a unique, real-time introduction to the world of pathology and its connection to patient care. The program offers one-on-one, recurring mentoring from working experts and familiarity with laboratory science careers through observation of the critical work done by MSK's scientists.

The first group of mScope participants will start in June 2020. High school and undergraduate students who are interested in applying must have at least a 3.0 GPA and an interest in laboratory sciences. They must be willing to commit at least one hour a week for eight weeks. Participants will do two-week rotations through four different areas within the Department of Pathology.

HOW TO APPLY

Applicants need to submit a complete application and participate in an on-site interview. To learn more about the mScope program,

visit www.mskcc.org/departments/pathology/mscope-program



Visiting students from East Orange STEM Academy



The Department of Pathology's Annual Alumni Meeting and Fred W. Stewart Award LINDA FERRELL, MD

By Jinru Shia, MD

Linda Ferrell is the 2019 recipient of the Fred W. Stewart Award, given annually by Memorial Sloan Kettering's Department of Pathology to an individual who has made outstanding contributions to the understanding of human neoplastic disease.

Dr. Ferrell is a world-renowned liver pathologist. Her stellar career achievements exemplify how dedicated surgical pathologists can have a momentous impact on the field of medicine.

Dr. Ferrell obtained an MD degree from the University of Kansas, where she also completed pathology residency training. She did fellowship training at the University of California, San Francisco (UCSF), then joined the faculty there, remaining at the university until 2015, when she retired to emeritus status. Over the years, Dr. Ferrell has served in multiple important roles at UCSF, including the distinguished Professor in Anatomic Pathology (Endowed Chair), Vice Chair of Clinical Affairs in the Department of Anatomic Pathology, Director of Surgical Pathology, Director of Surgical Pathology Fellowship, and Director of the Liver and Gastrointestinal Pathology Fellowship and Gastrointestinal Pathology Fellowship (2005 to 2014). At the national and international level, Dr. Ferrell has also played important roles: She is a past President of the Hans Popper Hepatopathology Society (2008 to 2009) and the United States and Canadian Academy of Pathology (USCAP) (2012 to 2013).



Dr. Ferrell has devoted her academic career to the study of liver pathology. As evidenced by her numerous publications (more than 200 original articles), she has made great contributions to the understanding of the pathology of liver tumors, particularly of well-differentiated liver tumors, including hepatocellular adenoma variants, focal nodular hyperplasia-like lesions, vascular lesions, and malformations in the liver. Through participation in major organizations, such as the Clinical Research Network in Nonalcoholic Steatohepatitis (a National Cancer Institute-sponsored consortium) and the International Liver Pathology Study Group (of which she was a founding member), Dr. Ferrell worked relentlessly to ensure the most effective integration of pathology into the various studies of liver diseases. Her seminal works on liver pathology in recurrent hepatitis C after transplantation and on the diagnosis of dysplastic nodules have gained worldwide attention, and a number of these studies have been recognized internationally as leading papers in the field.

Dr. Ferrell is also an ardent educator. She has nurtured generations of pathology residents and fellows. She chaired two major annual courses for pathologists for multiple years: at UCSF for 33 years and for the California Society of Pathologists for eight years. Through the years, she has served a wide variety of teaching roles via USCAP.

Her numerous book chapters and major liver pathology textbooks (including the premier text, *MacSween's Pathology of the Liver*, fifth, sixth, and seventh editions) have benefitted liver pathologists everywhere. Her contribution as the lead editor of *Liver Pathology* (part of the consultant pathology series from Demos Publishers), which emphasizes difficult diagnostic problems in liver pathology, has similarly offered invaluable guidance. Dr. Ferrell has lectured extensively both nationally and internationally. Her lectures are always very well received.

It is no surprise that numerous awards have been bestowed on Dr. Ferrell in recognition of her achievements. These include the 2008 Gold Headed Cane Award, the 2015 F. K. Mostofi Distinguished Service Award from USCAP, the 2016 Harvey Goldman Master Teacher Award from USCAP, the 2017 President's Award from the Arthur Purdy Stout Society of Surgical Pathologists, and numerous UCSF teaching awards for resident and medical student teaching.

Today, as we celebrate the memory of Dr. Stewart, a man who early on brought surgical pathology to the front lines of oncology, it is most fitting that the medal in his name be given to an individual who has dedicated her career to the practice of surgical pathology and contributed monumentally to the continued advancement of this discipline in modern times. We congratulate Dr. Ferrell on this well-deserved award.

“Today, as we celebrate the memory of Dr. Stewart, a man who early on brought surgical pathology to the front lines of oncology, it is most fitting that the medal in his name be given to an individual who has dedicated her career to the practice of surgical pathology and contributed monumentally to the continued advancement of this discipline in modern times.”



2019 MSK Pathology Alumni Dinner



MEERA HAMEED, MD



Embracing the Future of Pathology

By Kayt Sukel

Musculoskeletal tumors, or cancers of the bone and soft tissues, are both rare and complex. Which is exactly what sparked the professional interest of Meera R. Hameed, MD, Chief of the Surgical Pathology Service at Memorial Sloan Kettering Cancer Center, who was drawn to the challenge of specializing in this type of cancer.

“Compared to other types of cancers, there are fewer numbers of cases of bone and soft tissue,” explains Dr. Hameed. “Because of that rarity, there is a lot we still have to learn about these tumors. There are a host of challenges from diagnosis to treatment, and pathologists who work in this area have a unique opportunity to explore these cancers especially in this era of advancing technology.

Since coming to MSK in 2009, Dr. Hameed has worked to embrace new

technologies, including molecular diagnostics and digital and computational pathology, to help her and her colleagues better serve patients with rare cancers.

“The bone is a very difficult organ to access and treat,” she says. “With many of the bone and soft tissue cancers, if the tumor comes back after surgery, there are not many therapeutic options left. Being able to make the right diagnosis, which include working closely with our radiology, surgery and oncology colleagues, is of vital importance so that the right treatment is given from the start. It is important that all the modern technology tools are available and used appropriately to enhance diagnostic accuracy. For this, one has to start with even basic tissue preparation such as EDTA which allows preservation of DNA and RNA.

A SEARCH FOR UNDERSTANDING

Dr. Hameed and her colleagues have worked on a variety of musculoskeletal cancer types, including some of the more common of these rare cancers in bone such as chondrosarcoma, which starts in the cartilage cells; and osteosarcoma, a childhood cancer that develops from cells which make bone (osteoblasts). While osteosarcoma is sensitive to chemotherapy, she explains, chondrosarcomas are not sensitive to chemotherapy or radiation treatments — which is why it is imperative to get a better grasp of their underlying biology. Genetic studies are helping to do that. “We are learning that some of these cancers have specific genetic alterations,” says Dr. Hameed. “By studying the incidence of these alterations, as well as the outcomes in patients, we are learning about those that may have clinical relevance — there are even some clinical trials now for specific inhibitors related to some of the alterations.”

For example, through next generation sequencing, my colleagues and I have found certain alterations in osteosarcoma which may be of benefit for patients who have relapsed or refractory to conventional therapy. In chondrosarcoma, a driver mutation in the IDH gene has impact on recurrence free and metastases free survival.”

Dr. Hameed is also interested in very rare tumors, like chordomas, which are tumors that develop from notochordal cells which play an important role in spine development. Chordomas remain difficult to treat with complex surgeries and there are not many options for patients who have recurrent disease. In preliminary studies Dr. Hameed and colleagues have found that chordomas are tumors with predominantly copy number alterations and chromatin remodeling genes may play a role in their biology, and she is pursuing further studies to explore the epigenetic mechanisms in collaboration with other experts in the field.

“There are many challenges when we are talking about diagnosis, prognosis, and treatment for rare cancers,” she says. “But if we can understand the biology of how they develop

and the genetic changes involved, we may be able to find better diagnostic and prognostic markers, as well as treatments that can provide a better outcome for our patients.”

THE ROLE OF COMPUTATIONAL PATHOLOGY AND ARTIFICIAL INTELLIGENCE

Dr. Hameed has been a stalwart champion of implementing digital pathology and promoting computational pathology in the department of pathology at MSK. While many pathologists may be wary of new artificial intelligence (AI) or machine-learning algorithms coming to the field, Dr. Hameed sees them as a way of augmenting her and her colleagues’ abilities in ways that will benefit patients.

“Pathology is a field in which we look for patterns, and recognize those patterns that are indicative of disease,” she explains. “But there’s so much data on a particular slide, more than what the pathologist sees. These computational tools may offer us information that can be applied to further our diagnosis, prognosis, or in future how to treat an individual patient.”

With osteosarcomas, pathologists rely on their eyes to assess tumor necrosis following pre-operative chemotherapy as an indicator of prognosis and survival after therapy. This is a subjective measurement and can have interobserver disagreement as to the degree or percentage of necrosis. Dr. Hameed and Dr. Agaram (Bone and Soft Tissue team) are working with computational pathology colleagues (Dr. Fuchs’ laboratory) to develop machine learning tools and algorithms that can be trained to recognize necrosis in tumors. These algorithms will provide a more objective and quantitative measure than the unaided human eye. This will give the treating clinicians a more accurate assessment of how patients are responding to therapy.

“I think that as we adopt more of these algorithms, the field of pathology will become more objective,” she says. “We will be able to better assess prognostic factors in tumors. The computer algorithms will be able to pull data

“the combination of advanced molecular genetic techniques, new ways of imaging tumors, and new ways to harness the power of the computer to integrate and analyze the mass of data we collect from patient specimens will lead to significant improvements in patient care”

out of an image that we have not been able to by visual means. Then we, as pathologists, can analyze that information and determine how it relates to a particular patient’s disease.”

Dr. Hameed says that as pathology evolves to incorporate new technologies and tools in various cancers and rare tumors like the ones she studies, the specialty will benefit in a variety of ways. Put them together under the seasoned eye of a trained pathologist and the data will be more pertinent to the individual patient with the disease and will help inform clinical decisions for optimal treatment. She notes that “the combination of advanced molecular genetic techniques, new ways of imaging tumors, and new ways to harness the power of the computer to integrate and analyze the mass of data we collect from patient specimens will lead to significant improvements in patient care”.

