## MSK PATHOLOGY | INITIATIVES REVIEW | INITIATIVES INNOVATIONS ACCOMPLISHMENTS

# MSKCC Pathology Fellowship Directors





Memorial Sloan Kettering Cancer Center<sub>17</sub>  $\frac{1}{2018}$ 



Hannah Wen, MD, PhD, **Tackles Tough Breast Cancers** 

By Hope Cristol

### **Research Spotlight** HANNAH WEN, MD, PhD

Hannah Wen, MD, PhD, first came to Memorial Sloan Kettering Cancer Center as a fellow in 2008 before joining the Breast team in 2010. When she talks about her work, especiatlly her research, she sounds as enthusiastic as if it were her first day of fellowship.

"I love research! My clinical work is mostly breast cancer diagnosis, so I'll do research late in the day or come in on weekends," she says. "When you have such a rich environment, so many cases, and good technology, it's satisfying and fun."

Dr. Wen's projects include studies on triple negative breast cancer, tumor infiltrating lymphocytes, and more.

#### **Triple Negative Breast Cancer**

Dr. Wen's research interest is in triple negative breast cancer (TNBC), defined as breast cancer that does not express estrogen receptor (ER), progesterone receptor (PR), and HER2. Usually high grade with aggressive clinical behavior, TNBC constitutes one of the most challenging groups of breast cancers due to the lack of an effective targeted therapy.

In a study published in Modern Pathology, Dr. Wen and colleagues investigated the genetic alterations in TNBC using the MSK-IMPACT assay and correlated mutation profile with detailed histologic analysis. The study identified the most common somatic mutations in TNBC. The study also found that TNBC with apocrine differentiation constitutes a distinct subset, characterized by a high frequency of PI3K pathway alterations similar to luminal subtypes of breast cancer.

#### **Special Histological Subtypes**

Triple negative breast cancer isn't one type, but rather a heterogeneous group of breast cancers that don't have ER/PR/ HER2 expression. According to the World Health Organization classification, there are more than 17 special histologic subtypes of breast cancer. Some special histologic subtypes are triple negative but indolent.

"For diagnosis, it's important to recognize those that are indolent because they might not need the same treatment as the usual triple negative breast cancer," Dr. Wen explains.

She is working closely with Jorge Reis-Filho, MD, PhD, Director of Experimental Pathology, to characterize these special histological subtypes, some of which have distinct genomic alterations. Metaplastic breast carcinoma (MBC) for instance, is a rare and aggressive disease that tends to be triple negative. Drs. Wen, Reis-Filho, and other collaborators sought to define somatic alterations and mutational signatures of MBCs.

They compared the genomic landscape of MBCs with triplenegative invasive ductal carcinomas and assessed WNT and PI3K/ AKT/mTOR pathway activity. Among their findings, MBCs were genetically complex and tended to have a high frequency of PI3 kinase and WNT signaling pathways alterations. That's unusual for a triplenegative disease and good news from a treatment perspective, since they're targetable alterations.

#### **Tumor Infiltrating Lymphocytes**

Dr. Wen's work on tumor infiltrating lymphocytes, which are usually seen in triple negative breast cancer and HER2-positive cancer, shows promise for near-term clinical applications. "We believe those lymphocytes play an important role in the immune system, helping our body to defend against tumor cells," Dr. Wen says. "They're a good sign, a predictor of better response to neoadjuvant systemic therapy and a better prognosis."

For one of her projects, she says she was honored to collaborate with medical oncologist Larry Norton, MD, Medical Director of the Evelyn H. Lauder Breast Center. They examined genomic alterations of tumor-associated leukocytes in breast cancers, suspecting these had alterations that played a role in disease development, just as the tumor cells do.

Dr. Wen explains the technical approaches: "We isolated tumorassociated leukocytes from fresh tumor samples using fluorescent activated cell sorting, performed targeted capture sequencing and whole-exome sequencing analysis

in the sorted tumor-associated leukocvtes, and compared the mutation profile with that in lasercapture microdissected tumor cells and circulating blood cells."

Drs. Wen and Norton along with other collaborators, including Dr. Reis-Filho and Breast Pathology Director Edi Brogi, MD, PhD – demonstrated that somatic mutations were indeed present in the leukocytes in a subset of primary breast cancers. This observation may have implications in the response to systemic treatments, including immunotherapies.

**66** We isolated tumor-associated leukocytes from fresh tumor samples using fluorescent activated cell sorting, performed targeted capture sequencing and whole-exome sequencing analysis in the sorted tumor-associated leukocytes, and compared the mutation profile with that in lasercapture microdissected tumor cells and circulating blood cells."



## A New Approach to Endocervical **Cancer Classification:**

Gynecologic Pathology Director Robert Soslow, MD, is working to replace current guidelines for endocervical adenocarcinoma.

By Hope Cristol

## **Research Spotlight ROBERT SOSLOW, MD**

Robert Soslow, MD, Director of Gynecologic (GYN) Pathology, has spent much of his career studying endometrial carcinomas, particularly papillary serous carcinomas and mesenchymal neoplasms. "I think when people think of me, they think of me as an endometrial guy," he says. In the past few years, however, he's taken on an entirely new research challenge. He hopes to scrap the 2014 World Health Organization [WHO] classification for endocervical cancer and help establish a "much better" alternative for pathologists.

Although Dr. Soslow routinely handles diagnostic specimens from the cervix, they hadn't piqued his research interest until relatively recently. Partly he credits his GYN colleague Kay Park, MD, who has long been dedicated to cervical pathology research. "She has truly inspired me and has been a coauthor on all my work in this area," Dr. Soslow says.

