

# MSK PATHOLOGY REVIEW

INITIATIVES  
INNOVATIONS  
ACCOMPLISHMENTS



Memorial Sloan Kettering  
Cancer Center



Memorial Sloan Kettering  
Cancer Center™

3RD QUARTER  
2017

# TABLE OF CONTENTS

2	COMMENTARY FROM THE DEPARTMENT CHAIR
4	MULTIDISCIPLINARY EXPERTISE ADVANCES PATHOLOGY AT THE WARREN ALPERT CENTER
12	BEYOND BIOSPECIMENS: 5 PILLARS OF THE PRECISION PATHOLOGY BIO BANKING CENTER
15	THORACIC SERVICE EMPHASIZES COLLABORATION, DISCOVERY AND MENTORSHIP
16	Q & A WITH SARAH VIRGO
18	RETHINKING HEAD AND NECK TUMORS
19	A PATIENT CENTERED APPROACH TO FINE NEEDLE ASPIRATION
20	PATHOLOGY AT THE JOSIE ROBERTSON SURGERY CENTER
24	RESEARCH PROFILES
26	DERMATOPATHOLOGY AT MSK RESEARCH PROFILES
28	NEW FACULTY
30	2017-2018 CLINICAL FELLOWS
31	UPCOMING COURSES
32	4TH QUARTER 2017

Cover photo from left to right: S. Joseph Sirintrapun, MD, Director, Pathology Informatics, Yukako Yagi, PhD, Director, Pathology Digital Imaging, Jennifer Samboy, Senior Project Manager, Pathology Strategic Initiatives, Meera Hameed, MD, Service Chief, Surgical Pathology, David Klimstra, MD, Chairman, Department of Pathology, Victor Reuter, MD, Vice Chairman, Department of Pathology, Thomas Fuchs, PhD, Director, Computational Pathology.

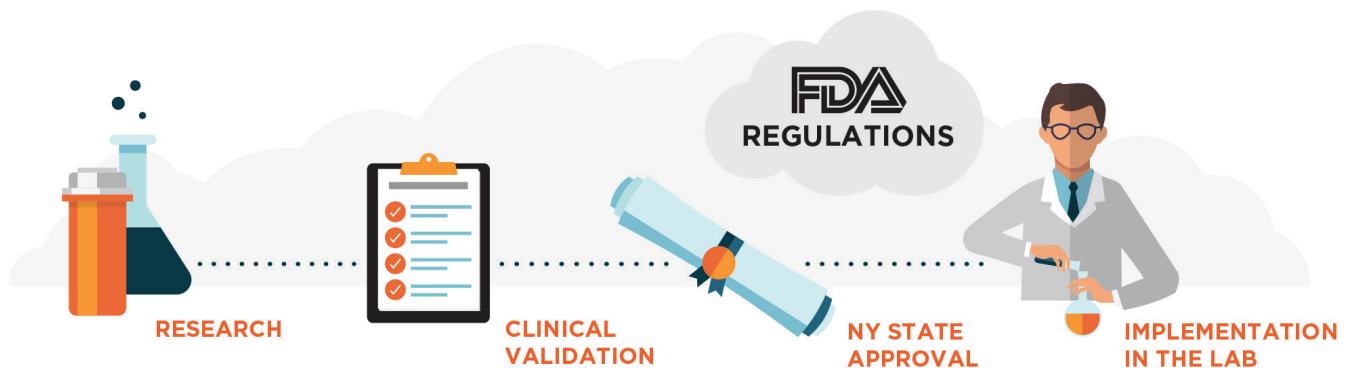
## THE EVOLVING REGULATORY CLIMATE FOR LABORATORY-DEVELOPED TESTS

Pathology laboratories are subject to a variety of regulatory oversights that govern our diagnostic processes. All laboratories must maintain CLIA compliance - in our case based on inspections and licensure by the New York State Department of Health (NYSDOH), but often provided by CAP - and we are additionally inspected and accredited by the Joint Commission (formerly, the Joint Commission on Accreditation of Healthcare Organizations or JCAHO), which has overlapping but not identical requirements to NYS. These organizations ensure that standard procedures are followed, quality is maintained, and appropriate records are kept. Pathology tests may be FDA-approved, entitling us to run them in our CLIA-compliant labs without the need for further test-specific approval. But the vast majority of our molecular diagnostic assays are not FDA approved and are developed in-house - so-called laboratory-developed tests (LDTs) or, in parlance currently more in vogue, in vitro diagnostics (IVDs). New York State, uniquely, also regulates the performance of each LDT, requiring submission of a detailed validation package and approved by the Department of Health before the test can be offered to patients. NYS approval is generally required for us to bill for the test as well. Currently, our Molecular Diagnostics Service performs more than 350 different LDTs, which range from relatively standard assays such as FISH for a specific gene fusion to complex multianalyte assays such as MSK-

IMPACT, which includes multiple steps and various pieces of equipment manufactured by different vendors. The use of LDTs allows laboratories like ours to develop tests quickly to meet the rapidly evolving needs of the oncology community, using technologies that are ideally suited to the testing needs in our environment. It can take many years for an FDA-approved test to emerge, and some are essentially obsolete by the time they become available. Many FDA-approved tests are also for single analytes, whereas current technologies such as next generation sequencing allow the simultaneous assessment of hundreds of genes, while maximizing the use of precious biopsy or cytology samples.

The development of a new molecular pathology LDT at MSKCC is driven by clinical need. Methods suitable for a clinical diagnostic setting are established, and validation experiments test the performance of the assay, to ensure reliability, specificity, and reproducibility. Then, a detailed description of the new test, including the specific conditions, reagents, and data analysis process, along with the results of the validation experiments, is prepared by our molecular diagnostics faculty for submission to the NYSDOH. These documents are truly formidable; the initial MSK-IMPACT submission ran 535 pages. The process from the conception of a new test through submission to NYS can take 12-15 months depending on the complexity of the test and the novelty of the technology employed. Formal NYSDOH review can also take months, although assays deemed by NYS to be lower risk can be awarded quicker provisional approval, allowing us to offer the test to patients. Generally, the NYSDOH raises questions after their review, requiring

## LABORATORY TEST APPROVAL IN NEW YORK



clarification or additional experiments, with resubmission of a revised document. Acceptance of the revised submission constitutes final NYS approval.

Based on our many years of test validation and NYS approvals, our molecular diagnostics laboratories have established a good working relationship with the regulatory group in Albany. The requirement for pre-test approval does ensure that our tests are of uniformly high quality; outside New York, issues with LDTs may not be uncovered until a periodic inspection by other regulatory groups, if at all. Nonetheless, the enhanced test quality in New York comes with a price. The time required to undertake all of the validation experiments and compile the package for submission remains a bottleneck in the launching of new assays, putting us at a competitive disadvantage relative to academic departments in other states. But in the end, we believe in the process and are proud of the resulting high quality tests we offer. In fact, the lack of pre-test approval requirements in other states has led to the proliferation of various assays that offer results of dubious quality or with unverified clinical significance. A number of high profile examples brought this situation to national attention, and three years ago the FDA announced in a draft guidance that it was planning to assume responsibility for the review and approval of LDTs. The draft provided a potential framework for FDA oversight but also raised significant concerns and left many unanswered questions, sending shock waves through the laboratory community. Of particular concern to MSK and other NYS laboratories was the potential that FDA regulations would be overlapping but not identical to those of NYS, resulting in redundancy of regulatory oversight and the need for additional (and costly) pre-test regulatory submissions.

Many individuals, institutions, and professional organizations then voiced strong opinions on both sides of the issue during a comment period allowed by the FDA. Some of the loudest voices were largely uniformed by the actual practice of laboratory diagnostics, frustrating those enmeshed in the daily activities of molecular testing, who more clearly understood the implications of excessive or duplicative regulations on the delivery of innovative testing to patients. In the following years, as the debate simmered, the U.S. Congress became aware of the issue and decided to conduct hearings to help formulate a plan, which could include a legislative rather than regulatory solution. On this backdrop, the U.S. Senate Committee on Health, Education, Labor, and Pensions (HELP) invited me to testify, representing institutions in NYS that have experience with pre-test approval. The majority of my testimony (memorialized on video on the Senate HELP website) was focused on explaining the process already in place under the NYSDOH, but our message that additional regulation was unwarranted and, potentially, cripplingly expensive came through as well. In particular, the implication that test approval could necessitate, in addition to our current analytic validation, clinical validation raised the specter of requiring exorbitant clinical trials to ensure the results are truly impactful for patient care. When asked by the committee chair, Senator Lamar Alexander, what would happen if all 350 LDTs conducted at MSK were subjected to the requirement for clinical trial validation, with its attendant costs, I logically replied that we would be forced to close the lab. Overly dramatic, perhaps, but valid points were made – including from other experts testifying about

the need for rational and comprehensive regulation to ensure the safety of patients and the efficacy of diagnostic tests – also laudatory goals.

In the months following the Senate hearings, a range of interactions took place involving MSK. Interestingly, the first formal contact came directly from the FDA. The group overseeing the approval of LDTs (there is already a mechanism for their review and approval, of course – it is simply voluntary at this time) contacted us to establish a dialogue about test evaluation and approval. Members of the Molecular Diagnostic Service and Pathology administration conducted conference calls with the group at the FDA, and the interchange was collegial and productive. Late last year, the FDA introduced a revised “white paper” that both addressed many of the ambiguities in their 2014 draft guidance and also clarified the nature of the proposed regulatory review, using a risk stratification system also recently deployed by the NYSDOH that would target only the highest risk tests for early FDA oversight. Tensions eased, but to date the issue has not been resolved, perhaps in part due to other political machinations taking place in Washington.

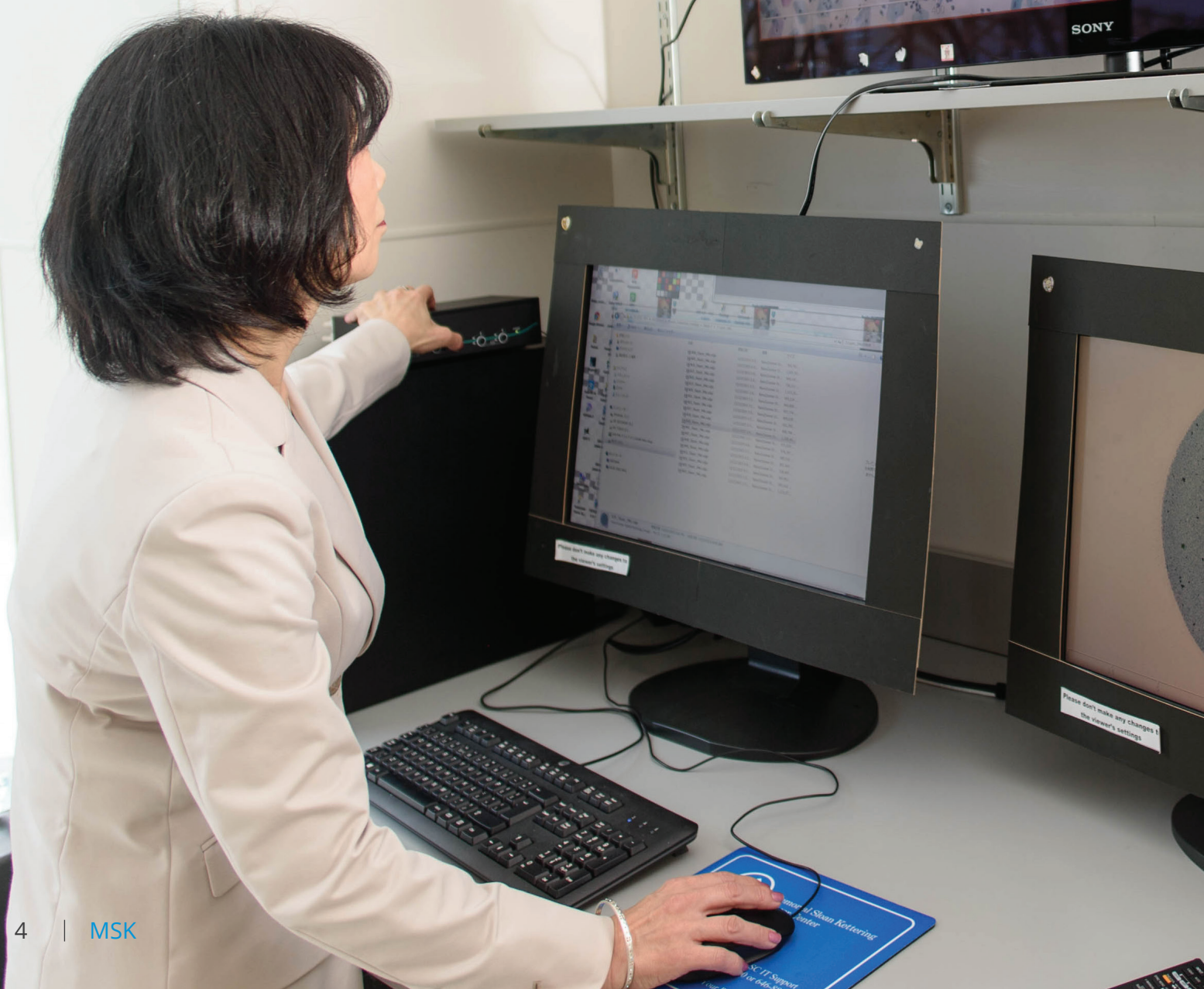
In the process of working with the FDA, an interesting opportunity presented itself. The group was curious to review the submission for MSK-IMPACT that had been approved by NYS, to assess the proposal made by us and others that NYS pre-test approval criteria be adopted by the FDA. We sent the corresponding regulatory tome and were pleasantly surprised when the FDA informed us that we had already completed the majority of the work needed for formal FDA clearance of our assay! They encouraged us to formally submit the package for FDA approval and even offered to help complete portions of their submission process not encompassed by the NYS documents.