The Pathology of NEOPLASTIC DISEASES COURSE

April 29 - May 3, 2019

2019 Course Directors



Meera Hameed, MD

Lung Cancer Classification

William D. Travis, MD

Molecular Pathology of Lung Cancer

Jason C. Chang, MD

Emerging Issues in Lung Adenocarcinoma

William D. Travis, MD

Immunohistochemistry for Lung Tumor Diagnosis and Biomarker Testing: An Update

Natasha Rekhman, MD, PhD

Diagnosis of Lung Cancer in Cytology and Small Biopsies

Darren J. Buonocore, MD

Neuroendocrine Tumors of the Lung

Natasha Rekhman, MD, PhD

Pleural Tumors

Jennifer L. Sauter, MD

Frozen Section Diagnosis of Thoracic Tumors

Darren J. Buonocore, MD

Mediastinal Tumors

Jason C. Chang, MD

Pulmonary Lymphoproliferative Disorders

Ahmet Dogan, MD, PhD

Ductal Adenocarcinoma of the Pancreas

Olca Basturk, MD

Solid Nonductal Neoplasms of the Pancreas

David Klimstra, MD

Cystic Neoplasms of the Pancreas

Olca Basturk, MD

Cytology of Pancreas Neoplasms

Carlie Sigel, MD

Neuroendocrine Neoplasms of the GI Tract - Conundrums and Caveats

Laura Tang, MD

Molecular Diagnostics of GI Tumors

Jaelyn Hechtman, MD

Appendiceal Epithelial Neoplasms - Bewildering Between Goblet and Bucket of Mucin

Laura Tang, MD

Gastroesophageal Adenocarcinoma and Their Precursor Lesions - The Barrett's Anxiety

Laura Tang, MD

Gastric Polyps and Other Epithelial Neoplasms

Michael Roehrl, MD

Biomarker Testing in Upper GI Tumors

Michael Roehrl, MD

Selected Issues in Colorectal Tumor Pathology

Jinru Shia, MD

GI Tumor Diagnosis: Lessons from Prior Mistakes

Jinru Shia, MD

Biopsy Diagnosis of Hepatic Tumors

David Klimstra, MD

Ductal, Intraductal and Cribriform, Oh My! The Differential Diagnosis of Large Gland Lesions of the Prostate and its Clinical Import

Samson Fine, MD

Essential Data Elements for Prostate Cancer Reporting in 2019

Samson Fine, MD

Risk Stratification in Prostate Cancer; the Role of Contemporary Tissue, Urine and Serum-Based Assays

Anu Gopalan, MD

Two Cases to Remember: Presentation by the Genitourinary Pathology Subspecialty Fellows

Liwei Jia, MD, Sounak Gupta, MD

Mimics of Urothelial Carcinoma

Victor Reuter, MD

Prognostic and Predictive Factors in Urothelial Carcinoma; Grading, Staging and Beyond

Hikmat Al-Ahmadie, MD

Urothelial Tumors of the Upper Urinary Tract

Hikmat Al-Ahmadie, MD

A Practical Approach to the Morphological Evaluation of Tumors of the Testis and Its Adnexa

Satish Tickoo, MD

Renal Neoplasia: Morphologic Spectrum and Differential Diagnosis

Satish Tickoo, MD, Yingbei Chen, MD

Germline Mutations in Urogenital Tumors; Disease Spectrum and Clinical Implications

Maria Carlo, MD

New and Emerging Variants of Renal Neoplasms

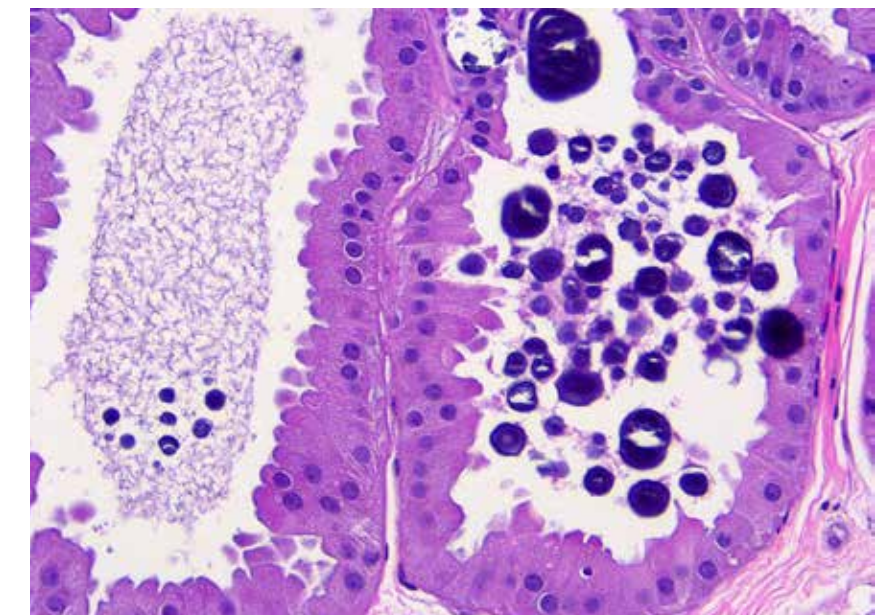
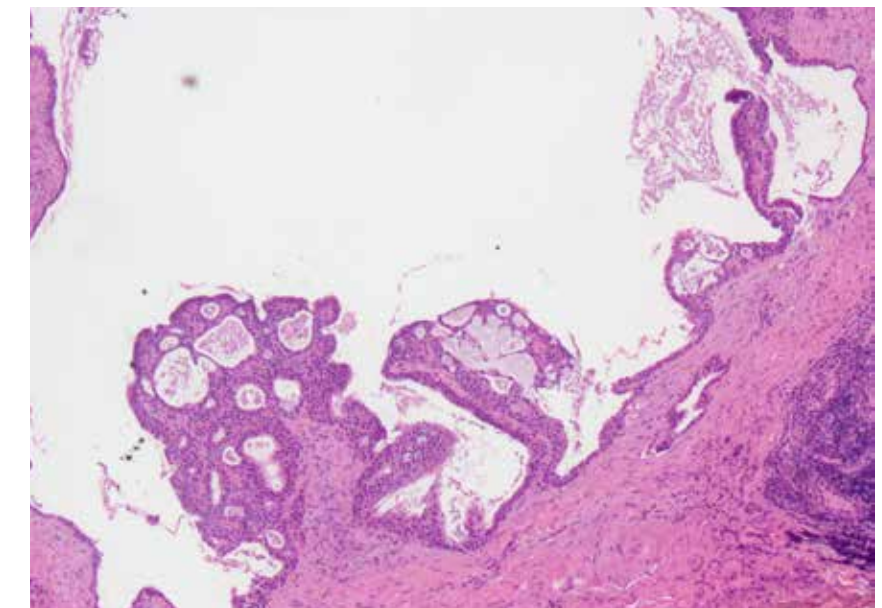
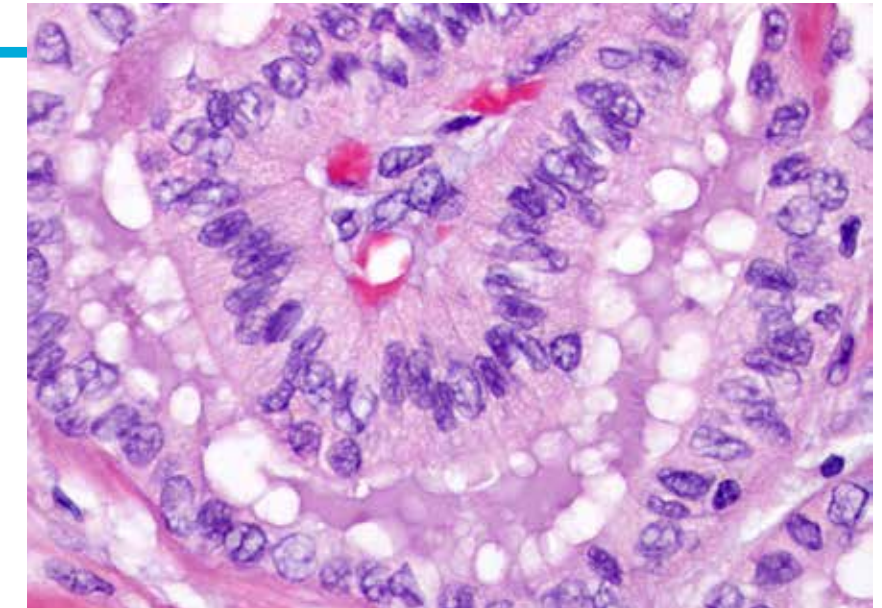
Yingbei Chen, MD

Implementation of Whole Slide Imaging in Your Laboratory; Challenges and Opportunities

J. Sirintrapun, MD

The 2020 Pathology of Neoplastic Diseases Course will take place from Monday, April 27- Friday, May 1 and will feature Head and Neck Pathology, Breast Pathology and Gynecological Pathology under the direction of Drs. Hameed, Ghossein, Brogi, Wen and Ellenson.