This story is not complete. The proposal for universal FDA regulation of LDTs seems stalled between the regulators and the politicians for now, and leadership of the FDA and of the specific group involved in LDT regulation has changed. So for now we are able to continue our prior practices, with NYS oversight, just as other labs across the country continue to offer assays without the need for pre-test approval. The fate of our own MSK-IMPACT assay with the FDA is also unknown, although all signals we have received are encouraging. But these experiences are reinforcing the role MSK Pathology can play in helping set standards and influence national practice and policies. While the final chapters in this saga remain to be written, I promise to bring them to you in future updates, perhaps with a bit of fanfare. Please stay tuned . . .

-David S. Klimstra, MD

# MSK PATHOLOGY-EARLY ADOPTERS OF DIGITAL PATHOLOGY

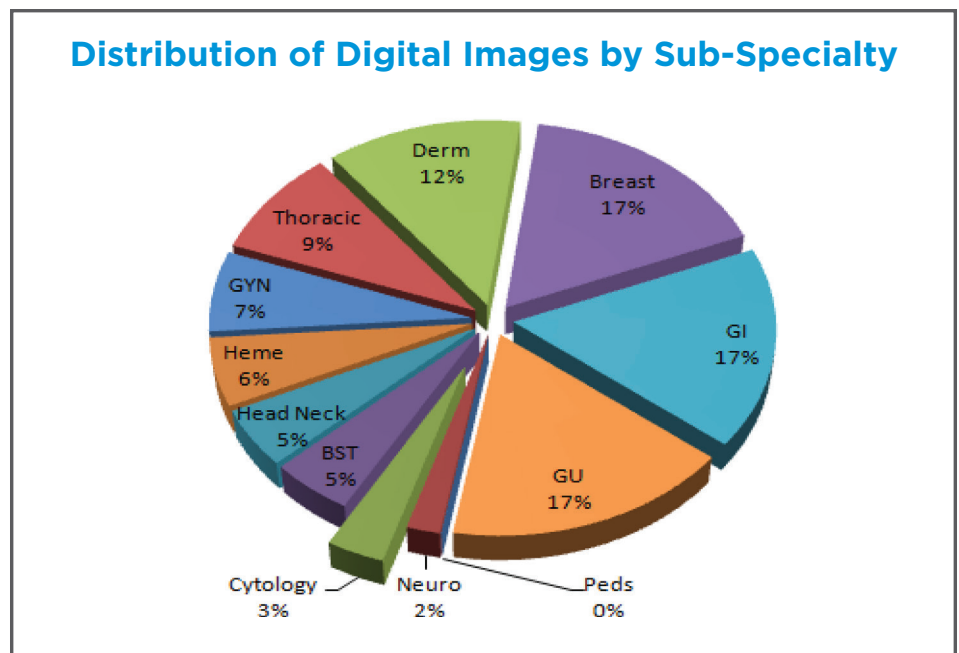
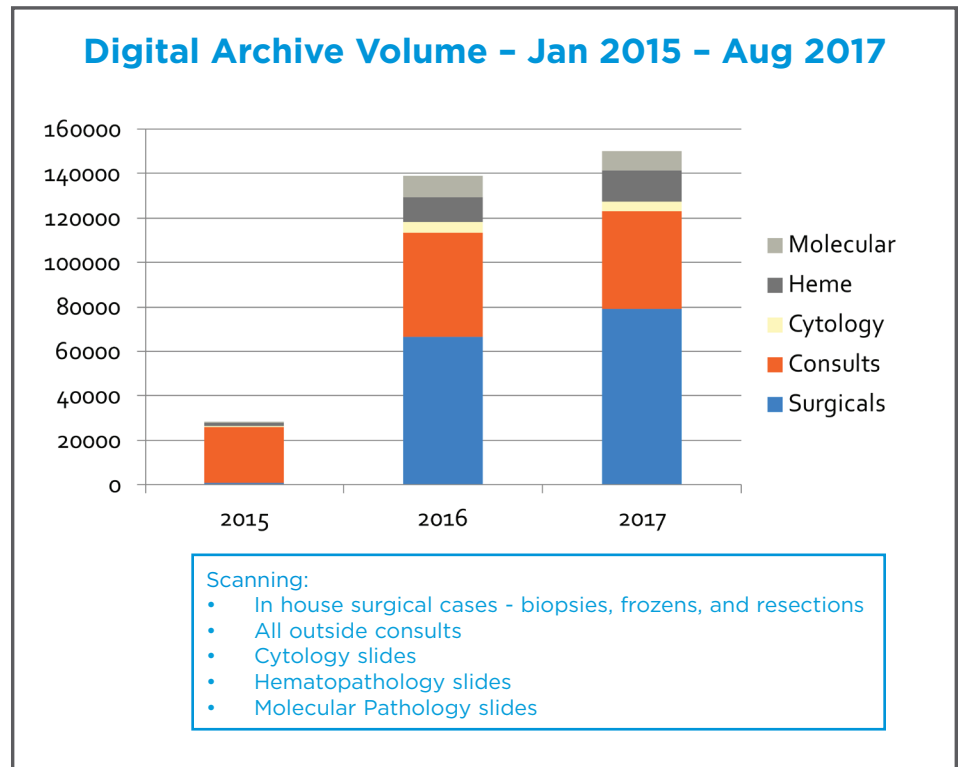
## INTRODUCTION TO THE **WARREN ALPERT CENTER FOR DIGITAL AND COMPUTATIONAL PATHOLOGY AT MSK**



## MULTIDISCIPLINARY EXPERTISE ADVANCES PATHOLOGY, CREATING A DIGITAL PATHOLOGY WORKFLOW

Digital pathology involves conversion of tumor tissue samples from glass slides to digital images to improve diagnosis while providing an infrastructure for computational pathology, which is based on quantitative measurement, mathematical modeling, and development of algorithms that can inform and improve the interpretation of disease processes on digitized slides, while integrating genetic and clinical information with the morphometric analysis of the image to provide higher level understanding of the tumor pathology.

The practice of anatomic pathology remains firmly based on the evaluation of glass slides of tissue sections or dispersed cells using a microscope, as it has been for 150 years. Inherent in the use of glass slides are logistical issues of slide transport, archiving, and retrieval as well as limitations in remote review, conferencing, and consultation capabilities; a challenge most pathology laboratories face. The capability to create whole-slide digital images (WSI) has existed for over a decade but has not yet been embraced for routine practice, and consequently the use of digital slides for higher level computational analysis has been limited. Improvements in technology and recent FDA approvals have created the opportunity to overcome some of these barriers and to incorporate digital pathology, along with machine learning-based computational analysis, into routine practice. A rapidly growing clinical practice, demand for pathology consultation by MSK pathologists, and the operational challenge of managing an archive of almost 25 million (and growing) glass slides strongly motivated the

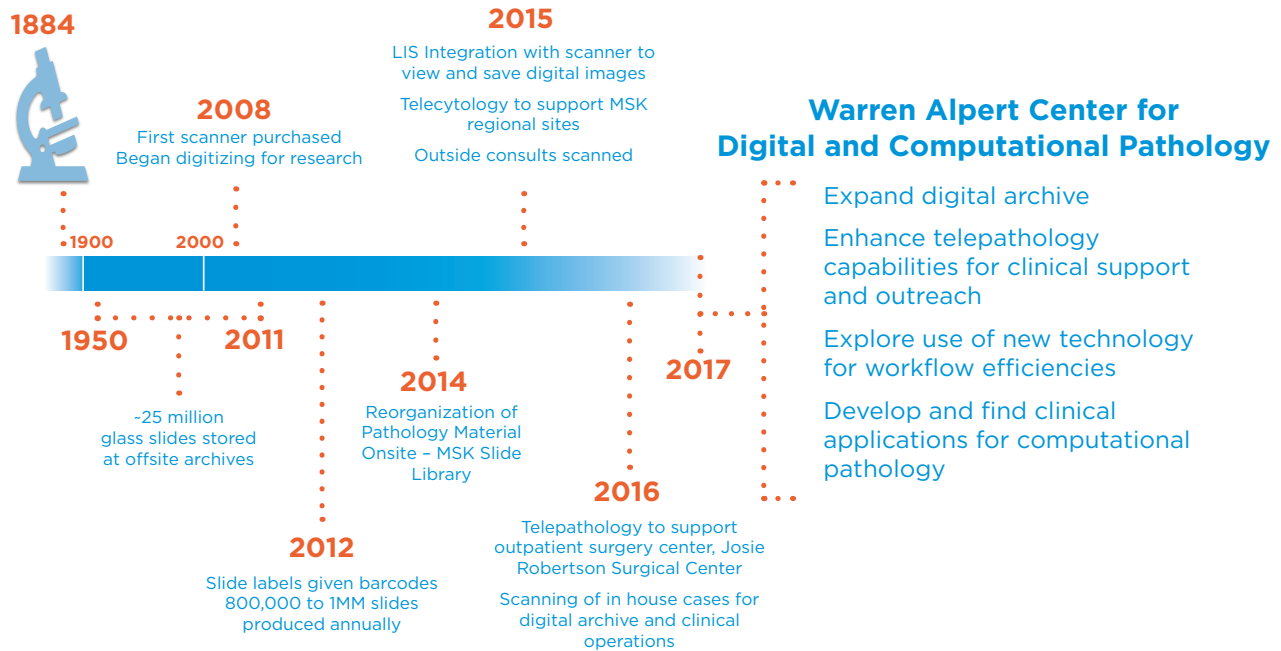


Department of Pathology at MSK to venture into the world of digital and computational pathology and it has been transformative for our practice.

With the support of a \$10 million gift, the Warren Alpert Foundation Center for Digital and Computational Pathology will help to position MSK as a major center for digital imaging and computational pathology,

providing a key component of the institutional focus on precision medicine. Though several other major institutions have begun programs in digital pathology or advanced imaging, few, if any, have tapped into both of these disciplines to foster a synergistic relationship with other clinical and basic disciplines as proposed by the Department of Pathology. Although MSK received the

## OPPORTUNITY FOR IMPROVEMENT-DIGITAL PATHOLOGY AT MSK



award this year, the groundwork began years ago with the purchase of the department's first scanner in 2008. The Department of Pathology has since taken the critical steps towards implementing a digital pathology workflow and partnered with industry leaders to become a national leader in the development, integration, and advancement of digital and computational pathology.

Under the leadership of Pathology Chairman David Klimstra, MD; Vice Chairman Victor Reuter, MD; and Surgical Pathology Service Chief Meera Hameed, MD, the Department of Pathology implemented digital scanning for archiving in 2015 after successfully establishing a secure image file management workflow to facilitate access of the digital slide via the department's laboratory information system (LIS). The department currently has a digital slide archive of more than 300,000 slides (~100K cases) and will soon scan 40,000 slides per month prospectively and from the archives.

The expansion of MSK clinical operations outside of the hospital's main campus, which required pathology support, led to the department's exploration of telepathology technology. Cytology Service Chief Oscar Lin, MD, PhD led the charge of incorporating telecytology for remote adequacy assessments to support MSK's regional sites. The opening of the Josie Robertson Surgical Center at MSK allowed the department to validate and use telepathology for frozen section consultations. Surgical pathologists at

JRSC can consult with their colleagues remotely when another opinion is needed. The experience gained from viewing digital slides for consultations made it easier for the MSK Pathologists to adapt to a telepathology workflow. The digital archive also helped provide easy access to prior pathology material, minimizing the need to transport glass slides between the two sites.

### THE WARREN ALPERT CENTER FOR DIGITAL AND COMPUTATIONAL PATHOLOGY AT MSK PATHOLOGY AT THE CUTTING EDGE

The Warren Alpert Center will play a critical role in the implementation of a fully digital workflow in the Department of Pathology and will harness the advantages of new imaging capabilities to extract advanced information on a cellular and sub-cellular level, for both clinical cancer care and research. Under the leadership of the Warren Alpert Center, the department will capitalize on MSK's extensive clinical and genetic data to pioneer computer-augmented cancer diagnosis and lead the transition of pathology from a qualitative to a quantitative discipline. Coupled with our engineering expertise, led by Yukako Yagi, PhD (Director of Digital Pathology) and Thomas Fuchs, PhD (Director of Computational Pathology), digital technology will allow novel methods for the morphologic evaluation of tissue samples. The move

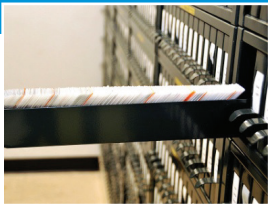
to a fully digital workflow will be led by the Warren Alpert Center's clinical leadership, Co-Directors David S. Klimstra, MD and Meera Hameed, MD, Medical Director Victor Reuter, MD, and Director of Pathology Informatics S. Joseph Sirintrapun, MD.

Dr. Yagi's digital pathology laboratory at the Josie Robertson Surgical Center will provide an incubator to explore and evaluate new technology to advance digital pathology in a clinical setting and actively engage vendors to help improve the technology and develop clinical applicability. Collaborations with clinical departments (e.g., Surgery), Radiology, Medical Physics, and Informatics groups will enhance the assessment and create opportunities for multidisciplinary applications. Dr. Yagi is currently working on four major projects: high resolution histology 3D imaging, validation of FISH image analysis, use of MicroCT in Pathology, and multiplex Histology 3D Imaging. With 20 years of experience in the field of digital pathology, Dr. Yagi has an enormous amount of first-hand experience and in depth knowledge of the technology and an innovative vision for future applications.