For more information or to register for the course, please visit: www.mskcc.org/neoplasticdiseases2020



2019-2020 FELLOWS

Oncologic Surgical Pathology Fellows



Cameron Beech, MD



Wissam Dahoud, MD



Liz Edmund, MD



Leone! Maldonado
Gonzalez, MD
Chief Fellow



Yan Huang, MD, MS



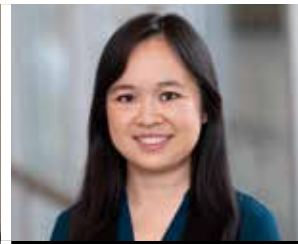
Yiang Hui, MD



Rami Imam, MD



Elizabeth Kertowidjojo,
MD, PhD, MPH
Chief Fellow



Anna Lee, MD



Fanni Ratzon, MD



Abeer Salama, MBBS



Christopher Schwartz, DO



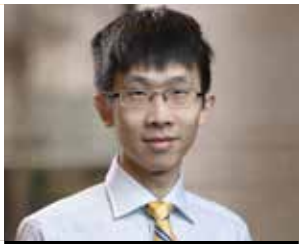
Shenon Sethi, MBBS



Brandon Umphress, MD



Alan Xinyu Wu, MD, PhD



Chen Yang, MBBS



Lingxin Zhang, MBBS

Specialty Fellows



Raza Hoda, MD
Breast Pathology



Marjorie Perron, MD, PhD
Breast Pathology



Willard Wong, MBBS
Breast Pathology



Jose Scarpa Carniello, MD
Cytopathology



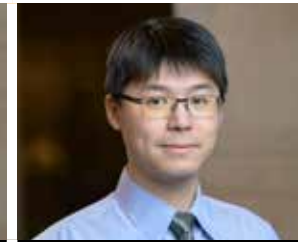
Bogdan Isaila, MD
Cytopathology



Roshan Raza, MBBS
Cytopathology



Laura Battle, MD
Dermatopathology



Kevin Yen Chen Ko,
MD, DMD
Dermatopathology



Mahra Nourbaksh,
MD, PhD
Gastrointestinal Pathology



John Kennedy, MD
Genitourinary Pathology



Pavel Kopach, MD
Genitourinary Pathology



Amir Momeni
Boroujeni, MD
Gynecologic Pathology



Akanksha Gupta,
MBBS, MD
Hematopathology



James Van Gurp, DO
Hematopathology



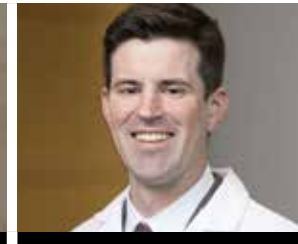
Menglei Zhu, MD, PhD
Hematopathology



Donna Ferguson, MD
Molecular Pathology



Ying Liu, MD, PhD
Molecular Pathology



Douglas Mata, MD, PhD
Molecular Pathology



Rohit Sharma, MD
Molecular Pathology



Stewart Soo
Ryum Yang, MD
Molecular Pathology



Marina Baine, MD, PhD
Thoracic Pathology

MSK CELEBRATES LAB WEEK 2019

By Julie Grisham

Medical Laboratory Professionals Week is a national celebration that takes place every year during the last full week of April. It was established to recognize the medical laboratory professionals who play a vital role in every aspect of health care.

At Memorial Sloan Kettering, Lab Week activities are jointly sponsored by the Department of Pathology and the Department of Laboratory Medicine. This event has incorporated events like “Family Feud: Lab Week Challenge” and “The Great Escape” provide an extra level of fun and bonding.

“Lab Week is full of great team-building events,” says Sarah Virgo, Assistant Manager and Chair, Laboratory Professionals

Week Committee. “So much of what our two departments do is behind the scenes, so it’s great to celebrate everyone and highlight the important work that they do. Without the essential work being done in the lab by our wonderfully talented staff, our patients couldn’t receive the excellent care they receive here at MSK.”

In 2019, Lab Week featured scientific talks from researchers throughout MSK, career-building sessions, and activities ranging from scavenger hunts to trivia to kickball. The week was rounded out on Friday with a luncheon held in the Rockefeller Research Laboratories building.



LAB WEEK TABOO

Rochelle Lopez
Laura Coyoy
Christina Lugo



LAB WEEK COSTUME CONTEST

Janet Guthrie
Judy Zhu
Luciana Kimmel
Kimberly Lauderman
Sylvie Wiener- Fedus
Nora Plante
Camille Ramkaran
Lily Zhuo



LAST PERSON STANDING TRIVIA

Viktor Moroz



LAB WEEK FAMILY FEUD CHALLENGE

Jean Allen
Madeline Cioffi
Nora Plante
Jessica Bautista
Joann Rittersbach
Ana Perez
Cathy Tan
Tasfina Yousuf
Matthew Brady
Richmond Serofica
David Puma



LAB WEEK GREAT ESCAPE

David Puma
Melissa Fonseca
Utsav Patel
Meiyi Wang
Anita Yun
Roger
Gavin Guy
Laura Coyoy
Christina Logo
Jonatan MontesDe Oca
Dondre Clarke
Rochelle Lopez
Bryan Lu
Julia Im
Judy Zhu
Yessica Saenz



LAB WEEK PERIODIC TABLE BINGO

David Puma
Rachel Oconnor
Doris Wong
Linda Moody Brow
Michael Sandino
Kerry Mullaney
Debby Melgar



LAB WEEK PHOTO CONTEST

Kerry Mullaney
Ana Perez
Kelsy Merck



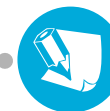
MUSIC VIDEO

Cytogenetics
Koch Center



EXTRA EFFORT AWARDS

Bryan Lu
Madeline Cioffi
Kerry Mullaney
Gloria Flamenco
Janet Guthrie



LAB WEEK AMAZING RACE SCAVENGER HUNT

Dondre Clarke
Melissa Fonseca
David Puma



Lab Week Family Feud Challenge 2nd Place Winners (from left to right): Cathy Tan, Tasfina Yousuf, Ana Perez, David Puma, Matthew Brady, Richmond Serofica



Lab Week Family Feud Challenge 1st Place Winners (from left to right): Joann Rittersbach, Jean Allen, Madeline Cioffi, Nora Plante, Jessica Bautista



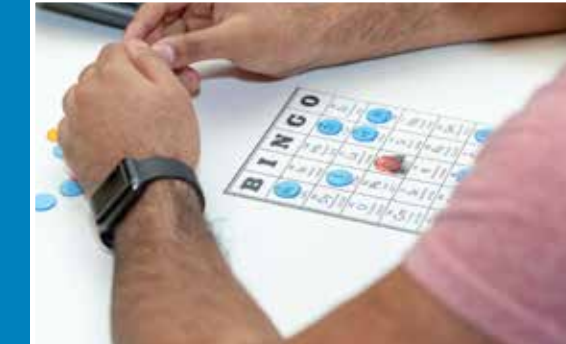
Towards Predictable Immune Reconstruction After Allo-Hematopoietic Cell Transplantation and Cellular Therapies
Dr. Jaap J. Boelens

Modalities and Applications for Quantitative Multiplexed Immunostaining in Immuno-Oncology
Dr. Travis Hollmann

Laboratory Professionals: Keynote Speaker
Dr. Sergio Giralt

Mass Spectrometry Assays for Detecting Monoclonal Immunoglobulins
Dr. Katie Thoren

Artificial Intelligence and the Clinical Lab
Dr. Jamal Benhamida



GASTROINTESTINAL PATHOLOGY



Jinru Shia, MD
Director, Gastrointestinal Pathology
Attending Pathologist



David S. Klimstra, MD
Chair, Department of Pathology
Attending Pathologist



Laura H. Tang, MD, PhD
Attending Pathologist



Christine Iacobuzio-Donahue, MD, PhD
Director, David M. Rubenstein Chair
for Pancreatic Cancer Research
Attending Pathologist



Michael H. Roehrl, MD, PhD
Director, Precision Pathology
Biobanking Center
Associate Attending Pathologist



Jaclyn F. Hechtman, MD
Assistant Attending
Pathologist



Olca Basturk, MD
Associate Attending
Pathologist



Carlie S. Sigel, MD
Associate Attending Pathologist



Efsevia Vakiani, MD, PhD
Associate Attending Pathologist

Setting the Standards

The Gastrointestinal Pathology team strives to provide the most accurate and relevant diagnostic information clinicians use to make treatment decisions for patients, and researches promising avenues that inform the future of that care.

By Kayt Sukel

Gastrointestinal (GI) cancers, which include esophageal, gastric, colorectal, liver, gallbladder, and pancreatic cancers, are among the most commonly diagnosed cancers across the globe. Over the past decade, the incidence rates for many of these cancers, including colorectal and liver cancer, have significantly grown. That is one of the main reasons Jinru Shia, MD, Director of the GI Pathology team, and her team stay so busy at Memorial Sloan Kettering Cancer Center.

“The GI service here is one of the busiest in the pathology department,” says Dr. Shia. “When we looked at our service load for the year recently, we saw that our group had already signed out more than 14,000 cases for 2019. That accounted for more than 16% of the total service volume.”

Those cases include in-house biopsies and resections, and consultation cases from other hospitals. It is a lot of work, Dr. Shia acknowledges — but in her view, such a heavy volume is a “welcome challenge” — one that she and her colleagues meet head on.

“Our main goal, always, is to stay at the forefront of clinical service, by both providing accurate pathology information for all the cases we see and ensuring effective integration of that information into clinical treatment decision-making,” she says,

“The service work may seem like regular, routine kind of work, but we make sure each case is done in the right way — the best way — so we can set the standards for the best pathology practice; our team is committed to that.”

AN EVOLVING SERVICE

When Dr. Shia came to MSK Pathology in 1998 as a fellow, there were 2 attending pathologists that had a special interest in GI. Today, there are 9 dedicated GI pathologists, forming the GI pathology team and working nimbly together, integrating new technologies that have enabled them to provide ever more valuable and targeted information that, in turn, helps inform treatment selection and disease management for the MSK patients. Everyone in the service, says Dr. Shia, shares the same dedication. “We all love what we do — and are passionate about doing really good work.”

Within the subspecialty of GI pathology, the team has further sub-specialized. Each team member is focused on a particular part of the GI system: upper GI tract, lower GI tract, or hepato-pancreato-biliary system. “For each of those three major areas, we have dedicated expert pathologists who can take our pathology diagnosis and help translate it to the best clinical effect,” explains Dr. Shia.

While most people think of pathologists working hard behind the scenes, spending more time with their microscope than with clinical colleagues, members of the GI pathology team play key roles within MSK’s signature disease management teams (DMTs), helping zero in on treatment selections that best benefit individual patients.