The practical use of digital pathology for primary diagnosis requires the development of useful analytic algorithms to compensate for the reduced efficiency of slide review inherent in current digital slide interface applications, and at MSK, we are uniquely positioned to develop these algorithms while addressing the user experience (MSK Universal Viewer). The technology will further enrich our knowledge of disease by integrating computational pathology data with other specimen-related data (genomics, proteomics, radiographic imaging, etc.). This will bring an unprecedented breadth and depth of information to each individual case and yield a comprehensive, multidimensional

## Transformative for Pathology Practice

2015



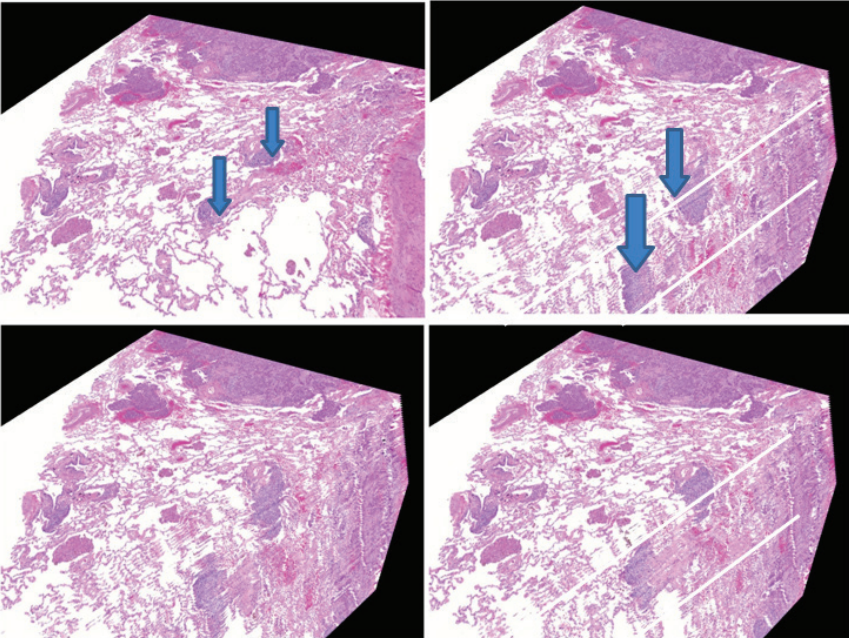
2016



**MSK Pathologists' Feedback on Digital Archive:**

- Instantaneous availability of prior material
- Improved efficiency in sign out
- Immediate feedback to clinicians
- Conference preparation
- Supports education
- Better patient care

## Future of Digital Pathology Imaging 3D Histology



**3D Reconstruction of Lung Adenocarcinoma**

analysis that would otherwise be impossible. Examples are nuclear detection, nuclear classification, tissue segmentation, staining estimation, and quantifying morphology. These features form the basis for the higher-level tasks of cancer detection,

grading, staging, micrometastasis detection, and quantifying immune cell infiltration. The basis for machine learning is the analysis of numerous parameters in huge numbers of well-annotated cases. Computational pathology expert, Thomas Fuchs, PhD, and his



# Pathology Material Management Today at MSK

MSK Slide Library – Glass Slide Archive



Storage for 4 million slides onsite for last 5 years

MSK Server Room – Digital Image Archive



Storage of ~1 petabyte of compressed image data

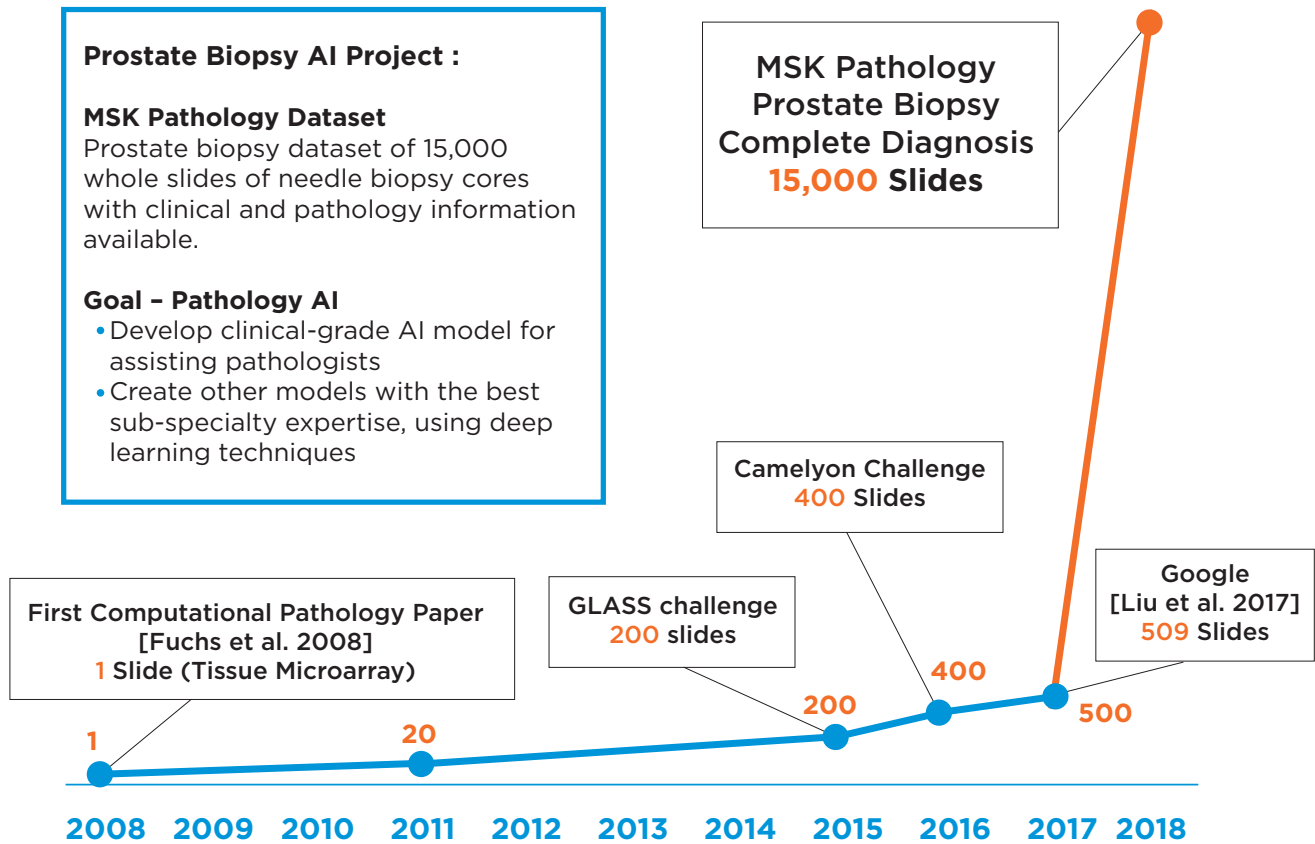
### Immediate Benefits:

- Less chance of losing glass slide
- Redundancy of material
- Decrease in request for glass slides when digital images are available

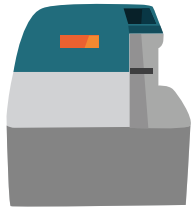
### Short Term Challenges:

- Added expense in redundant storage
- Redundancy in resources to manage both
- Does not eliminate the need to create a glass slide and retain it

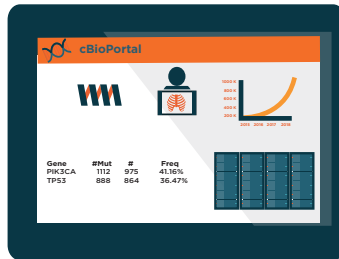
## Computational Pathology – Changing Diagnostic Practice



# MSK UNIVERSAL SLIDE VIEWER



Any Scanning Platform



Clinical Information i.e. Darwin, cBio Portal



Pathology Consult Portal



MSK Universal Slide Viewer



MSK Artificial Intelligence Model decision support



Laboratory Information System (LIS)

computational pathology laboratory and team lead these initiatives and are currently developing what we hope to be the first clinical grade AI model for prostate cancer, among many other projects.

Artificial intelligence as a digital assistant will revolutionize diagnostic pathology and research. It will enable pathologists to be faster, more efficient, and more accurate by supplanting subjective with objective criteria. Decision support tools can help identify regions of interest, match unusual

morphologic features among similar cases, and rapidly calculate microscopic measurements, cell counts, and other quantitative metrics. In addition to clinical care, archiving, and education activities with the departments of Radiology and Medical Physics, this work will facilitate large scale, quantitative correlations between tumor characteristics, protein expression, and genetic panels like MSK-IMPACT.

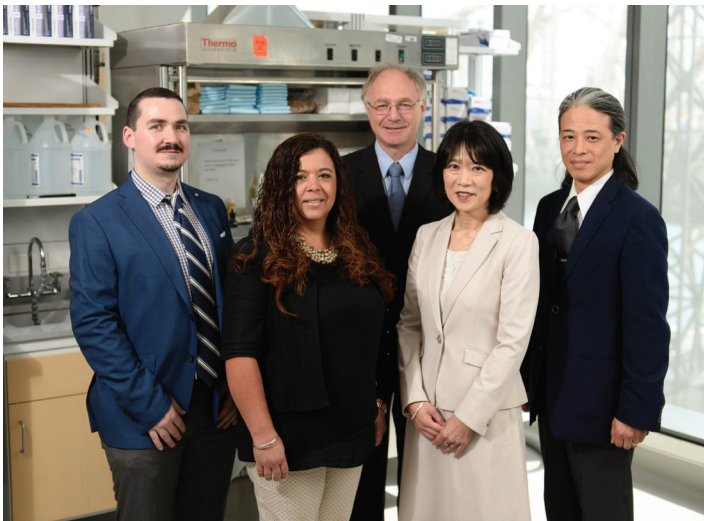
-Hope Cristol and Jennifer Samboy

# MEET THE WARREN ALPERT CENTER TEAM

The Warren Alpert Center vision and mission requires strong collaboration between pathologists and informatics experts, computer-assisted machine learning specialists, and sub-specialized and molecular pathologists.

In addition to the leadership and support of MSK's world-renowned pathologists, the Warren Alpert Center is supported by the research fellows, post docs, machine learning experts, software engineers, technicians, and administrative staff that support

both Dr. Yagi and Dr. Fuchs and their laboratory and research operations. Jennifer Samboy, MHA is the Warren Alpert Center's Senior Project Manager. The digital scanning operations are led and supported by the Digital Imaging and Graphics Team and Pathology IT Team. The Slide Library Team played a major role in helping the department reorganize its archives to facilitate a digital scanning workflow. This has been a department wide initiative and without everyone's support and collaboration, it wouldn't be possible.



Dr. Yagis' Digital Pathology Laboratory (L-R): Paul Matises, Patricia Ashby, Alexei Teplov, Yukako Yagi, Kazuhiro Tabata



Thomas Fuchs Computational Pathology Laboratory (L-R, Top row then bottom): Hassan Muhammad, Yubin Xie, John S. Ziegler, Andrew Schaumberg, Jeremy Kunz, Gabriele Campanella, Peter J. Schueffler, Talia Wise, Christina M. Virgo, Thomas Fuchs, Arjun Raj Rajanna, Luke Geneslaw



Digital Imaging and Graphics Team (L-R, Top row then bottom): Lisa Ricketts, Jamaal Spencer, Jason Dehaney, Kwadwo Akosah, Jordana Shapiro, Marguerida Bertie, Ali Manzo, Lorraine Corsale, Christian Ruiz

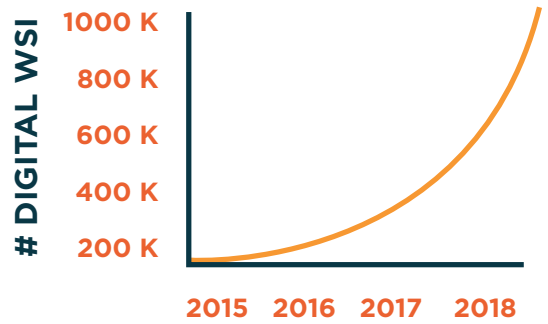


Pathology IT Team (L-R): Jennifer Samboy, Christopher Attard, Naveel Butt, Evangelos Stamelos, Lev Sipershteyn, Faith Cao