“Our approach ensures that we can have close communication with the clinical team early on and play a major part in the process of determining care,” says Dr. Shia. “We meet regularly to discuss ongoing cases — and treatment decisions are made during that meeting. All the different disciplines at MSK contribute to these clinical-based DMT meetings. By working together and sharing our expertise, we can help ensure the best possible outcome for our patients.”

BIOMARKER REPORTING

When asked about specific examples of innovative approaches the GI pathology team has brought on in the arena of clinical service, Dr. Shia mentions biomarker reporting as an example. “In the current era of precision oncology and targeted therapy, accurate reporting of biomarkers is of great importance,” Dr. Shia explains. And she is particularly referring to what is known as predictive biomarkers, tumor tests that can predict whether the tumor is likely to respond to a given targeted therapy or not.

“Immunotherapy is particularly pertinent to GI tumors,” says Dr. Shia. “One of the predictive markers for immunotherapy is the tumor’s microsatellite instability (MSI) status. So, today, every patient with a GI tract carcinoma gets tested for MSI markers (as well as some other markers). To effectively report the results of the various biomarkers, the GI team has worked closely with MSK’s medical oncologists, and together they implemented standardized biomarker reporting systems for both upper and lower GI tract malignancies. Such systems not only offer the data that is needed for the oncologists to make treatment decision based on current guidelines, they also capture additional information that can benefit future retrospective studies, and can potentially help further improve our understanding of tumor behavior and how best to achieve better treatment response.

WORLD-CLASS RESEARCH

While Dr. Shia is undeniably pleased to speak about the robust clinical services her team provides at MSK, she’s also proud of her colleagues’ contributions on the research front.

“Using the phrase ‘world-class’ to describe what they do is not an exaggeration,” she says. “The World Health Organization recently updated its GI tumor classifications. Many of our team members directly participated in this new, fifth edition of these classifications. And if you open the book and look at the different tumor subtypes, you’ll see that, quite often, the references that serve as evidence for each came from members of our group. It feels good to see what a difference we are making.”

Similarly, her team members’ great work as evidenced by the numerous publications has also earned them authorships and co-authorships of other major text

“The service work may seem like regular, routine kind of work, but we make sure each case is done in the right way—the best way—so we can set the standards for the best pathology practice; our team is committed to that.”

books as well including several *AFIP* fascicles. Dr. Shia was particularly proud to mention that one of the team members, Dr. Christine Iacobuzio-Donahue, also the Director of MSK’s David M. Rubenstein Center for Pancreatic Cancer Research, was recently named a recipient of the Ruth Leff Siegel Award from Columbia University Irving Medical Center as the investigator with the most impactful contribution to the understanding of pancreatic cancer over the past year.

Dr. Shia is also anticipating the ways in which the team’s research will enhance the standard of care for GI tumors worldwide, and seeing what sort of insights future investigations may spark. “Many exciting research projects are being carried out by our team members”, she says. Some examples she has provided are: the heterogeneity of MSI cancers at both the molecular and phenotypical level and how that may translate to tumor response to immunotherapy; the role of gut microbiome on tumor development and behavior; and the clinical and diagnostic application of digital and computational pathology. “All such efforts carry the promise of providing meaningful data and ultimately helping advance the field of GI oncology”.

THE NEXT GENERATION

Dr. Shia says she and the GI team greatly enjoy working with their fellows. “The fellows’ unique perspective brings on views that we would otherwise have not seen; such views often help improve the way we work and teach,” Dr. Shia says. For the fellows — both the first-year fellows and the GI subspecialty fellows, the GI service provides a nurturing and supportive environment that allows them to freely absorb knowledge and grow.

Dr. Shia has served as Director of the Gastrointestinal Pathology Fellowship Program at MSK for the past 10 years. In 2020, her teammate Dr. Carlie Sigel will take over this role. “Carlie has already been an integral part of our GI Fellowship Program for many years. Carlie is a wonderful teacher and has mentored many fellows on various research projects,” says Dr. Shia.

Whether she is discussing the past, present, or future, Dr. Shia exhibits great pride in the work that the GI pathology team contributes to MSK. There is good reason she’s remained in her post at MSK for more than two decades: the kind of work the service does is simply unparalleled. “GI pathology at MSK has always performed at a very high level. Between our clinical service, research, and educational efforts, you can count on it always being that way,” Dr. Shia concludes.

14,000

“When we looked at our service load for the year recently, we saw that our group had already signed out more than 14,000 cases for 2019. That accounted for more than 16% of the total service volume.”

SHADI HADDAD

1982-2019

By Carlie S. Sigel



The Cytology Service is nested within the Pathology Department and the services it provides require consistent trust and interconnectedness among the cytology staff. We are tethered to each other by Vocera, we cover those taking lunch, delayed by transit, or away on unexpected absences, and we suffer such intimacies as having to recognize and decipher the worst of our colleagues' handwriting. Bonded in this way, we frequently choose to gather by circling around the office, eating cake by the cubicles in the spirit of celebration for life's milestones such as new students, marriages, baby showers, holidays, promotions, and retirements. We are a close-knit group, and when Shadi dropped out of our lives so tragically sudden, I felt unraveled and deeply sad.

I've been keeping his spirit alive in my mind and in my heart since June by remembering the qualities I admired most in him. He was a model of positivity. Shadi was never simply present and working for the sake of completing a task. He aimed to be as helpful and available as possible and he always had a good attitude. Another one of his admirable qualities was his accountability. Consistently, he was free to admit uncertainty or his role in a mishap. Incapable of lying, he would never obscure any details. I knew I could trust anything he said even if I couldn't trust that the words he used were

present in the dictionary. He told me his wife Meghan called his language, "Shadanese" and the entry I will make in that lexicon is "subsequential" which means the thing that happened after the one we were talking about. And if Chloe, his daughter, ever finds herself having trouble pronouncing names, it is safe to say she inherited that from her father. Shadi deeply cared about his family. They understood his work family was an extension of theirs and gathered from near and far to attend the MSK memorial. My favorite memories of him will be when he would poke his head into my office and ask me if I was busy. "Of course, but c'mon in," I'd say, and then he'd bound over to my desk with his phone out and show me the latest cute Chloe pic. The pureness of his excitement and joy in being a dad and loving his baby girl was endlessly uplifting. Shadi had an awesome sense of humor and an innate sense of when to be serious and when it was okay to cut loose a little.

I count myself among the many who think of Shadi frequently. I will honor his life by trying to embody in myself these traits that left such a deep impression on me and those of us who continue to grieve. If you want to add a little Shadanese to your life, just say "cool beans" when you agree with something and I guarantee it will help you smile through the sadness.

“The sudden passing of cytotechnologist Shadi Haddad on May 31, 2019 shocked and saddened all of his extended 'work family', who he touched both professionally and personally.” - David Klimstra, MD



“

I will always remember Shadi's laugh – it was like no other laugh I have ever heard. He will always be in our hearts.”

MARIA MAUGERI

“

A Bosnian and a Jordanian walk into a bar..... No, it's not the beginning of a joke, but the beginning of a friendship! Shadi and I, with a couple of other members of the cytology service, had a tradition of going to a local bar before our yearly departmental Christmas party. Early on, our conversations focused on craft beers and cars. He loved Volvo's. As the years progressed, our conversations turned to married life, our kids, family, and Bitcoin. Shadi enjoyed discussing the intricate details of the cryptocurrency process. Shadi was genuine and caring. He loved his family. We will miss his laid-back attitude, his laugh, and helpful nature.”

RUSMIR FERATOVIC

“

Shadi was always calm, humble, and cordial towards other people. He brought positive attitude and effort every day in our Cytology Service. Amazing colleague.”

HANDY OEN

“

I had the privilege of working with Shadi at MSK. He was a kind, smart, friendly soul. My deepest condolences to Shadi's family. He will be dearly missed.”

LORRAINE CORSALE

“

Dearest Shadi- One of the sayings that has always struck a cord in my heart is “Only the good die young”. Some things in life are not meant to be explained, just accepted, and your passing is certainly one of them. We miss you, today and always.”

VERONICA KIM



QUALITY IMPROVEMENT FAIR XVI

Pathology Project Recognized at MSK Quality Improvement Fair

By Julie Grisham

Every year, Memorial Sloan Kettering’s Quality Improvement (QI) Fair showcases various improvement efforts and initiatives across the Center. The institution-wide event is hosted by the Division of Quality and Safety.

The QI Fair was created to increase awareness of various projects and initiatives, improve collaboration, and emphasize patient safety and quality of care as top priorities, among other objectives.

In April 2019, a project from the Department of Pathology won two of the three awards at the QI Fair: the Judges’ Choice Award and the Patients’/Caregivers’ Choice Award.

The project, called “Pathology Consultations 2.0: Empowering Users, Improving Turn Around Time, and Embracing the Digital Age”, was aimed at improving workflow in the acquisition and analysis of pathology specimens obtained through MSK’s personal consultation (PC) service. These specimens are sent by non-MSK patients and physicians located anywhere in the world who are seeking a second opinion from MSK’s expert team of sub-specialized pathologists. They make up about 10% of the department’s volume.

“I’ve spent my entire career at MSK in the Department of Pathology and received cancer care as a patient here; therefore I understand the unique perspective of both needing an expert opinion and being acutely aware of the knowledge my colleagues offer to the world. Perfecting our personal consultation service while increasing awareness of options available to patients, augmenting our revenue streams and making the overall cancer care process easier for our patients has been incredibly rewarding. I’m very proud of the team that allowed these goals to come to fruition.” says Sarah Virgo, Project Lead and Assistant

Manager, Pathology Communications for the Department of Pathology.

The project identified several areas for improvement in the PC service, including common reasons that these cases are delayed and issues with communication, billing, and workflow. The leaders of the project focused on specific measures for improvement.

The initiative included implementing a new digital portal for the electronic submission of PC cases, streamlining workflows for easy submission of PC cases, and increasing marketing efforts to solicit more PC submissions and recruit new patients to MSK. The goals were to increase overall volume of PC cases, change the way billing information is collected, and establish a revenue stream through the portal.

As presented at the QI Fair, the results of these efforts were a reduction in overall turnaround time for these samples as well as in the number of misdirected cases or cases with missing information or material. In addition, the portal greatly exceeded the anticipated number of PC portal submissions – by 433% – and increased overall annual volume by 12%.

The portal also increased web traffic and revenue for the Pathology Department. As a result of the project, 224 non-MSK patients chose to receive care at MSK after using the portal and more than \$20 million in revenue was generated as a result of these new patients.



The Life Changing Magic of Tidying Up HR Files: A Paperless Personnel File Management System

Monika Kamalska-Cyganik • Robert Citera • Rose Khoobyar • Brian Murphy • Justyna Sadowska • Paulo Salazar • Angela Scalise • Joshua Somar • Nicole DeGroat • Maria A. Friedlander
Molecular Diagnostic Service, Department of Pathology

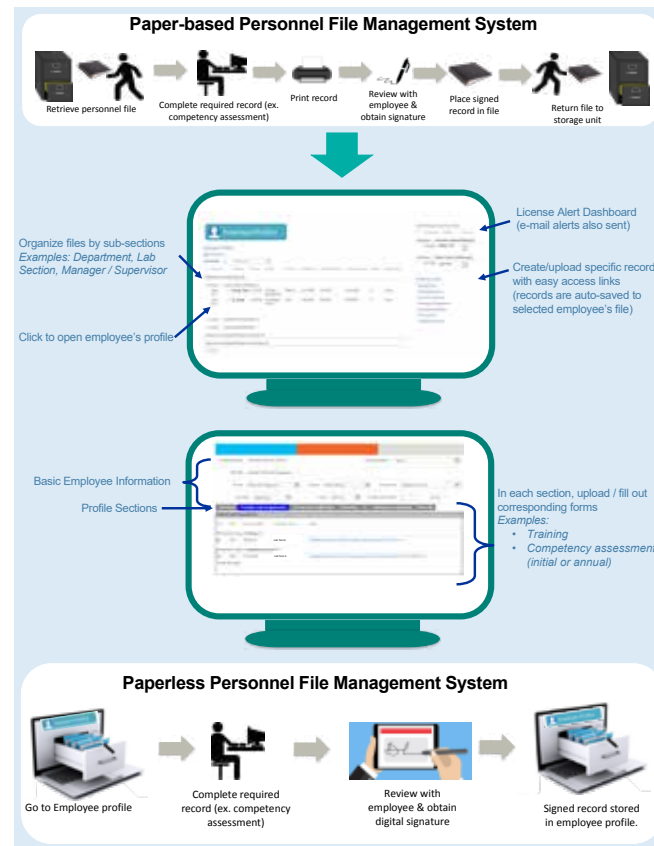
Goals and Objectives:

- Transition to paperless-based personnel files
- Minimize misfiled HR records
- Enhance HR file access for relevant staff while maintaining security and confidentiality
- Engage alert notifications for records associated with expiration dates
- Utilize current available resources (no additional software cost)
- Enhance compliance with HR-personnel records maintenance



Implementation steps:

- Designed user-friendly employee profile template on MSK's SharePoint platform
- Employee profile tailored to include dedicated areas to archive various HR record requirements
- Secure and access controlled site
- Incorporated email alert notifications for relevant records
- Trained lab managers/ supervisors in a use of the new portal
- Solicited user feedback and modified the portal accordingly



Key features

Available and customizable when designing the Employee Files Management Portal:

- Access Control
- Cloud Storage
- Indexed Filing
- Multi file type Compatibility
- E-Signature Integration
- Auditing Function
- File Alerts
- File Checklist

Impact to MSK:

- Positive feedback from managers/supervisors using the portal to maintain personnel files
- Enhanced compliance with HR regulatory, accreditation & institutional requirements
- Gain in physical space previously used for file storage
- Potential use and customization by other MSK departments challenged with HR personnel file management with current available platform
- Sparking joy

Sustainability/Green Impact:

- 15,000 pages saved per ~116 employees
- Elimination of plastic binders and dividers used to store paper HR records



MSK Pathology Scan Operations Journey to a Full Digital Workflow

Radhangle Seenauth • Lorraine Corsale • Shirley Vargas • Christine England • Jennifer Samboy • Chris Attard • Jamaal Spencer • John McDonough • Cindy McCollum



Problem Statement

The Pathology department's scan operations consists of many manual steps resulting in ample delays. In an 8 hour shift. Digital Scanning Assistants spend 50% of the time adjusting and reprinting labels adding non-value added time to the process. Labeling issues prevent streamlined scan operations which limits the pathologists' ability to consult more quickly on complex cases, correlate outside diagnoses to a patient's MSK diagnoses, and support the department's transition to full digital sign-out.



Smart Goal

Reduce percent of current clinical slides that require relabeling by 50% and increase the number of current clinical slides submitted weekly from 8,000 slides to 10,000 slides per week by April 30th, 2019.

Benefits

- Use of Digital Pathology to Support OR Operations
- Telecommunication
- Improvement in Pathology Material Management
- Opportunity for Savings in Vendor Services

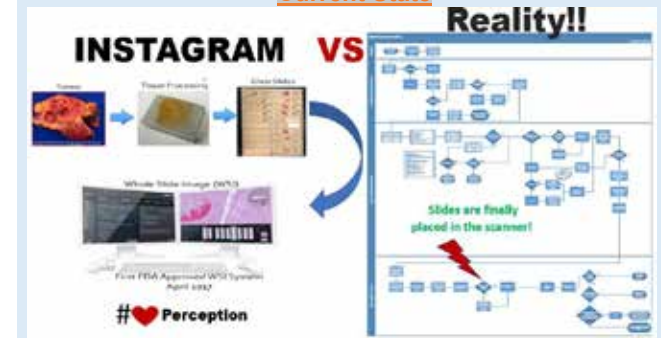


Background

- In 2015, pathology's clinical workflow was introduced to Digital Scanning. **-DIRECTLY IMPACTS PATIENT CARE**

Scan Operations 2019 YTD Volume - Monthly Scan Updates				Scan Volume Totals:	
2019	Current	Archive	Total		
Jan	38,774	29,082	67,856	Inception - 2018	830,262
Feb	34,614	27,955	62,569	Jan - YTD 2019	184,580
Mar	30,353	23,802	54,155		
Apr					
May					
Totals	103,741	80,839	184,580	Grand Total:	1,014,842

Current State



Long Term Goal

of slides generated by the Histology Lab daily = approx. 3,000 slides/day
Lab -> Scanner -> DIGITAL IMAGES -> Pathologist -> Diagnosis



Root Cause Analysis

- Common Themes:
- Barcodes on Slide Labels
 - Placement of Labels
 - Reprinting of Barcoded Labels
 - Quality Control (Pre & Post Scan)
 - Scanner Software Limitations
 - QLIS (CoPath) Limitation
 - Lack of Education

Propose & Test Solutions

- Rapid Cycle Testing:
- Involvement of Staff on Scan Operations
 - Printer Maintenance Schedules
 - Modify Barcode Labels and Tracking Capability
 - Manufacturing Pre-Scans and Post-Scan Image Review Processes



Implement & Sustain

Implemented	Continue to Roll	Next Steps
Pre-Scans Schedule	Out Process	Lab Manager and Staff
Standardized Case Tracking	Relabeling Optimization	Digital Scanning Assistant
Standardized QC Pre-Post Image Review	Controlled Scanning Operations (Scan)	History Department Consult Labels
Standardized Barcode Labels	Controlled Scanning Operations (Scan)	Standardize Labels
		Planwork in Case Files



PLATFORMS

Agaram, Zhang, Antonescu—Bone and Soft Tissue Pathology. *GLI1-Amplified Soft Tissue Neoplasm: A Novel Entity Showing Morphologic Overlap with Tumors with GLI1 Gene Fusions*

Al-Ahmadie—Genitourinary Pathology Society. *Pathology and Molecular Features with Clinical Implications: Lower Tract Urothelial Tumors*

Al-Ahmadie, Fine, Gopalan, Sirintrapun, Tickoo, Chen, Reuter—Genitourinary Pathology. *Revisiting Prognostic Significance of ClinicoPathological Features in Type 1 Papillary Renal Cell Carcinoma*

Antonescu—International Society of Bone and Soft Tissue Pathology. *Epithelioid Hemangiioendothelioma—Histologic and Clinical Spectrum and New Genetic Variants*

Antonescu—Pathobiology. *Genomic Progression in PDG-FRA-Mutant Gastrointestinal Stromal Tumors (GISTs)*

Antonescu—Genitourinary Pathology. *BCOR-Overexpressing Malignant Renal/Perirenal Solitary Fibrous Tumor: A Close Mimic of Clear Cell Sarcoma of the Kidney*

Arcila—Biocartis—*Potential of Ultra-Rapid Mutational Analysis in Oncology-Based Applications: Ultra-Rapid Mutational Analysis Complementing NGS Workflows in High-Volume Laboratories*

Arcila—*Practical Molecular Diagnostics for the Practicing Surgical Pathologist*

Basturk—*Surgical Pathology and CytoPathology of the Pancreas and Ampulla*

Boroujeni, Arcila, Ladanyi, Dogan—Pathobiology. *Genomic Profiling of Mucinous Adenocarcinomas Can Assist in Determination of Site of Origin*

Chen—International Society of Urological Pathology. *The Importance of Pathologic Evaluation in Active Surveillance of Small Renal Masses*

Chen—International Society of Urological Pathology Special Conference on Molecular Pathology of Urogenital Cancers—Molecular Pathology Kidney Cancer Working Group. *Eosinophilic Solid and Cystic Renal Cell Carcinoma and Renal Tumors Associated with TSC-mTOR Pathways; Distinguishing Papillary Renal Cell Carcinoma and Mucinous Tubular Spindle Cell Carcinoma*

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

Chen, Fine, Gopalan, Sirintrapun, Tickoo, Reuter, Al-Ahmadie—Genitourinary Pathology. *Expression of Insulinoma-Associated Protein 1 (INSM1) in Small Cell Carcinoma of the Bladder*