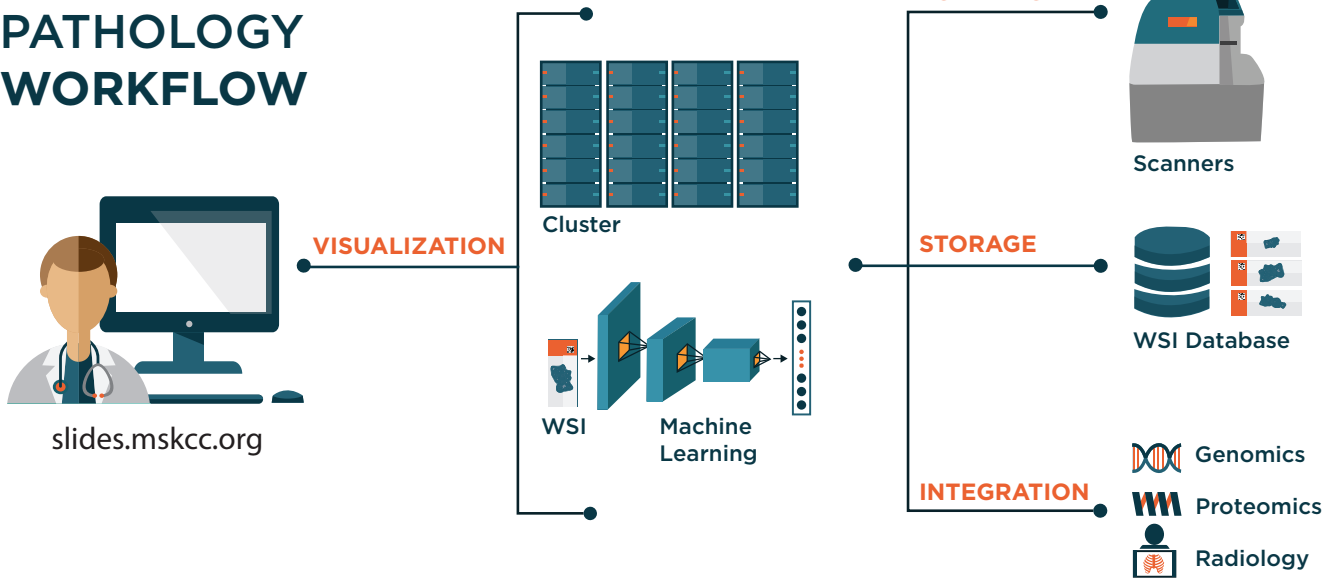
# DIGITAL AND COMPUTATIONAL PATHOLOGY AT MSK



- 10** WSI scanners for clinical & research
- 300K+** WSI available in LIS
- 100K+** Cases have WSI
- 98%** Outside consults have WSI
- 40%** Surgical cases have WSI
- 40K** Slides scanned monthly (4<sup>th</sup> QTR)
- 25MM** Glass slides in archive



## COMPUTATIONAL PATHOLOGY WORKFLOW



## DIGITAL PATHOLOGY WORKFLOW

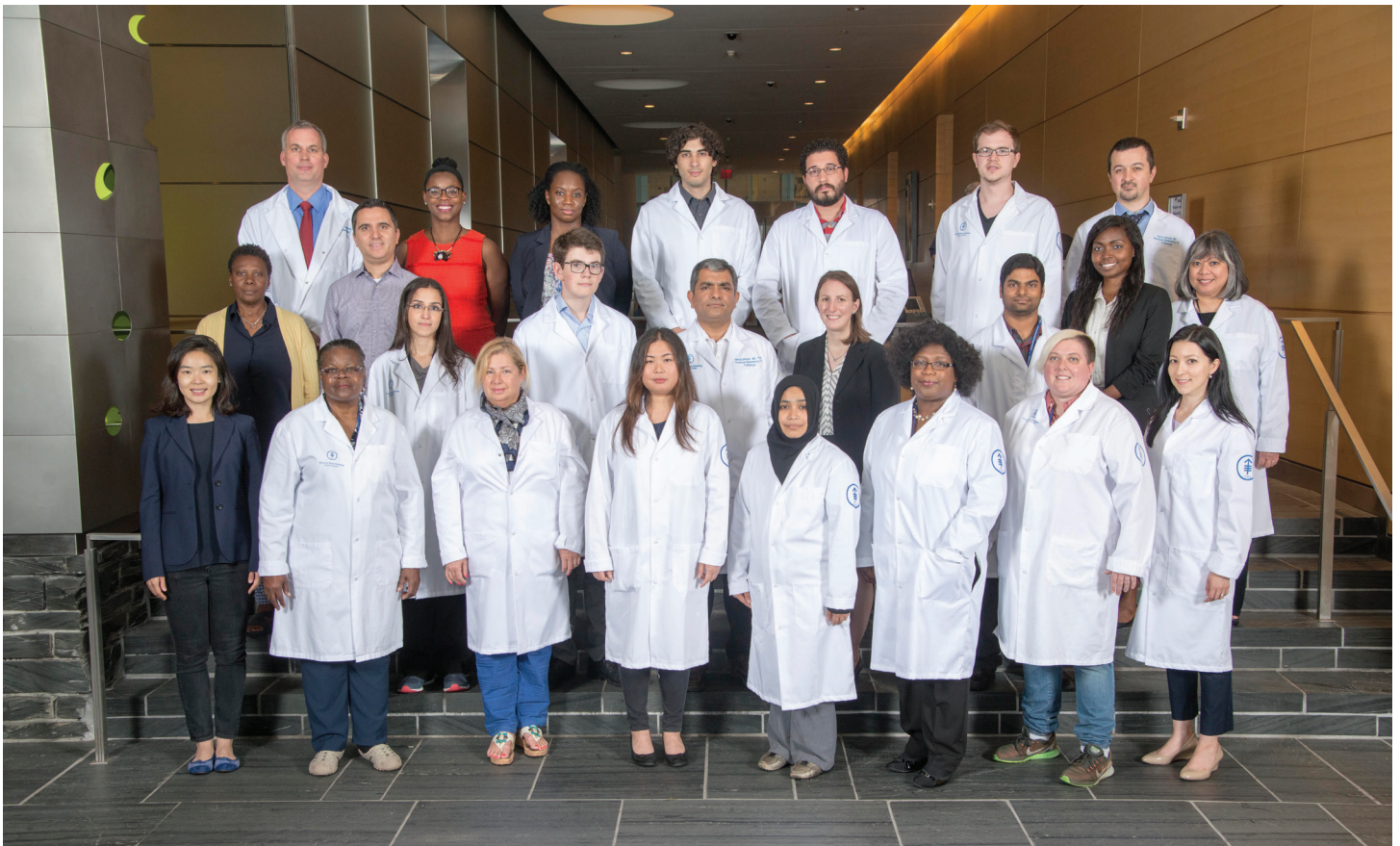


# BEYOND BIOSPECIMENS

## 5 PILLARS OF THE PRECISION PATHOLOGY BIOBANKING CENTER

Most people know biobanks as repositories for biospecimens, primarily for research purposes, but the new Precision Pathology Biobanking Center (PPBC) at Memorial Sloan Kettering is significantly more than that.

Michael Roehrl, MD, PhD, joined the staff here about two years ago as PPBC Director. His goal is to build it out as a collaborative research center – an entity at MSK that brings together lab investigators and clinicians from different disciplines. Joachim Silber, PhD, Director of PPBC Operations, joined the team about seven months ago, and has taken an active role in not only executing the vision for PPBC, but bringing together various MSK investigators to carry out their research projects. Dr. Silber takes the time to understand the goals of each investigator and together with the PI, outlines a plan to ensure samples are captured appropriately to carry out the research project. “Even though the name has biobanking in it, that’s only one [out of five ] of our major pillars, historically the one that was most developed,” says Dr. Roehrl, who is also a practicing pathologist with a specialty in gastrointestinal pathology.



PPBC (L-R, Top row then bottom): Michael H. Roehrl, Tanisha Daniel, Jordana Ray-Kirton, Eric Gaal, Miguel Santin, Peter Ruh, Guray Aktruk, Faye Taylor-Mason, Joachim Silber, Enmily Hernandez, Max Widmann, Umesh Bhanot, Nicole Degroat, Satish Ramakrishnan, Christina M. Virgo, Maria Corazon Mariano, Young Suk Kim, Priscilla McNeil, Irina Linkov, Emily Lin, Katrina Allen, Nurul Alhamid, Jessica Kenney, Aziza Hamrokulova

# THE FIVE PILLARS OF THE PPBC

## 1. WORLD-CLASS BIOBANKING

The PPBC Biobank is proficient in 13 international testing schemes, including tissue histology, DNA and RNA extraction from whole blood, FFPE and frozen tissue, and viable PBMC isolation. It's awaiting accreditation from the College of American Pathologists (CAP), which is required for collaborations with pharmaceutical and biotech companies. Historically, the biobank only banked nunc, frozen, specimens; however, this paradigm has shifted recently and we have introduced creating a research repository of FFPE blocks and blood. Additionally, slide scanning has been introduced to the daily workflow, thus allowing a digital archive of research samples. These efforts ensure a robust bank so MSK investigators are on the cutting edge of their research.

## 2. PRECISION PATHOLOGY INFORMATICS

Big-data analytics are and will continue be vital to the vision for the PPBC, with goals of developing tools for data federation and making big data accessible for clinicians and researchers. In July the PPBC team launched a new, internal site for MSK users: <https://one.mskcc.org/sites/pub/Pathology/Pages/PPBC.aspx>. It offers a wealth of information - on various surgical tissue availability and molecular diagnostic data via query tools. Our PPBC informatics team has also engaged in conversations with the Darwin, Digital Pathology Center, and IBM Watson teams to begin undertaking the enormous task of natural language processing as it pertains to pathology reports. Working collaboratively to develop algorithms that can be shared across pathology specialties will go a long way towards defining true metrics for rendering a diagnosis.

## 3. NEW PATHOLOGY TECHNOLOGIES

Pathologists at MSK already use state-of-the-art technology and advanced diagnostic techniques, including tissue microarray profiling and immunohistochemical analysis. New technologies in the PPBC will include:

- Proteogenomic diagnostics (mass spectrometry)
- Living biobank of disease models
- Computational pathology and data analytics
- Companion diagnostics development

## 4. R&D PARTNERSHIPS

The CAP accreditation will be an essential step toward enabling R&D partnerships that can advance precision pathology to the next level. Dr. Roehrl expects the PPBC will collaborate with partners in academia, pharma and biotech on projects including, but not limited to: companion diagnostics development, biomarker discovery and validation, and preclinical and clinical trials.

## 5. PATHOLOGY HUB FOR CLINICAL TRIALS

As with the other four pillars, precision pathology is at the heart of this one. Some ways the PPBC will play a leading role in clinical trials:

- Selecting histologic types of tumors to be targeted with new agents
- Design of pathology and specimen components of a new trial (what tissues to sample, how often, what types of specimens, etc.)
- Development of emerging molecular technologies to use in trials, with the goal of rapidly translating them for routine diagnostic use

While Dr. Roehrl developed the PPBC with these five strategic pillars in mind, he notes that they're not actually separate in practice - that therapy, diagnostics and other aspects of pathology - are increasingly interconnected.

"The diagnostics and other work we're doing as pathologists are intimately linked with choice of therapy. Increasingly, it will be a continuous circle: You put a patient on therapy and through careful pathology - DNA based and increasingly protein based, etcetera - assess how the tumor responds in real time," he says.

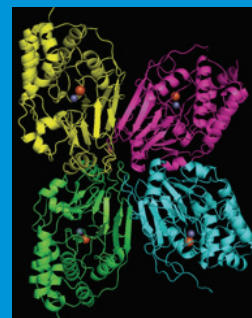
Dr. Roehrl anticipates the PPBC, and indeed the entire pathology department, will be driving significant progress in precision medicine. "People here are really leaders in their field. Moving things forward in an innovative way is just in the DNA here," Dr. Roehrl says. "We recognize that pathology is the central discipline in precise medicine because everything starts with a deep, functional analysis of a patient's disease."

## CANCER PROTEOMICS - THE NEXT FRONTIER FOR FUNCTIONAL PATHOLOGY

In July 2017, Dr. Roehrl was awarded funding as MSKCC Principal Investigator of the National Cancer Institute's Clinical Proteomic Tumor Analysis Consortium (CPTAC). CPTAC is a national effort to accelerate the understanding of the molecular basis of cancer through the application of large-scale integrated proteome and genome analysis, or proteogenomics. With essentially all targeted cancer therapies directly interacting with protein partners (e.g., kinases), the direct quantitative study of proteins and their activities will be of paramount importance for the next generation of precision diagnostics.

The goals of CPTAC are to develop innovative proteomic methodologies (such as mass spectrometry), to discover of proteome-centric cancer subtypes, to functionally rank driver mutations by correlative analysis of genomic and transcriptomic alterations with actual protein abundance, and to understand cancer-relevant biochemical pathway activation states through post-translational modifications.

CPTAC is currently leveraging its investment in cancer proteogenomics by characterizing additional cancer types, expanding its application through open-source community resources, and accelerating precision oncology by applying proteogenomics to questions of toxicity and resistance in clinical trials.



# PRECISION PATHOLOGY BIOBANKING CENTER (PPBC)



## JANUARY-JUNE 2017

**37,633** Histology slides prepared for research

**4,487** H&E stained slides prepared for research

**7,033** IHC stained slides prepared for research

**50** Research IHC staining protocols used per month



## JANUARY-JUNE 2017

**13,672**

Fresh tissue aliquots generated

**1,253**

Aliquots distributed to investigators for research

**3,179**

Fresh tissue cases handled from **3,111** unique MSK patients



**65**

College of American Pathologists accreditation-related policies established

**13**

international IBBL/ISBER-certified proficiency testing schemes



## JANUARY-JUNE 2017

**2,791** FFPE blocks generated

**1,986** Slides generated for PPBC Biobank digital archive



## TOTAL INVENTORY

PPBC Biobank holds

**350,632**

sample units from

**87,887** unique MSK patients

# THORACIC SERVICE EMPHASIZES COLLABORATION, DISCOVERY AND MENTORSHIP

Ask William Travis, MD, Director of the Thoracic Pathology team, to talk about his work, and instead he'll focus on his team: How their expertise spans services. How their collaboration supports the institution.

"They're thoracic pathologists, but each of them do cytology," Dr. Travis says of Natasha Rekhtman, MD, PhD; Jennifer Sauter, MD; and Darren Buonocore, MD. "It's a great advantage because about two-thirds of our patients present with advanced unresectable lung cancer, so their diagnosis is based upon small tumor specimens collected with less invasive techniques - such as core and fine

needle aspiration (FNA) biopsy."

In fact, he adds, Dr. Rekhtman has published multiple critical papers on the topics of immunohistochemistry and molecular features of lung carcinomas, which provided a strong foundation for major changes in the recent WHO Classification. In collaboration with Drs. Rekhtman and Arcila, recent thoracic team addition Dr. Buonocore was a major contributor to a recent study demonstrating how endoscopic bronchial ultrasound (EBUS)-FNA cytology samples showed a high success rate (86%) in identifying molecular alterations by next generation sequencing. He also

works closely with Jean-Marc Cohen, MD, Director of the FNA Biopsy Clinic - "which is a huge growth opportunity for the department and institution," Dr. Travis says, taking another opportunity to shine a light on his pathology colleagues.

Another exciting new area of evolving discovery is the topic of SMARC-A4 and SMARC-B1 deficient thoracic neoplasms in which both Drs. Jennifer Sauter and Natasha Rekhtman are making significant contributions. In collaboration with Drs. Cristina Antonescu, Mrinal Gounder and the thoracic medical oncology team, they are helping to develop novel diagnostic



From left to right: Natasha Rekhtman, MD, PhD, Marc Ladanyi, MD, Maria Arcila, MD, William Travis, MD, Darren Buonocore, MD, Jennifer Sauter, MD



approaches and new therapies for these rare but highly aggressive thoracic tumors.

The Thoracic Service supports the thoracic disease management team in a multidisciplinary way, working closely with thoracic surgeons, oncologists, radiologists and molecular biologists. Dr. Travis adds that Drs. Marc Ladanyi and Maria Arcila, who lead the Diagnostic Molecular Pathology laboratory in the Molecular Diagnostics Service, are a critical part of our team. “Their research efforts in thoracic molecular biology have pioneered new advances in the genetics of lung cancer frequently contributing to novel molecular targeted therapies,” he says. Another contribution to the department is the efforts of Drs. Rekhtman and Sauter to validate useful immunohistochemical markers in collaboration with Achim

Jungbluth, MD, PhD and the clinical immunohistochemistry laboratory. In the last year, the group initiated and participated in the validation of new neuroendocrine markers (ASCL1, INSM1), markers for assessment of SMARCA4-deficient tumors (Claudin-4, SMARCA2/BRM), and PD-L1. Dr. Sauter, a recent addition to our group, obtained a departmental grant to study PD-L1 and other predictive markers in cytology specimens and is the lead pathologist working on pleural malignant mesothelioma with the multidisciplinary team on clinical and research projects.

Dr. Rekhtman has been the lead pathologist on multiple multidisciplinary collaborative projects involving Molecular Diagnostics Service Chief Marc Ladanyi, MD, Diagnostic Molecular Pathology Director, Maria Arcila, MD and others

at MSK including the thoracic oncology team. These studies have helped to define comprehensive molecular characteristics of lung adenocarcinoma, squamous cell carcinoma and neuroendocrine carcinomas which have defined personalized therapeutic strategies for lung cancer patients. These have involved molecular targeted inhibitors involving the EGFR, ALK, RET, MET, EZH2-SLFN11, PIK3CA/AKT1 and PD-L1 pathways. Dr. Rekhtman also recently was awarded a Grant from the Drukenmiller Center for Lung Cancer Research to study the genetics and pathology of pulmonary neuroendocrine tumors.

The thoracic pathology team is also committed to education, and offers a biennial course: Thoracic Pathology New York City with Multidisciplinary Correlations. This is one of the few comprehensive courses covering most

# Q & A

## WITH SARAH VIRGO



### **Q: What does your role as Education & Communications Coordinator entail?**

As Pathology’s Education & Communications Coordinator, I manage everything related to our internal and external websites, including the internal OneMSK platform and the external mskcc.org sites. I also coordinate and maintain our CME and non-CME educational initiatives, serve as a public relations liaison, coordinate the new *MSK Pathology Review*, provide new staff with a departmental orientation, manage our very popular Lab Week events and the Translational Research Symposium, organize the Pathology Leadership Lecture Series as well as Grand Rounds, and lead digital enhancement projects.

### **Q: What are some of the most exciting things you’ve seen happen in the department?**

There are so many! The establishment of the Warren Alpert Center for Digital and Computational Pathology, the launch of the Precision Pathology Biobanking Center and the ongoing success of the IMPACT initiative, to name a few. Since I started my career here 11 years ago, I’ve seen the addition of at least 35 faculty members, the introduction of digital slides, enhancements to the molecular genetics division and the establishment of pathology at four off-site locations, including the

major neoplastic and non-neoplastic thoracic topics including lung, pleura and mediastinum. It is attended by pathologists and clinicians from around the world

Naturally Dr. Travis also has an extensive list of clinical and research accomplishments. In the past 20 years, he has served as the lead editor of the 1999, 2004 and 2015 World Health Organization Classifications of Tumors of the Lung, Pleura, Thymus and Heart. In addition, beginning in 2008, through the International Association for the Study of Lung Cancer (IASLC), Dr. Travis led a proposal with nearly 30 colleagues from around the world to reclassify lung adenocarcinoma. The effort culminated in the 2011 IASLC/American Thoracic Society/European Thoracic Society International Multidisciplinary Classification of Lung Adenocarcinoma.

“It was the culmination of a variety of observations in different arenas including histopathology, radiology, molecular biology, thoracic surgery and medical oncology,” Dr. Travis says. “It crystallized an extraordinary decade of advances in a way that has transformed clinical practice.” This led to reclassification of bronchioloalveolar carcinoma (BAC) into five distinct entities and one of the first evidence based recommendations that EGFR mutation testing should be performed on all advanced lung adenocarcinomas.

Of course, not all thoracic service work leads to such sweeping achievements. There is also the daily clinical work of the department. Dr. Travis and his colleagues receive a substantial number of personal consultations – many related to non-neoplastic disease, one of Dr. Travis’s main interests. These cases “help round

out our clinical experience, so our case material is not so heavily weighted on cancer,” Dr. Travis says.

One reason that’s important to him: Dr. Travis has dedicated his career to training the next generation of thoracic pathologists. When he came to MSK in 2005, he spearheaded the establishment of MSK’s ACGME accredited thoracic pathology fellowship program.

“Even though we’re a cancer center, the fellows benefit by exposure to non-neoplastic lung disease as well as cancer cases,” Dr. Travis says. And he feels the exchange of diverse knowledge goes both ways. “These are young, bright minds who ask great questions and have good ideas.”

–Hope Cristol

Josie Robertson Surgical Center. The clinical and academic achievements of my colleagues along with the application of applied technology has amplified Pathology’s critical role in the clinical environment.

### **Q: How can social media benefit the Pathology Department?**

Cancer patients and their families see surgeons, oncologists and nurses, but rarely interact directly with pathologists. Social media allows pathologists to connect directly with the communities they serve – not just patients, but also clinicians and researchers. A recent article in the *Archives of Pathology* (<http://archivesofpathology.org/doi/pdf/10.5858/arpa.2016-0612-SA?code=coap-site>) highlighted many examples of the value of Twitter for pathologists, from fostering collaborations to increasing the influence of publications.

### **Q: Where do you see Pathology at MSKCC in 5 years?**

I envision our department extending its dominance in the areas of pathology education, reference and digital archiving. Pathology at MSKCC continues on its mission and vision towards extending its reach as the leader in the realm of digital advancements for both research and precision medicine. The department’s talented physicians, researchers,

and technologists, along with the support and technological infrastructure already in place, will redefine the role of pathology in both the laboratory and in the clinical setting for years to come.

### **Q: If I’d like more info about current initiatives and upcoming events happening in Pathology, where can I look?**

Check out our website ([mskcc.org/departments/pathology](http://mskcc.org/departments/pathology)) for information on our faculty, how to send a consult to the members of our department, upcoming educational events, and other topics of interest. Stay tuned for a full relaunch later this year! Additionally, we’re now on Twitter! Follow @mskpathology for weekly updates from our full range of subspecialty teams.



# RETHINKING HEAD AND NECK TUMORS

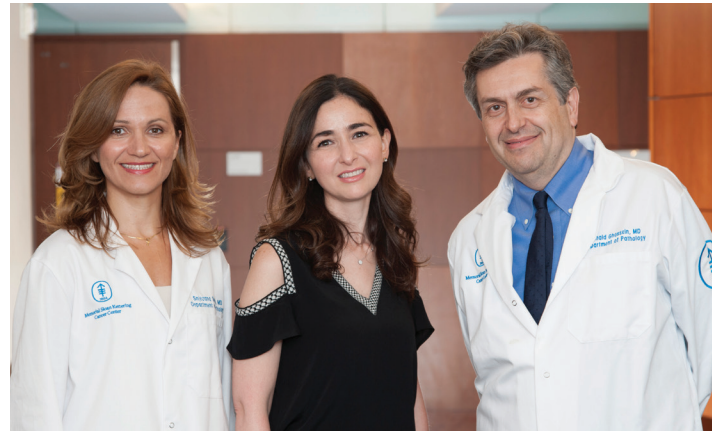
Some big news for thyroid cancer made media headlines last year. From *The New York Times*: “It’s Not Cancer: Doctors Reclassify a Thyroid Tumor.” The UK’s *Daily Mail* offered more detail: “Not All Cancerous Tumours Are Actually Cancer: Thyroid Growths Are First Ever to be ‘Downgraded’ to Prevent Patients Having Unnecessary Treatment.”

These and other lay press articles were based on a paper in *JAMA Oncology*. After 35 years of being considered malignant, a type of thyroid tumor – encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC) – was reclassified as non-cancerous. Now it’s called noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

Ronald Ghossein, MD, Director of the Head and Neck Service at MSK, was a senior author on the reclassification paper – along with a large consortium of other experts. But Dr. Ghossein and a small group of colleagues first recommended the change years earlier. Their 2006 paper in *Cancer* noted that this tumor doesn’t behave like a malignancy and should not be treated as such. Yet because of the words “thyroid carcinoma,” many physicians continued to overtreat patients with the non-invasive lesion.

“After 10 years, an international group changed the name to a tumor that doesn’t have the term cancer in it,” Dr. Ghossein says. “Basically, by doing this, we calculated that every year, 10,000 patients in the United States will not be subjected to the side effects of taking out the thyroid or to the psychological effects of a cancer diagnosis.” Worldwide, he estimates close to 40,000 patients could be spared overtreatment.

Dr. Ghossein says this change was “a big contribution from the head and neck service.” Of course, he and colleagues regularly make important contributions. They review approximately 290 cases



From left to right: Snejjana Dogan, MD PhD, Nora Katabi, MD, Ronald Ghossein, MD

per month, and their research is leading to better patient care.

Head and neck pathologist Nora Katabi, MD, who subspecializes in salivary gland cancer, has conducted extensive research to help stratify which patients will benefit from different treatments. “She was also one of the important contributors of the World Health Organization (WHO) classification of head and neck tumors, including salivary gland tumors,” Dr. Ghossein says.

In fact, the *WHO 2017 Blue Book* includes a new chapter, co-authored by Dr. Katabi, on tumors and tumor-like lesions of the neck and lymph nodes. Many of these have previously been diagnosed as unknown primary tumors but can now be identified as oropharyngeal and nasopharyngeal carcinomas. The new *Blue Book* chapter helps aid pathologists in the diagnosis and management of these tumors.

The third member of the head and neck team, Snejjana Dogan, MD, subspecializes in sinonasal tumors. With clinical expertise in molecular diagnostics, she recently identified a mutation with a therapeutic target – IDH2 R172 – in sinonasal carcinomas. Dr. Dogan detailed this recent finding as lead author of a June paper in *The Journal of Pathology*.

All three pathologists in the head and neck service also conduct research on squamous cell carcinoma. One potentially significant finding for tongue cancer: “Local recurrence-free survival was significantly affected only with surgical margins of less than or equal to 2.2 mm,” the authors wrote in their June 2017 paper in *JAMA Otolaryngology-Head and Neck Surgery*. “This new definition of close margins stratifies the risk for local recurrence better than the arbitrary 5.0-mm cutoff that has been used.” The upshot: If the finding is validated in future research, fewer tongue cancer patients may need painful chemoradiation after surgery.

-Hope Cristol

## Research Highlight

The Head and Neck service is currently involved in an important collaborative research program at MSK: A Specialized Programs of Research Excellence (SPORE) grant on the thyroid, led by endocrinology service chief James Fagin, MD. Dr. Ghossein is director of the pathology component of this grant.

# A PATIENT CENTERED APPROACH TO FINE NEEDLE ASPIRATION



From left to right: Maria Maugeri, Narsi Agaram, MBBS, Jean-Marc Cohen, MD, Carlie Sigel, MD, Oscar Lin, MD PhD, Allix Mazzella, MPH, Darren Buonocore, MD

In 2015, Jean-Marc Cohen, MD, came onboard as director of the Fine Needle Aspiration (FNA) Biopsy Clinic, which is part of the Cytology Service at Memorial Sloan Kettering. One of his primary aims has been to improve the clinic's availability to perform FNAs and to offer real-time service for patients in need of diagnostic procedures.

The numbers speak to his success: procedures performed in the clinic doubled within the first year.