D' Alfonso—*Challenging Frozen Sections: When Do I Stick My Neck Out...and How Far?*

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

Fine, Al-Ahmadie, Chen, Gopalan, Sirintrapun, Tickoo, Reuter—Genitourinary Pathology. *Practice Patterns in Reporting Tertiary Grades at Radical Prostatectomy: Survey of a Large Group of Experienced Urologic Pathologists*

Fine—*Dynamic Evolution in Prostate Cancer Diagnosis and Reporting: What the Pathologist Needs to Know*

Fuchs—International Society of Breast Pathology. *Artificial Intelligence (AI) in Breast Pathology*

Fine, Tickoo, Al-Ahmadie, Chen, Sirintrapun, Ladanyi, Reuter, Gopalan—Genitourinary Pathology. *Immunohistochemical Detection of Androgen Receptor in Metastatic Castrate Resistant Prostate Cancer*

Grabenstetter, Brogi—Breast Pathology. *Flat Epithelial Atypia (FEA) in Breast Core Needle Biopsy (CNB): Is Excision Necessary?*

Hechtman—*Incorporating TRK Inhibition into the Treatment Paradigm: The Pathologist's Role—What Methods are Appropriate for Detecting TRK Fusion Cancer in Daily Practice*

Hechtman, Vakiani, Klimstra, Shia—Gastrointestinal Pathology. *Inter-Tumoral Discordance in Mismatch Repair Protein Expression in Synchronous or Metachronous Gastrointestinal Tumors:*

Biological Significance and Clinical Implications

Ho—HematoPathology. *Clinico- Pathologic and Genetic Characterization of non-AML NPM1-Mutated Myeloid Neoplasms*

Jungbluth, Katabi, Xu—Genitourinary Pathology. *Expanded Characterization of the Immune Microenvironment in High-Grade Urothelial Carcinoma of the Bladder*

Katabi, Jungbluth, Xu—Quality Assurance. *Inter- and Intra-Observer Agreement of PD-L1 Scoring in Hypopharyngeal Squamous Cell Carcinoma (HSCC), Urothelial Carcinoma (UC), and Breast Carcinoma (BC)*

Kezlarian, Dogan, Lin—CytoPathology. *CytoPathologic Characterization of SMARCB1-Deficient Malignancies of the Head and Neck Region*

Klimstra—*Acini, Islets, and Associated Pancreatic Neoplasia: A Journey of Technological Evolution in Research and Diagnostics*

Nafa, Hameed—Bone and Soft Tissue Pathology. *Comprehensive Genomic Profiling of the Primary Craniofacial Osteosarcomas*

Pareja, Jungbluth, Giri, Weigelt, Reis-Filho, Brogi—Breast Pathology. *Immunohistochemical Analysis of IDH2 R172 Hotspot Mutations in Breast Papillary Neoplasms*

Park—International Society of Gynecological Pathology. *HPV- Independent Cervical Adenocarcinomas (Including Relationship to Silva Classification and Molecular Abnormalities)*

Rekhtman—Pulmonary Pathology Society. *Update on SMARCB4 Deficient Lung Tumors*

Reuter—Arthur Purdy Stout Society of Surgical Pathologists. *The Disease Doesn't Know Your Age: Adults and Children with the "Wrong Affliction"? GU Pathology*

Soslow—Gynecologic Pathology. *ClinicoPathologic Analysis of MMR-Deficient Endometrial Carcinosarcomas*

Shia, Gopalan, Chen, Fine, Sirintrapun, Arcila, Tickoo, Berger, Reuter, Al-Ahmadie—Genitourinary Pathology. *Detailed Morphologic and Genetic Features of Urothelial Carcinoma in Patients with Lynch Syndrome*

Sigel, Basturk—CytoPathology. *Fine Needle Aspiration Findings in Pancreatoblastoma (PBL): An Analysis of 10 Cases Reveals Helpful Cytologic Criteria in Their Distinction from Common Mimics*

Sirintrapun—Association for Pathology Informatics. *Robotic Telecytology for Remote Diagnosis*

Soslow—GYN Pathology. *The Evolving Landscape of Endocervical Adenocarcinoma, What Matters?*

Tang—Pancreatobiliary Pathology Society. *Pancreatic*

Neuroendocrine Neoplasms—Landscape and Horizon

Travis—Pulmonary Pathology Society. *Lung Adenocarcinoma: Emerging Histologic Patterns*

Travis—Pulmonary Pathology. *Importance of Distinguishing Adenocarcinoma and Squamous Cell Carcinoma in Assessment of Pathologic Response After Neoadjuvant Chemotherapy*

Travis, Sauter—Pulmonary Pathology. *Pericardial Mesothelioma: A Multi-Institutional Study of 61 Cases*

Vakiani, Shia, Klimstra—Gastrointestinal Pathology. *Massive Parallel Sequencing of Neuroendocrine Carcinomas of the Large Bowel Reveals Distinct Molecular Subsets and Patterns of Genomic Evolution*

Weigelt—*Molecular Diagnostic & Genomic Applications in Cancer: A Primer for the Pathologist*

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

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

Xu—Genitourinary Pathology. *Protein and Transcriptomic Characterization of the Immune Milieu of High-Grade Bladder Cancer*

Zhang, Antonescu—Bone and Soft Tissue Pathology. *Novel Recurrent PHF1-TFE3 Fusions in a Subset of Ossifying Fibromyxoid Tumors*

Zhou, Tanaka, Hendrickson, Wang, Roehrl—Techniques. *Developing a Robust Sample Preparation Procedure for Depp Fourier- Transform Mass Spectrometric Profiling of Formalin-Fixed Paraffin-Embedded Clinical Tissue Specimens*

POSTERS

Al-Ahmadie—Genitourinary Pathology. *Urothelial Carcinoma in Situ Versus Early High-Grade Papillary Urothelial Carcinoma: A Survey of Pathologist and Urologist Interpretations*

Antonescu—Bone and Soft Tissue Pathology. *Pericytoma with t(7;12) and ACTB-GLI1 Fusion Involving the Musculoskeletal System and Ovary: A Report of Three Cases*

Arcila, Nafa, Ho, Roshal—HematoPathology. *Sensitive and Ultra-Rapid BRAF V600E Mutation Assessment in Hairy Cell Leukemia from Stained Smear Slides, Blood and Bone Marrow without Pre-Extraction*

Askan, Olca Basturk—Pancreas Pathology. *Do We Still Really Need to Count Mitoses for Pan-NETs? Proper Ki67 Counting Negates the Need for the Cumbersome and Problematic Mitotic Count Required in the Current WHO-2017 Grading Scheme*

Basturk—Pancreas Pathology. *Frequency of Dysplasia/ Carcinoma and Foveolar Atypia Associated with Gallbladder Cancer Risk: Comparative Analysis in Mapped/Totally Sampled Gallbladders from High-Risk Versus Low-Risk Regions*

Basturk—Pancreas Pathology. *Field Risk ("Field-Effect"/ "Field-Defect") in the Gallbladder and Biliary Tree: An Under-Recognized Phenomenon with Major Implications for Management and Carcinogenesis*

Benayed, Ladanyi, Hechtman—Pathobiology. *NTRK Fusion Detection Across Three Assays and 29,000 Tumors*

Bhanot, Roehrl—Informatics. *Digital Imaging for Systematic Validation of Spatially Annotated Mirror-Image Simultaneous Flash Frozen and FFPE Tissue Banking for Research*

Boroujeni, Al-Ahmadie, Reuter, Gopalan, Arcila, Fine, Ladanyi, Yao—Pathobiology. *Genomic Profiling of Prostate Cancer with EGFR Family Gene Alterations—Potential of Clinical and Therapeutic Implications*

Boroujeni, Arcila, Ladanyi, Soslow, Chang—Gynecologic Pathology. *Evaluation of Copy Number Alterations of MYC Family of Genes, RB1 Gene and AURKA in Endometrial Carcinomas*

Brogi, Pareja, Murray, Weigelt, Reis-Filho, Wen—Breast Pathology. *Secretory Carcinoma of the Breast: ClinicoPathologic Profile of 14 Cases Emphasizing Distant Metastatic Potential*

Brogi, Murray—Breast Pathology. *Core Needle Biopsy Diagnosis of Fibroepithelial Lesions: Features Predictive of Upgrade to Phyllodes Tumor at Excision*

Chan, Lewis, Arcila, Zhang, Roshal, Xia—HematoPathology. *Blast to Plasmacytoid*

Dendritic Cell Ratio is Predictive of Progression in Low Grade Myelodysplastic Syndromes

Chen, Al-Ahmadie, Fine, Gopalan, Sirintrapun, Tickoo, Reuter—Genitourinary Pathology. *SMARCB1 Alterations and Protein Expression in Non-Medullary Renal Cell Carcinoma*

Chen—Genitourinary Pathology. *Clear Cell Renal Cell Carcinoma with a Poorly-Differentiated Component: A Novel Variant Causing Potential Diagnostic Difficulty*

Chen, Tickoo, Fine, Gopalan, Al-Ahmadie, Sirintrapun, Antonescu, Ladanyi, Arcila, Reuter—Genitourinary Pathology. *TFEB Expression Profiling in Renal Cell Carcinomas*

Dogan, Xu, Vanderbilt, Berger—Head and Neck Pathology. *Genomic Analysis of 134 Squamous Cell Carcinomas Arising in the Base of Tongue Diagnosed from 1985 to 2017*

Dogan, Arcila, Katabi, Ladanyi, Benayed—Head and Neck Pathology. *Novel Rearrangements in Salivary Gland Tumors Detected by an RNA-Based Targeted Next-Generation Sequencing Assay*

Dogan, Ghossein, Reis-Filho, Xu, Katabi—Head and Neck Pathology. *Inter-Observer Variation in the Histologic Classification of Polymorphous Adenocarcinoma (PAC) and Cribriform Adenocarcinoma of Salivary Gland (CASG)*

Fine, Al-Ahmadie, Chen, Gopalan, Sirintrapun, Tickoo,

Reuter—Genitourinary Pathology. *In Organ-Confining Prostate Cancer at Radical Prostatectomy, neither Total Tumor Volume nor Maximum Tumor Diameter of the Index Lesion Aids in Prediction of Biochemical Recurrence*

Fine, Reuter—Genitourinary Pathology. *Reporting Practices and Resource Utilization in the Era of Intraductal Carcinoma of the Prostate (IDCP): A Survey of Genitourinary (GU) Subspecialists*

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New Pathology Faculty

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Lora Hedrick Ellenson, MD
Attending Pathologist
Director, Gynecologic Pathology



M. Herman Chui, MD
Assistant Attending Pathologist



Pallavi Galera, MD
Assistant Attending Pathologist



Brie Kezlarian, MD
Assistant Attending Pathologist



Alexander Chan, MD
Assistant Attending Pathologist



Andrea Moy, MD
Assistant Attending Pathologist



Maksym Misyura, PhD
Assistant Attending Molecular Geneticist



Judy Sarungbam, MD
Assistant Attending Pathologist



Xiao Jun Wei, MD, PhD
Attending Pathologist



Debyani Chakravarty, PhD
Assistant Attending Molecular Geneticist



Angela Rose Brannon, PhD
Assistant Attending Bioinformatician



Joachim Silber, PhD
Assistant Attending Laboratorian

Featured (Newly) Available IHC Protocols

DAXX

New Protocol: DAXX

Reagent: rabbit mAb

Protein: DAXX (Death domain-associated protein 6)

Protein Description: Corepressor of transcription that interacts with several transcription factors. It is part of the Histone remodeling complex ATRX/DAXX.

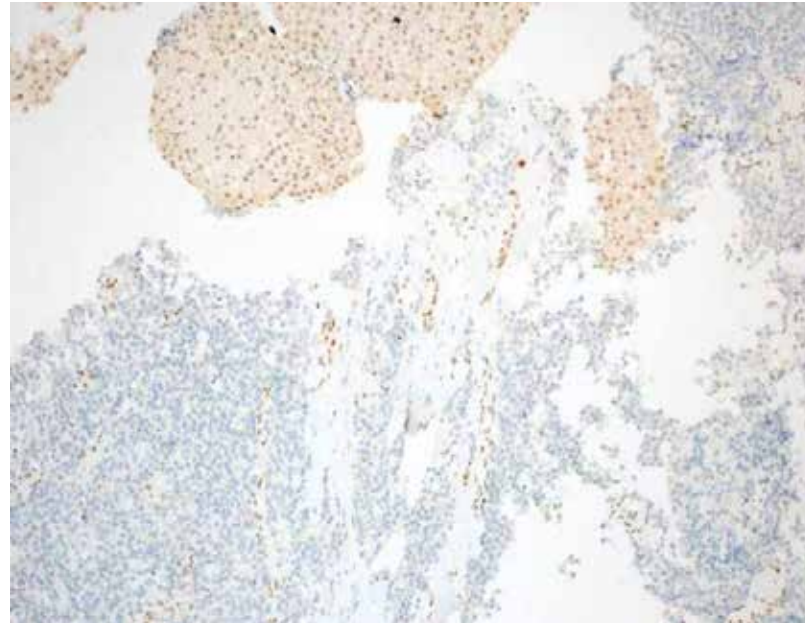
Manufacturer: Abcam (ab32140)

Clone: E94

Clinical Use: Loss of DAXX in pancreatic neuroendocrine tumors is associated with DAXX mutations, alternative lengthening of telomeres, and poor prognosis.

Reference:

<https://www.ncbi.nlm.nih.gov/pubmed/30747827>



DAXX (mAb E94), liver biopsy, DAXX-mutated pancreatic NET metastatic to the liver

MUC5AC

New Protocol: MUC5AC

Reagent: mouse mAb

Protein: MUC5AC (Mucin 5AC, oligomeric mucus/gel-forming)

Protein Description: Mucins are carbohydrate rich glycoproteins with a protein backbone linked to a wide variety of oligosaccharide side chains; so far 20 mucins have been identified, which are expressed in a tissue-specific manner. MUC5AC is expressed in surface-epithelial (foveolar) mucin of the gastro-intestinal tract, including the ampulla, as well as in other tissues.

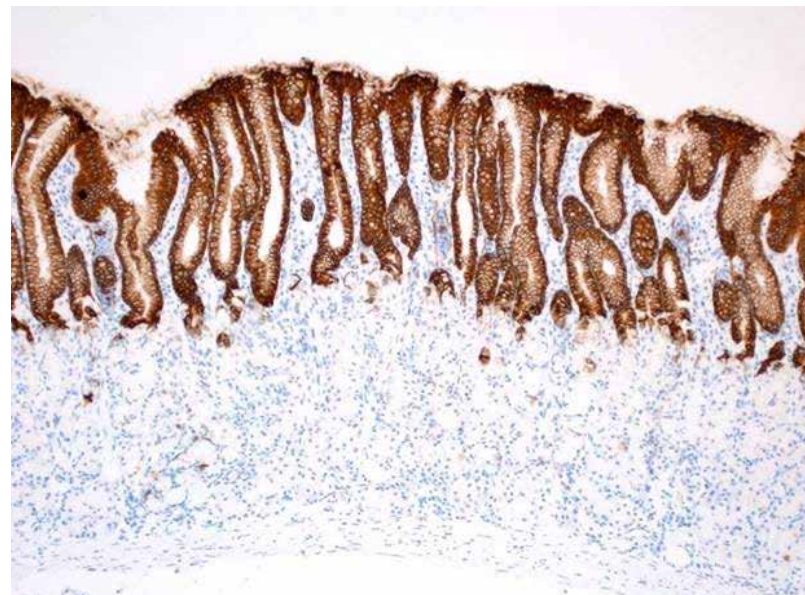
Manufacturer: Santa Cruz (SC-33667)

Clone: CLH2

HGNC: MUC5AC

Syn.: MUC5, TBM, leB, mucin, mucin 5AC, oligomeric mucus/gel-forming

Clinical Use: Differential diagnosis of pancreatic intraductal neoplasms; distinction of IPMNs from ITPNs (IPMNs usually positive for MUC5AC and negative for MUC6; ITPNs usually positive for MUC6 and negative for MUC5AC).



MUC5AC (mAb CJLZ), stomach mucosa

References:

<https://www.ncbi.nlm.nih.gov/pubmed/28776573>

<https://www.ncbi.nlm.nih.gov/pubmed/27984235>

MUC6

New Protocol: MUC6

Reagent: mouse mAb

Protein: MUC6 (Mucin-6, oligomeric mucus/gel-forming)

Protein Description: Mucins are carbohydrate rich glycoproteins with a protein backbone linked to a wide variety of oligosaccharide side chains; so far 20 mucins have been identified, which are expressed in a tissue-specific manner. MUC6 (pyloric type mucin) is expressed in gastric pyloric glands, Brunner glands as well as in other tissues.

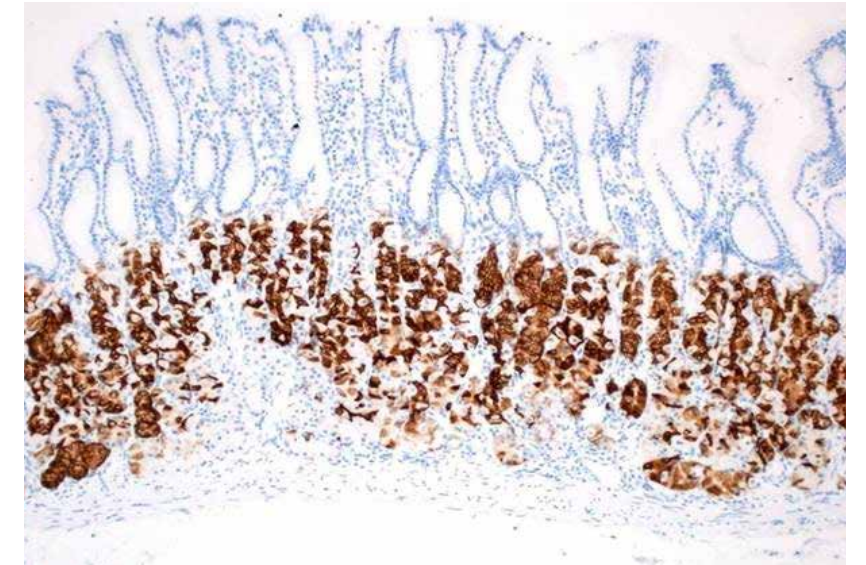
Manufacturer: Santa Cruz (SC-33668)

Clone: CLH5

HGNC: MUC6

Syn.: Muc-6, Gastric mucin6

Clinical Use: Differential diagnosis of pancreatic intraductal neoplasms; distinction of IPMNs from ITPNs (IPMNs usually positive for MUC5AC and negative for MUC6; ITPNs usually positive for MUC6 and negative for MUC5AC).



MUC6 (mAb CHL5), stomach mucosa

References:

<https://www.ncbi.nlm.nih.gov/pubmed/27984235>

<https://www.ncbi.nlm.nih.gov/pubmed/28776573>

EGFRvIII

New Protocol: EGFRvIII

Reagent: rabbit mAb

Protein: EGFRvIII (Epidermal Growth Factor Receptor deletion mutation VIII)

Protein Description: Deletion mutation of EGFR with loss of exons 2-7; also called EGFRd2-7.