Over the past two years availability of cytopathologists in the clinic has increased, making it much more patient-centric. Now clinicians can send patients to the clinic without appointment. Walk-ins can generally be seen within the hour.

"It's a structural change. People working in the pathology lab tend to be behind their microscopes even though some of them have excellent training in interventional cytopathology. The flexibility to offer fine needle biopsies at any time is a big thing," Dr. Cohen says.

Another change, which Dr. Cohen and his team have been working on for the past year, is increasing outreach beyond MSK. The clinic now provides fine needle aspiration biopsies to those outside the institution.

This service enables MSK pathologists to provide diagnostic expertise and capabilities for advanced diagnostic testing to patients in the greater community. The Cytology Service offers the combination of our pathologists' technical and diagnostic expertise and availability of modern ancillary studies results in

diagnoses that optimize patient care and outcomes. These include flow cytometry, which can identify and quantify subsets of cells, and molecular testing, which can reveal DNA mutations, chromosomal translocations and other features that can help pinpoint a diagnosis and guide the treatment.

Patients seen at the FNA clinic may seek referrals to MSK clinicians to manage the conditions diagnosed by Dr. Cohen's team. It is a great way to improve the care of patients. They can have streamlined access to MSK care if they are diagnosed with cancer.

These shifts at the FNA clinic have not required an influx of additional resources or training, he adds. "It's a change in mentality, a change in the way people think about their role." What that means for the pathologists is that there is nothing close to a "typical" workday, at least not in the clinic, which offers FNA biopsies of palpable and nonpalpable superficial lesions, including those of the thyroid, salivary glands and lymph nodes. Ultrasound guidance is often used to enhance the accuracy of sampling the lesion. The changes and success of the clinic is based on an integrated effort from the Cytology administrative and professional staff and hospital administration to improve the patient experience at MSK.

Dr. Cohen's focus on cytopathology and FNA reflects decades of experience. Shortly after arriving in the United States from France more than 30 years ago, he did his fellowship under the late Leopold G. Koss, MD - a pioneer of the field of cytopathology and former faculty member in Pathology at MSK - at Montefiore Hospital in the Bronx. Dr. Cohen later co-ran the FNA unit at NYU School of Medicine, and then opened and became director of the FNA service at Beth Israel Medical Center, where he worked until he joined MSK.

Like most pathologists, he has published research throughout his career, but he primarily considers himself an interventional cytopathologist. "Compared to the other pathologists in the department that really have a significant amount of research, I am more interested in cytopathology and FNA," Dr. Cohen says. "I was hired to develop the FNA clinic and I'm geared toward [serving] patients and doctors in order to facilitate that."

*-Hope Cristol*

# PATHOLOGY AT THE JOSIE ROBERTSON SURGERY CENTER

Cutting-edge surgery equipment and secure doctor-patient video conferencing are just some of the sophisticated features earning high praise at MSK's new Josie Robertson Surgery Center (JRSC). Less touted – though no less impressive – are the pathology labs.

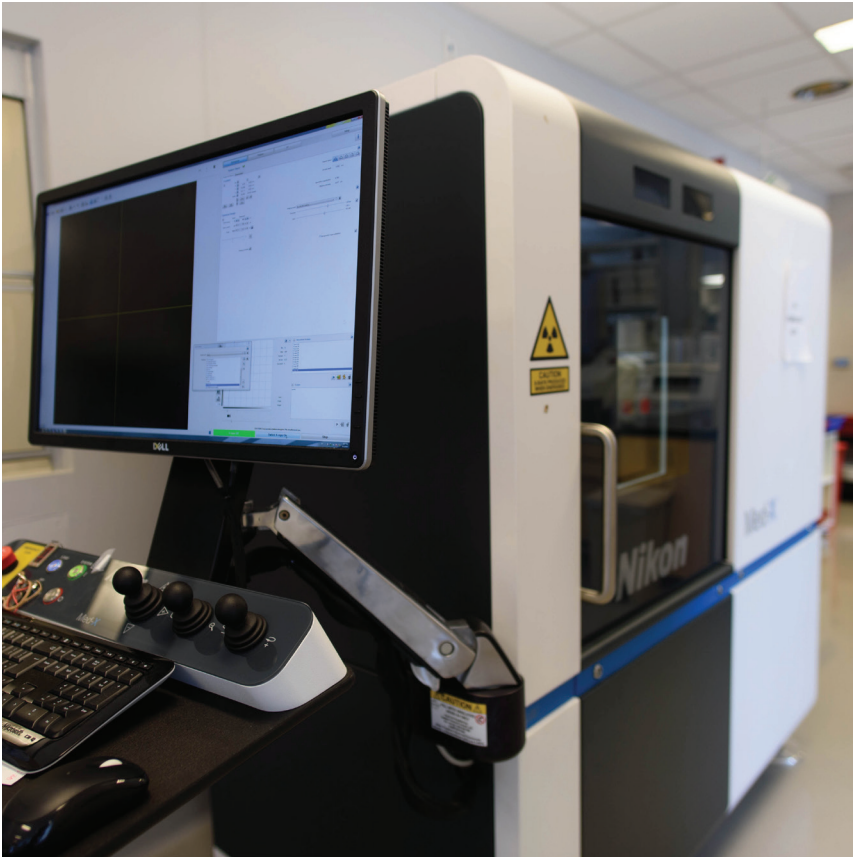
There are accession assistants who transcribe specimen information and patient demographics into the laboratory information system rather than sending specimens to the main campus for accessioning. “Josie,” as the center is known to many, also has a gross room staffed by pathologist assistants and a frozen section lab.

Pathologists from the main building rotate duty at Josie, but it's not just a center for clinicians. Yukako Yagi, PhD, Director of Pathology Digital Imaging, works out of Josie, focusing on the development and validation of digital imaging techniques. The Center is also home to a biobank, one essential component of the Precision Pathology Biobanking Center, or PPBC. (See page 12 for more on the PPBC.)

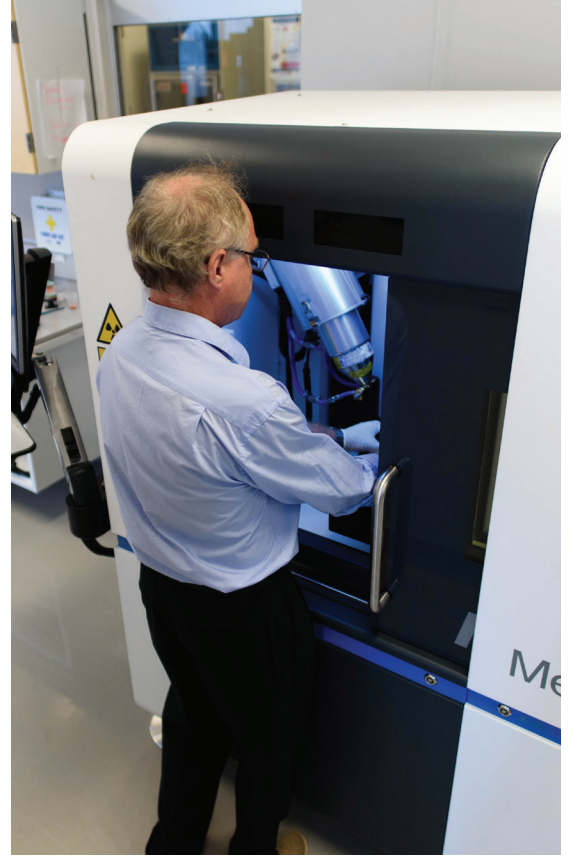
Here's an insider's look at pathology in the Josie Robertson Surgery Center.



Precision Pathology Biobanking Center (PPBC) at JRSC



MicroCT from Nikon at JRSC



Imaging technician, Alexei Teplov loading fresh specimen for scanning in MicroCT



Use of telepathology at JRSC for frozen section review



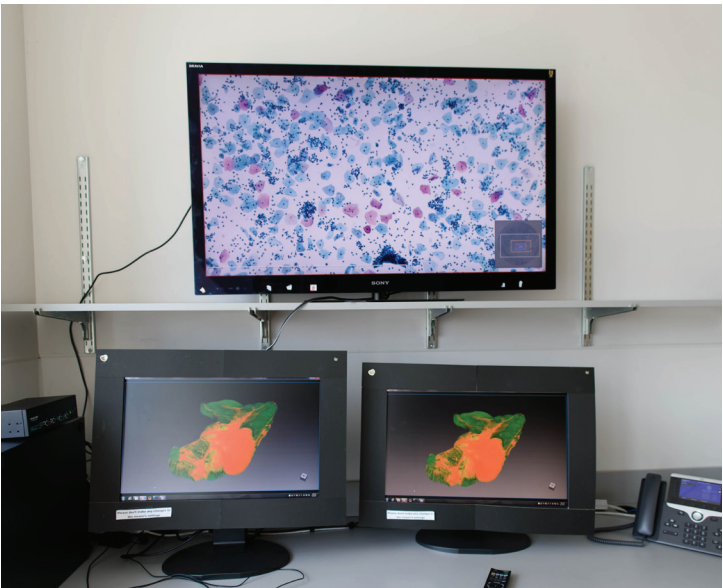
Surgical Pathology fellow reviewing clinical cases with pathologist at JRSC



Histology technician, Larry Jordan in frozen section lab



Histology technician prepping frozen section specimen in cryostat



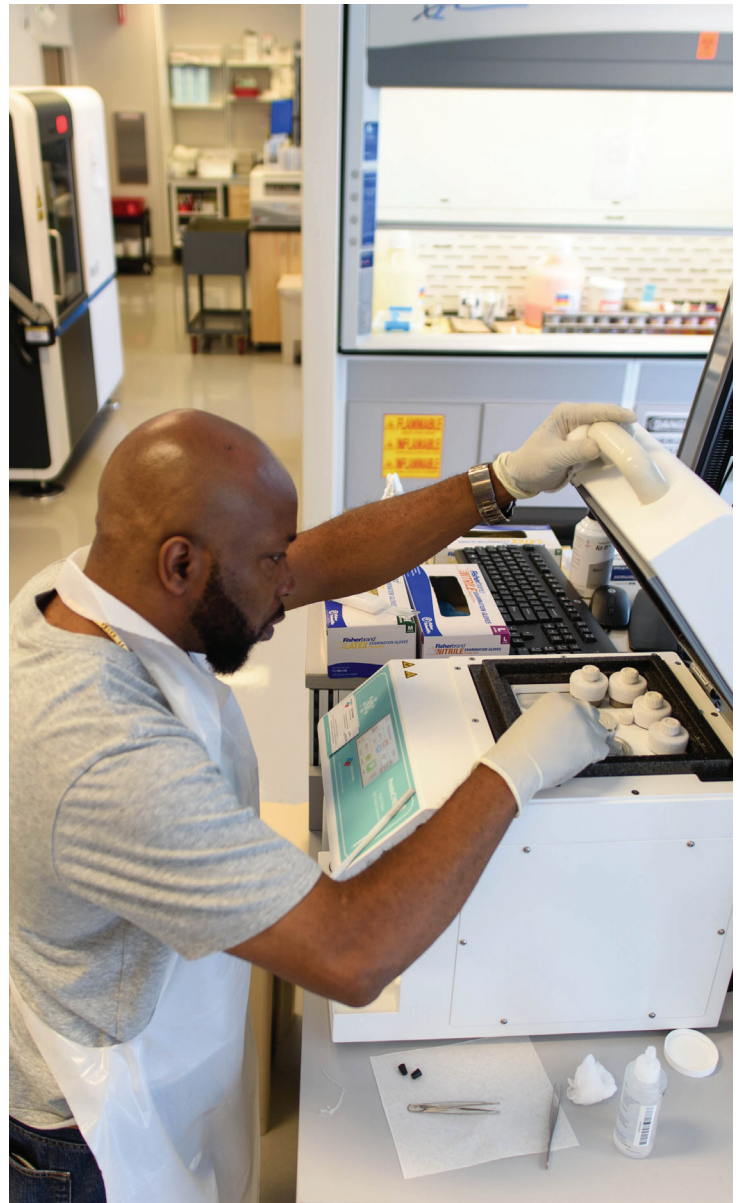
Dr. Yagi's Digital Pathology lab at JRSC



Pathologist Assistants (PA) grossing specimens in gross room at JRSC



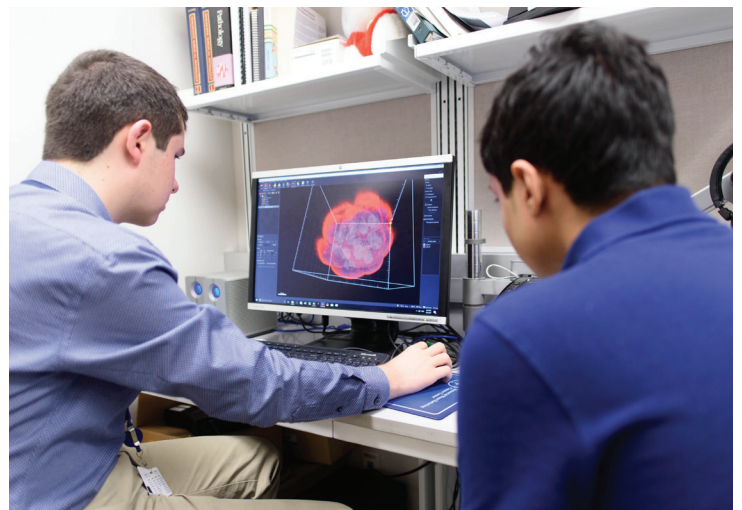
Laboratory bench at JRSC for histology technologists preparing recuts



Histology technician using new technology for processing specimens at JRSC



Joseph Sirintrapun, MD prosecting specimen for frozen evaluation



2017 summer interns-introduction to digital pathology with Yukako Yagi, PhD



Surgical Pathology accessioning workroom at JRSC



# RESEARCH PROFILES



**JINRU SHIA, MD**

Jinru Shia, MD, joined MSK in 1998 as a pathology fellow. The changes from then to now, both in the department and in the field of pathology, have been extraordinary. Dr. Shia has not only witnessed the sea change, but like so many of her MSK colleagues, she also contributed to it.