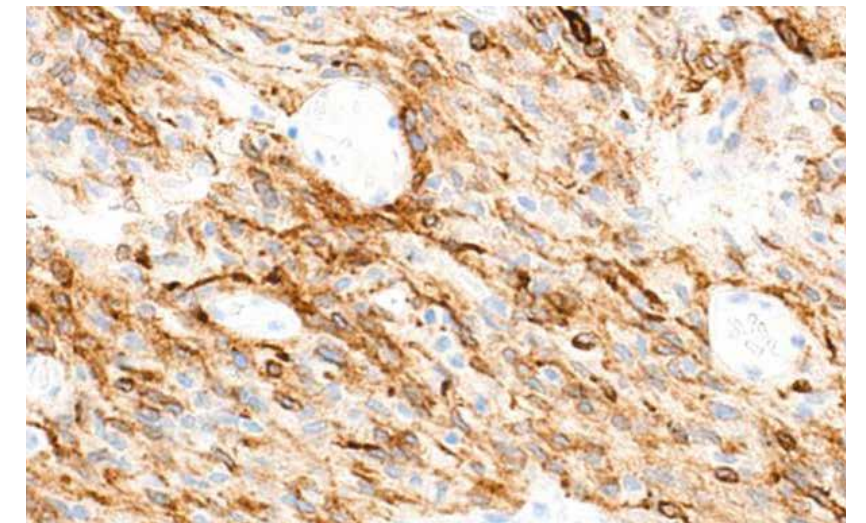
Manufacturer: Cell Signaling Technologies (CST), (#64952)

Clone: D6T2Q

HGNC: n/a

Syn.: EGFRd2-7

Clinical Use: EGFRvIII is a common mutation in glioblastoma (GBM). It involves the deletion of exons 2-7 and is associated with protein overexpression; it is thought to be a late event after amplification of EGFR. The present antibody detects EGFRvIII. While the pro-tumorigenic effects of EGFRvIII have been demonstrated in several model systems of GBM, it can also be rarely encountered in other tumor types, where its significance is less clear.



EGFRvIII (mAb D6T2Q), EGFRvIII-positive glioblastoma

References:

<https://www.ncbi.nlm.nih.gov/pubmed/1584765>

<https://www.ncbi.nlm.nih.gov/pubmed/21170331>

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ERIC KLEIN

Senior Financial Manager

By Kayt Sukel

Q What are you responsible for in your current role?

A My primary responsibility is ensuring the fiscal health of the department. It may sound simple, but it involves being aware of all the different priorities from all the different services and stakeholders here in Pathology and ensuring that they have the resources they need to meet their individual, departmental, and institutional goals. I also oversee all of the research administration within the department. That includes helping to prepare research and grant applications for faculty, reporting their progress to granting agencies, and working with other departments to help connect them with the right people in our department to meet their pathology needs.

Most people think my job is all about numbers on a spreadsheet. But they don't see the behind-the-scenes part where I work with clinicians, investigators, lab managers, suppliers, and administrators to make sure that all of the pieces of the puzzle come together in such a way that there's a seamless flow of resources when it's time to get the

work done. If I've done my job well, it appears effortless to everyone else. But there's an enormous amount of work involved, and a large support structure to make sure that can happen. We work together closely to integrate finance, operations, clinical care, and research in a holistic way.

Q What brought you to Memorial Sloan Kettering?

A My father worked in hospital administration and I knew early on that I wanted to work in a hospital setting where there was a strong mission to help people as well as advance the field of medicine. MSK offers the pinnacle of cancer treatment, research, and education. It's an internationally renowned institution and I'm proud to have joined it two years ago. Pathology is a critical part of that mission. Without the clinical care going on in our department, the rest of cancer treatment falls apart. Pathology provides a unique way of understanding, identifying, and optimizing the treatment of cancer.

Q What's the most enjoyable part of your work?

A I get a lot of satisfaction out of working hand in hand with clinicians, lab managers, and investigators to understand what resources they need to perform clinical care or conduct their research and delivering those resources seamlessly so that they may focus on their work and not the support structure behind it. I work closely with them to help them understand what they need to do their work to treat and cure cancer as well as generate results that

will further advance cancer insights and treatment in the future. I try to incorporate my personal interests in digital technology and efficiency when delivering support so that we can ensure high quality of care and optimization of resources to reduce patient costs and provide education for the different services in the Department of Medicine.

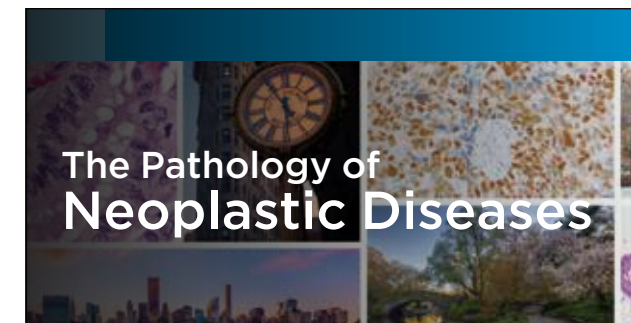
Another large part of my role is research. I help coordinate collaborations with industry, which involves working with them to determine the scope of work, preparing a budget, working with legal to review contracts, and coordinating the logistics of a study.

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

A It's all about the translational science. We provide the best clinical care to our patients. We also have a strong research program and some of the brightest minds in the field. But our department is unique in bridging the two together. And that's important because one can't grow without the other. Our work is helping to not only advance the field through research or improving patient outcomes, but combining the two to advance the standards of cancer care across the industry. And in doing so, we create new and innovative technologies and treatments and quickly move them from the bench to the bedside to help our patients.



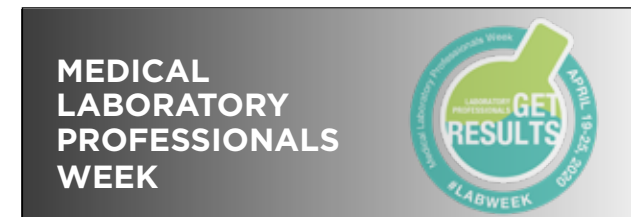
March 26, 2020
Memorial Sloan Kettering Cancer Center
 Zuckerman Research Center
www.mskcc.org/trs2020



April 27-May 1
Memorial Sloan Kettering Cancer Center
 Rockefeller Research Laboratories
www.mskcc.org/neoplasticdiseases2020



June 24, 2020
Memorial Sloan Kettering Cancer Center
 Zuckerman Research Center




April 19-25, 2020

DR. CHRISTINE IACOBUZIO-DONAHUE
 was named as the 2019 recipient of the
 Ruth Leff Siegel Award


The Pancreas Center of Columbia University has been entrusted by the Siegel family to identify the investigator who has had the most impactful contribution to the understanding/treatment/advancement of pancreatic cancer over the past year. Their research can be in any field of pancreatic cancer research, including but not limited to basic biology, population biology, public health, and/or translational science. Not only must the investigator have a track record of high quality work in this field, but also must have contributed to our understanding of pancreatic cancer in the past year, and will continue to do so for years to come.



 **@MSKPathology** is excited to announce that workshop proposals for ICLR 2020 entitled “AI for Overcoming Global Disparities in Cancer Care” have been accepted! Congrats to **@marciaedelweiss** and Dr. Ntiamoah for their contributions! ai4cc.org

 **#GrandRounds2019** First lecture of the 2019-2020 academic year **@MSKPathology**: Dr. Jason Huse of **@MDAndersonNews** “Characterizing and Targeting Epigenetic Dysfunction in Malignant Glioma”

 Congratulations to **@MSKPathology** faculty members Drs. Jorge Reis-Filho and Samson Fine (**@rovingatuscap**) for their inclusion in **@pathologistmag’s** 2019 Power List which features 100 of the industry’s top trailblazers!!

 Our **#liquidbiopsy** test at **@sloan_kettering** has received NY State DOH approval for clinical use! MSK-ACCESS captures 129 genes, selected from MSK-IMPACT, for high sensitivity, non-invasive cancer genomic profiling and disease monitoring in plasma cell-free DNA **#ASC019**



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

Memorial Sloan Kettering Cancer Center
Attn: Sarah Virgo
 1275 York Avenue
 Department of Pathology,
 H-504
 New York, NY 10065

212-639-5696
 cooks@mskcc.org
 www.mskcc.org/departments/pathology

Twitter & Instagram:
@MSKPathology

1st Quarter 2020

Research Profile: Jennifer Sauter, MD

Research Profile: Maurizio Scaltriti, PhD

Research Profile: Mikhail Roshal, MD

Service Spotlight: Autopsy Service

Cover: Protein Based Diagnoses

Q & A with Jessica Chapman, PhD



MDs who tweet



- Jackie Hechtman **@JackieHechtman**
- Ahmet Zehir **@ahmetz**
- Christine Iacobuzio- Donahue **@ciacobu**
- Natasha Rekhtman **@natasharekhtman**
- Michael Berger **@MFBerger1**
- Ryma Benayed **@RymaBenayed**
- Samson Fine **@rovingatuscap**
- Jennifer Sauter **@JL_Sauter**
- Marcia Edelweiss **@marciaedelweiss**
- Thomas Fuchs **@ThomasFuchsAI**
- Edi Brogi **@EdiBrogi**
- Bin Xu **@BinXu16**
- Marc Ladanyi **@MLadanyi**
- Hikmat Al-Ahmadie **@h_ahmadie**
- Hannah Wen **@HannahYWen**
- Kay Park **@KayParkMD**
- Olca Basturk **@OlcaBasturk**

- Jamal Benhamida **@jamalbenhamida**
- Ozge Birsoy **@BirsoyOzge**
- Meera Hameed **@hameedm**
- DanaTsui **@DNA_tsui**
- Yukako Yagi **@YukakoYagi**
- Matthew Hanna **@MGHannaMD**
- Wenbin Xiao **@drwenbin_xiao**
- Yingbei Chen **@Unclassified1**
- Sahussapont Joseph Sirintrapun **@sirints**
- Ronald Ghossein **@ghosseir1**
- Nora Katabi **@katabinmsk**
- Timothy D’Alfonso **@tim_dalfonso**
- Anne Grabenstetter **@AGrabenstetter**
- Melissa Murray **@MelissaMurray17**
- Andrea Moy **@aprimi**
- Melissa Pulitzer **@MPulitzerMD**
- Debyani Chakravarty **@CDebyaniPhD**

USCAP 108TH ANNUAL MEETING

UNLOCKING YOUR INGENUITY