Back in 1998, there were maybe 20 attending pathologists “at the most. We had fewer cases and everybody did everything – we weren’t sub-specialized,” Dr. Shia says. “We had good expertise but it wasn’t as deep as it is now.”

The surgical pathologist credits her mentor, David Klimstra, MD, Chairman of the Pathology Department, with encouraging her to sub-specialize in gastrointestinal pathology years ago. Today, Dr. Shia is Director of Gastrointestinal Pathology and Director of the Gastrointestinal Pathology Fellowship Program. Her research focuses in part on the histological and molecular characteristics of familial and sporadic colorectal tumors, and her work has contributed to the understanding of microsatellite instability (MSI) in colorectal tumors and other solid tumors.

MSI in colorectal cancer was discovered in 1993, years before Dr. Shia entered practice. However, in the early 2000s, when Dr. Shia started her work on MSI, the methods of detecting MSI and the associated mismatch repair (MMR) protein deficiency were still at their early stages of development. It was work like hers and others’ that enabled the two key tests - MMR

protein immunohistochemistry (IHC) and MSI detection by PCR or sequencing- to evolve into efficient tools as they are today.

Like many surgical pathologists, Dr. Shia’s research isn’t done in a lab: She conducts clinical pathological and molecular correlative studies. A significant component of her MSI work was achieved by analyzing the MMR IHC staining patterns of large numbers of tumor cases. IHC “is a test that we do routinely as surgical pathologists, and we interpret what we see and correlate it with other findings,” Dr. Shia explains.

From extensive IHC based studies, Dr. Shia and her group proposed and validated a 2-antibody panel for MMR IHC that is reliable and more cost-effective than the commonly used 4-antibody panel. This 2-antibody panel is currently used by MSK and other institutions in appropriate clinical settings. Her group also validated the effectiveness of tumor biopsies as test samples for MMR IHC. They also illustrated clinically relevant scenarios where MLH1 IHC can be falsely normal and MSH6 can be “falsely” abnormal, and explained certain aberrant patterns such as concurrent loss of MLH1/PMS2 and MSH6 or concurrent loss of all 4 proteins in different clinical and molecular contexts.

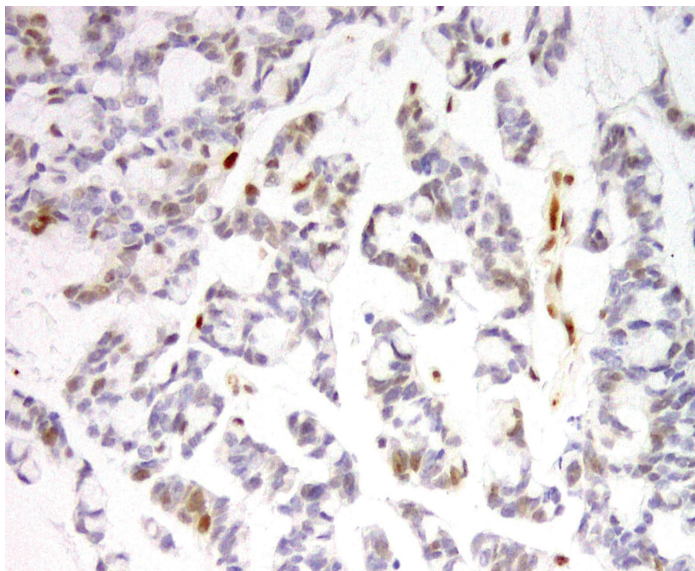
Dr. Shia’s ongoing research efforts will continue to help define and refine precision pathology, particularly where it concerns deeper understanding and characterization of MSI tumors – and especially those tumors associated with double somatic

mutations in the MMR genes. Preliminary data in some of these tumors have shown unique, clinically relevant characteristics.

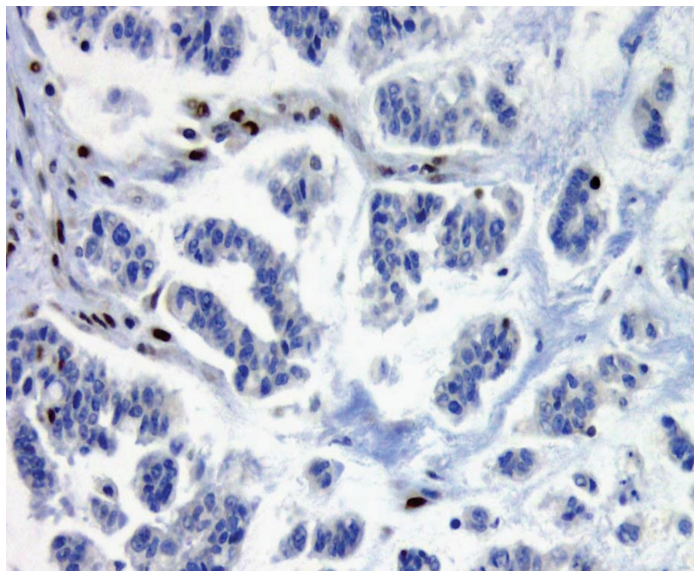
Dr. Shia is also exploring the relevance of MSH3 deficiency, which occurs in a substantial subset of colorectal cancers. Because of the specific type of mismatch repair function the MSH3 protein has, its deficiency results in a distinct form of microsatellite instability. That form of MSI is called elevated microsatellite alterations at selected tetranucleotide repeats (EMAST).

“Further delineation of these tumors not only carries the potential to allow better prognostication, it may also improve our understanding of the tumor’s immune microenvironment,” Dr. Shia says.

Another major ongoing MSI-related effort is characterization of unusual Lynch syndrome associated tumors. This, like her efforts on MSH3 may allow better prediction of tumor response to immunotherapy – and help clinicians determine how to select patients for treatment.



**MLH1 IHC: Staining present, weak**



**PMS2 IHC: Staining absent**

Immunohistochemistry studies of a colon cancer from a patient with a deleterious MLH1 germline mutation demonstrating weak staining of MLH1 and complete loss of PMS2 in the tumor cells. When coupled with loss of PMS2, weak MLH1 immunohistochemical positivity often points to abnormality in the MLH1 gene. Studies in the recent past have elucidated the clinical and biological implications of various intricate MMR protein expression patterns, and enhanced the utility of immunohistochemistry as a tool in the study of mismatch repair proteins. Other examples include loss or reduced MSH6 reactivity in treated tumors being more likely a result of secondary down regulation (possibly due to ischemia) and not MSH6 gene mutation; clonal or complete loss of MSH6 or MSH3 in tumors that are deficient in MLH1 and/or PMS2 being linked to instability of the coding microsatellites in MSH6 or MSH3, respectively; and MMR protein loss in certain non-colorectal type tumors proven to be a manifestation of an underlying pathogenic MMR gene mutation but not always accompanied by detectable microsatellite instability by either conventional PCR method or NGS based programs such as MSIsensor.

## 2017 RESEARCH HIGHLIGHTS

For a surgical pathologist, Dr. Shia is prolific on the research side. These are some of the articles that she (along with other MSK colleagues) published in 2017.

1. Modern Pathology: Morphological characterization of colorectal cancers in The Cancer Genome Atlas reveals distinct morphology-molecular associations: clinical and biological implications.
2. Familial Cancer: Immunohistochemical null-phenotype for mismatch repair proteins in colonic carcinoma associated with concurrent MLH1 hypermethylation and MSH2 somatic mutations.
3. Familial Cancer: Universal screening for microsatellite instability in colorectal cancer in the clinical genomics era: new recommendations, methods, and considerations.
4. Clinical Colorectal Cancer: Molecular Screening for Lynch Syndrome in Young Patients With Colorectal Adenomas.
5. Human Pathology: Diagnosing Colorectal Medullary Carcinoma: Interobserver Variability and Clinicopathological Implications.

# DERMATOPATHOLOGY AT MSK

## 5 HIGHLIGHTS FROM THE DERMATOPATHOLOGY TEAM

The Dermatopathology Team is a very busy clinical service with individual staff members dealing with a high volume of daily cases for review. Many of these cases are tedious and time-consuming, such as detailed margin assessments for melanomas of sun-damaged skin, or diagnostically very difficult and controversial neoplasms. The service also receives challenging non-neoplastic cases of skin rashes or hair loss related to various cancer treatments.

Dr. Busam sees a large number of personal consults from all over the USA and overseas, and has a few other roles as well. He is Director of the Dermatopathology Fellowship Program, Director of the Immunohistochemistry Operations Committee, and, along with Dr. I. Orlow, Director of the Biospecimen Core of an NIH-funded multi-institutional collaborative research effort to investigate molecular aberrations of primary cutaneous melanoma. His main academic interests in pathology are exploring new methods to improve the diagnostic accuracy of skin melanocytic tumors and prognostic models of melanoma.

Dr. Busam has been a fixture

in the pathology department at MSKCC for so long – more than 20 years – that his packed schedule and numerous roles are no surprise to many here. But the work he does, and the interdisciplinary teams he works with, are continually evolving. Here are five noteworthy highlights.

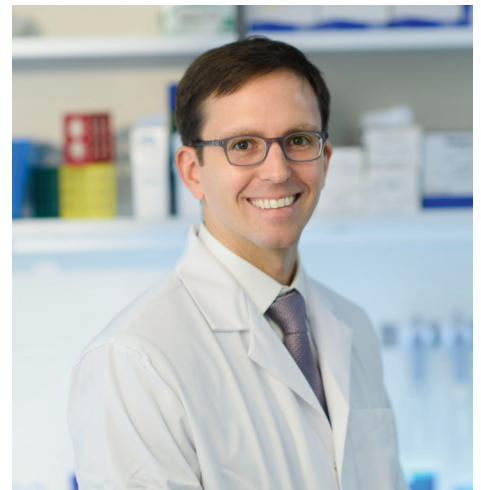
### 1. CUTTING-EDGE APPROACHES

The Dermatopathology Team offers a unique, efficient processing system for rapid histopathologic evaluation of staged excisions of skin tumors that affect skin of the face, where close coordination

with dermatologic surgeons is critical to excise just as much skin as needed to ensure complete removal the tumor, but as little as possible given the cosmetically sensitive location of the tumor. MSK Dermatopathology is also a national and international leader in using genomic methods as ancillary tools for diagnosis, which may prove especially valuable when the distinction between benign and malignant tumors is difficult under the microscope. “The genomic studies are part of research that suggests they may be beneficial for diagnosis. We feel compelled to try it here and bring it on early,



Klaus Busam, MD



Travis Hollmann, MD PhD

before many other institutions,” Dr. Busam says.

He adds that the same is true for immunohistochemistry. If new antigens are found in a research project to be of potential clinical use, Dr. Busam feels it’s vital to explore “to what extent the expression of distinct proteins may be helpful to type a tumor more precisely, or to use the information to improve prognostic models, or to help select the best treatment for those patients.”

Dr. Busam is also collaborating with data scientists led by Thomas Fuchs, PhD, to explore the use of machine learning for the diagnosis of skin tumors via digital images, to improve diagnostic accuracy, quality control, and workflow efficiency.

## 2. AN ALL-STAR TEAM...

Dr. Busam emphasizes that his service is a team effort and that he is proud of its accomplishments. The diversity of interests, background and experiences of the team members adds to the strength of the service and academic mission. In July, he welcomed the team’s newest member, Cecilia Lezcano, MD, a talented young physician who recently graduated from the Harvard dermatopathology program. The Dermatopathology Team at MSK also includes Travis Hollmann, MD, PhD, who has a strong background

in immunology and is interested in assessing biomarkers for predicting treatment response to metastatic melanoma and other cancers; and Melissa Pulitzer, MD, who is an expert in cutaneous lymphomas and has contributed novel insights into pathways associated with Merkel cell carcinoma.

## 3. EMPHASIS ON EDUCATION...

The Dermatopathology Team has two fellows per year as part of its ACGME-accredited fellowship program with Cornell, but Dr. Busam is individually committed to education as well. He lectures nationally and internationally, offers a CME course on melanocytic and non-melanocytic tumors, and is wrapping up a new textbook on melanocytic tumor pathology (co-edited by Drs. Gerami from Northwestern University, Chicago, and Richard Scolyer from the Melanoma Institute of Australia) among other opportunities to educate the pathology community.

## 4. MULTIDISCIPLINARY APPROACH TO PATIENT CARE...

The Dermatopathology Team also has weekly discussions of difficult cases with clinicians – plus many other meetings to assess, compare and learn from non-melanoma and melanoma cases. The entire team of dermatopathologists participates

in an upcoming CME course led by their clinical colleagues Drs. Nehal and Singh this fall (November 3<sup>rd</sup> and 4<sup>th</sup>) on the diagnosis and management of complex skin cancer.

## 5. CYTOGENIC ANALYSIS

Dr. Busam’s team, which sees a very high volume of unusual tumors, employs a range of diagnostic techniques not often used elsewhere. “We have taken the lead with a few other centers in the country to develop new diagnostic tools for lesions that frustrate pathologists because under the microscope they show ambiguous features and conventional parameters are not sufficiently sensitive or specific to determine whether a lesion is benign or malignant,” Dr. Busam says.

One technique is cytogenic analysis. For example, Dr. Busam explains, he might look at all the chromosomes in a tumor cell for aberrations, as melanomas typically have small segmental gains or losses, and most nevi don’t. “Using that technology helps us establish more accurate diagnoses than if we had to rely on the microscope alone.”

—Hope Cristol



Melissa Pulitzer, MD

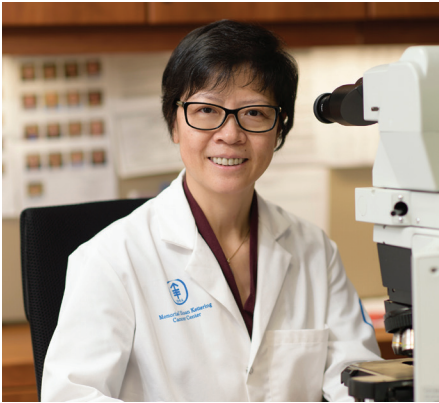


Cecilia Lezcano, MD

# NEW FACULTY

## Hong (Amy) Zhang M.D., Ph.D.

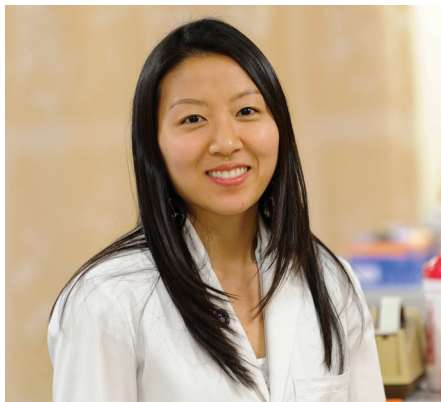
Attending Pathologist, Surgical Pathology Service,  
Department of Pathology



Dr. Zhang received her MD from Harbin Medical University in China and her PhD in Pathology/Structural Virology (Cryoelectron Microscopy) from the University of Texas - Houston Medical School. She also conducted AP/CP residency training at UT - Houston and then became a Surgical Pathology Fellow at MD Anderson Cancer Center. After a year as a staff pathologist in Pittsburgh, she returned to Houston as Assistant Professor at Baylor, subsequently moving to MD Anderson as Assistant Professor in 2009. Most recently she has been Associate Professor at MD Anderson. Dr. Zhang's diagnostic subspecialty is in breast pathology, and she has also conducted research related to breast cancer, both in her own lab at MD Anderson and as a collaborator with others in her institution and elsewhere. Her own work has focused on the significance of MAP3K3 amplification in breast cancer prognosis and chemoresistance, the potential for novel kinase and proteasome inhibitors to sensitize breast cancer cells to conventional chemotherapy, and the use of single cell sequencing to study the genetic evolution of breast cancers. In our Department, she will be working with Jorge Reis-Filho to further her experimental efforts.

## Christine Moung M.D.

Assistant Attending Pathologist, Molecular  
Diagnostics Service, Department of Pathology



Dr. Moung received her BS from the Sophie Davis School of Biomedical Education, City College of New York, and her MD from SUNY Stony Brook School of Medicine. After graduation she completed her AP/CP residency at Mount Sinai School of Medicine, where she also served as Chief Resident. She then trained as a fellow in Transfusion Medicine at UCLA, followed by a fellowship in Molecular Genetic Pathology in our Department. Upon completing her training in 2011, Dr. Moung became an Assistant Attending in Laboratory Medicine at MSK to work in the area of transfusion medicine. Over the ensuing years, however, she desired to return to the practice of Molecular Pathology, so she repeated our MGP fellowship in order to train fully in the era of next-generation sequencing. She now joins the Molecular Diagnostics Service as an Assistant Attending. Based on her experience in stem cell transplantation in the past, Dr. Moung forged relationships with the transplant team to pursue test development related to this discipline, and her diagnostic work will also involve molecular hematopathology, in keeping with that specialty interest.

## Kseniya Petrova-Drus M.D., Ph.D.

Assistant Attending Pathologist, Hematopathology  
and Molecular Diagnostics Services, Department of Pathology



Dr. Petrova-Drus received her BA from Barnard in 2003 and is a graduate of New York University School of Medicine, where she received her MD and PhD degrees in 2011 after conducting her PhD research in molecular oncology and immunology in the lab of David Ron at the Sackler Institute. Her graduate thesis related to the regulation of the unfolded protein response and the regulation of ER chaperones. She subsequently trained as an Anatomic and Clinical Pathology resident at Weill Cornell Medicine in 2011-2015. She took an Elective Rotation in Hematopathology as a Visiting Fellow at the NIH and completed her hematopathology fellowship in 2015-2016 at Weill Cornell Medicine, under the direction of Dr. Attilio Orazi. Last year, Dr. Petrova-Drus was a fellow in Molecular Genetics Pathology at MSKCC. Thus, she has excellent training in both hematopathology and molecular diagnostics, and she will participate in diagnostic work on both services. She will also be engaged in molecular test development, especially in the growing area of molecular hematopathology, and she will conduct research related to hematopathology topics, such as the diagnosis of myelodysplastic syndrome, one of her current interests.

# NEW FACULTY

## Tejus Bale M.D., Ph.D.,

Assistant Attending Pathologist, Surgical Pathology and  
Molecular Diagnostics Services, Department of Pathology



Dr. Bale is a summa cum laude graduate of Stony Brook University, where she received a Bachelor of Science in Biochemistry in 2006. She then received her MD-PhD (MSTP program) in Physiology and Biophysics, also from Stony Brook University, in 2012. Dr. Bale received several awards at Stony Brook for academic excellence and excellence in science. Her PhD thesis research on the role of 5HT<sub>2A</sub> receptor blockade on phrenic nerve discharge was conducted under the mentorship of Dr. Irene Solomon and published in *Advances in Experimental Medicine and Biology* as a first author paper. After graduation she completed residency training in Anatomic Pathology and Neuropathology, a 4-year program, at Brigham and Women's Hospital, with neuropathology rotations also at Boston Children's Hospital and BI Deaconess. She received ABP Board certification in Anatomic Pathology and Neuropathology in 2016. Currently, she is a Molecular Genetic Pathology fellow in the combined program at Harvard Medical School and will be Board eligible at the end of the 2016-2017 academic year. This program will expose her to most of the contemporary, complex molecular pathology assays we perform at MSK, including NGS-based panel sequencing assays. Thus, her combined training in both neuropathology and molecular pathology will fit a critical niche for us, providing a second neuropathologist who can also serve a liaison role between neuropath and molecular diagnostics, which we have previously lacked.

## Cecilia Lezcano, M.D.

Assistant Attending Pathologist, Surgical  
Pathology Service, Department of Pathology



Dr. Lezcano received her medical degree with honors at the Universidad Nacional de Asuncion in Paraguay. After graduation she became a research fellow in dermatopathology for 3 years at MGH and Brigham and Women's Hospital, working with Drs. Martin Mihm and George Murphy. She then undertook AP residency training at the University of Pittsburgh, where she also served as the Chief Resident. In 2016, Dr. Lezcano returned to the Harvard Combined Program in Dermatopathology to complete her clinical dermatopathology fellowship. Her initial research under the mentorship of Dr. Antonio Cubilla in Paraguay (a former MSK pathology faculty member) was focused on the clinicopathologic analysis of penile carcinomas, and collaborations on this topic continue. In her research fellowship, she collaborated on studies related to cutaneous GVHD and vasculogenic mimicry in melanoma - a phenomenon in which neoplastic cells achieve morphologic and biologic properties of endothelial cells, which is thought to contribute to the development of metastatic disease. She has also expanded this work to study vasculogenic mimicry in other tumors, such as Merkel cell carcinoma.

## Anne Grabenstetter, M.D.

Instructor, Surgical Pathology Service  
Department of Pathology



Dr. Grabenstetter completed her BA at Case Western Reserve University and her MD at Northeast Ohio Medical University. She trained in anatomic and clinical pathology at Rutgers New Jersey Medical School. She was selected as an oncologic surgical pathology fellow at MSKCC in 2015, and last year she completed our fellowship in breast pathology. As an outstanding diagnostic breast pathologist, Dr. Grabenstetter has been appointed to be an Instructor in Pathology. She is currently involved in two research projects; one analyzing CDH1 expression and mutations in lobular carcinoma and another to study breast implant associated anaplastic large cell lymphoma.

# 2017-2018 CLINICAL FELLOWS

## ONCOLOGIC PATHOLOGY FELLOWS



LAURA FAVAZZA  
Co-Chief



JENNIFER ZENG  
Co-Chief



ISABELLE CUI



CHRISTIAN CURCIO



ANDREW GOLDEN



MATTHEW HANNA



PATRICK HENN



LIWEI JIA



UPASANA JONEJA



BRIE KEZLARIAN



DANIEL LEVITAN



STEPHANIE MULLER



VIDARSHI  
MUTHUKUMARANA



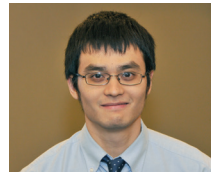
MARYAM SHAHI



JAMES SOLOMON



MONIKA VYAS



YOURAN ZOU

## SPECIALTY FELLOWS



SABINA HAJIYEVA  
Breast Pathology



ZENA JAMEEL  
Breast Pathology



KANT MATSUDA  
Breast Pathology



DEEPU ALEX  
Cytopathology



TIANHUA GUO  
Cytopathology



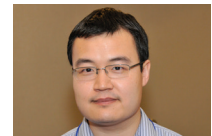
LEILI MIRSADRAEI  
Cytopathology



BRIANNE DANIELS  
Dermatopathology



ALLEN MIRAFLOR  
Dermatopathology



TAO WANG  
Gastrointestinal  
Pathology



YU-CHING PENG  
Gentiourinary Pathology



VITOR WERNECK SILVA  
Gentiourinary Pathology



GULISA TURASHVILI  
Gynecological  
Pathology



PRIYADARSHINI  
KUMAR  
Hematopathology



NATASHA LEWIS  
Hematopathology



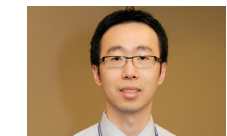
PALLAVI KHATTAR  
Hematopathology



FATIMA ZHARA  
JELLOUL  
Hematopathology



JAVIER ARIAS-STELLA  
Molecular Diagnostics



JASON CHANG  
Molecular Diagnostics



PAOLO COTZIA  
Molecular Diagnostics



SOUNAK GUPTA  
Molecular Diagnostics



CHAD VANDERBILT  
Molecular Diagnostics



JOHNATHAN VAUCHER  
Thoracic Pathology

# UPCOMING COURSES

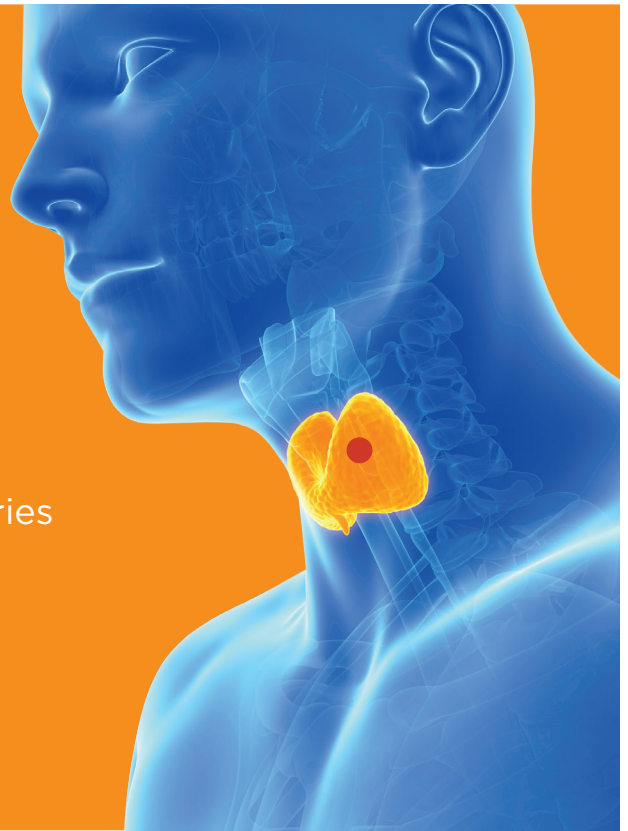
## THYROID NODULES: CANCER OR NUISANCE

A Multidisciplinary  
Approach

OCTOBER 13, 2017 • 5:00PM  
Rockefeller Research Laboratories  
Room 116



Memorial Sloan Kettering  
Cancer Center



Follow us on  
**TWITTER**  
@MSKPathology



# 4TH QUARTER 2017

## **MULTIPLEXED IMMUNOMORPHOLOGY PLATFORMS**

Travis Hollmann, MD, PhD

## **41ST FRED STEWARD AWARD PRESENTATION AND THE 41ST ANNUAL ALUMNI RECEPTION**

## **RESEARCH PROFILES**

Natasha Rekhtman, MD PhD & Yingbei Chen, MD PhD

## **GERMLINE IMPACT**

Liyong Zhang, MD PhD, Diana Mandelker, MD PhD & Ozge Birsoy, PhD

## **IMMUNOHISTOCHEMISTRY**

Achim Jungbluth, MD, PhD