Another reason for his shift in focus? Like any great pathologist, he can't resist a challenge. When Dr. Simona Stolnicu, his friend and research collaborator in Romania, suggested they take on a big project on the cervix, he was in. With a host of other colleagues, they have been working to establish and validate the novel, proposed International Endocervical Adenocarcinoma Criteria and Classification (IECC).

One key aspect of these guidelines is the separation of endocervical adenocarcinomas into two categories: HPV-associated and HPV-unassociated. Unlike the WHO system, the IECC system considers etiology and biological behavior as well as morphology and would provide objective criteria that is easily translatable to clinical diagnostics.

#### A Closer Look at Gastric-Type Tumors of the Cervix

Gastric-type endocervical adenocarcinoma was described just a few years before the 2014 WHO classification. "It's like a prototype of cervical adenocarcinoma that is not related to HPV infection," Dr. Soslow explains. Although it makes an appearance in the 2014 classification, Dr. Soslow feels it got short shrift.

"A lot of people still don't know how to recognize that tumor type, and it's an important one," he says. Unlike HPV-associated adenocarcinomas or squamous cell carcinomas, which tend to have well characterized and readily identified precursor lesions, gastrictype carcinomas often don't. When there is a precursor lesion, it can be hard to recognize under the microscope.

"Screening was designed for HPV-associated lesions, not for gastric-type adenocarcinomas," Dr. Soslow says.

He adds that the latter is likely to become more prevalent. Today, non-HPV-related tumors represent only about 15% of endocervical carcinomas. The number is expected to rise as HPV-related cases decline due to better screening methods and the HPV vaccine.

#### **Research Highlights**

Dr. Soslow and his colleagues have laid some important groundwork for improved classification of endocervical

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adenocarcinomas. Examples include:

Interobserver reproducibility of the IECC system. Using a cohort of 75 endocervical adenocarcinomas, researchers compared interobserver reproducibility in the IECC and WHO systems. They found the former to be superior. For example, under the IECC system, 97% of endocervical adenocarcinomas had majority agreement, while 56% had perfect agreement. Under the WHO system, 75% had majority agreement, while only 10% had perfect agreement. These and other findings from the study were published online in June in the American Journal of Surgical Pathology.

Silva classification. In July of this year, Gynecologic Oncology published a paper that examined whether the Silva classification system can be applied to all endocervical adenocarcinomas. The system, which is based on stromal invasion pattern, stratifies these of Gynecological Pathology characterized morphologic features lesions into three categories corresponding to risk of metastasis and using surgical biopsy and cytology specimens, which can be used recurrence. The researchers found the Silva system was effective at with ancillary studies to improve diagnostic accuracy. Biopsies identifying patients at lowest risk of metastasis in HPV-associated showed pale or foamy cytoplasm and well defined cytoplasmic endocervical adenocarcinomas. However, the researchers also found borders; nuclei exhibited mild-to-moderate pleomorphism with that Silva is not applicable to HPV-unassociated adenocarcinomas. small nucleoli. Cytology revealed tumor cells with pale, foamy, and/ Gastric type morphology. Misdiagnosis of gastric-type cervical or vacuolated cytoplasm and well-defined cytoplasmic borders; nuclei adenocarcinoma is common, in part due to lack of awareness of its were moderately pleomorphic, with one or more nucleoli.

morphology. A paper published in May in the International Journal

#### WHEN TO USE IN-SITU HYBRIDIZATION TO CONFIRM HPV

If you need to confirm HPV infection you have two options. The first is p16 immunohistochemistry. The stain can indicate infection, but it is not entirely specific and does not indicate whether HPV is in the cells. "It is more of a surrogate marker for HPV," Dr. Park explains.

The second option is in-situ hybridization, an assay that recognizes the HPV genome. In a study published this year in The American Journal of Surgical Pathology, Drs. Soslow, Park, and others directly compared the methods to confirm the presence of HPV. The researchers found that in-situ hybridization was slightly more sensitive and much more specific than the p16 stain.

"We were the first to do a discipline comparison between these," Dr. Soslow says. "Now our go-to first step [to identify cells with HPV] is the in-situ hybridization assay rather than the p16."

#### WHAT'S IN A NAME?

Do you know why gastric-type adenocarcinomas of the cervix are so named?

"It's because these tumors have the same kind of mucin in their cytoplasm as you would find in the pyloris of the stomach," Dr. Soslow says. Here are some other things to know about these recently described tumors, compared to the usual type endocervical adenocarcinomas.

- More aggressive
- HPV-unassociated
- p16 immunochemistry negative
- Chemorefractory
- Significant risk of recurrence
- Worse 5-year survival rates



THE **EVOLUTION OF** MSK'S PATHOLOGY **FELLOWSHIP PROGRAM** 

The MSK Pathology Fellowship Program has changed in ways large and small over the years. Pathology's Director of Education, Kay Park, MD, is in a unique position to highlight key improvements.

By Hope Cristol

**From left to right**: Kay Park, MD, Melissa Murray, DO and Nora Katabi, MD



The Pathology Department's fellowship program is robust to say the least. At any given time, there are at least 45 fellows in the program, examining hundreds of cases, honing their diagnostic skills, and expanding the possibilities for their futures.

Seventeen fellows are in the oncological surgical pathology program. Another 28 are fellows in an array of subspecialties, including:

- Breast Pathology •
- Cytopathology ٠
- ٠ Dermatopathology
- Gastrointestinal Pathology •
- Genitourinary Pathology .
- Gynecologic Pathology •
- Hematopathology

- Molecular Pathology
- Thoracic Pathology

At the head of it all is Kay Park, MD, the Pathology Department's Director of Education. This newly created position in Pathology, which also exists in several other departments at MSK, tasks her with oversight of each fellowship. In addition, Dr. Park also centralizes

**66** As a fellow during each subspecialty rotation, you are learning from the best of the best, thought leaders in their fields, those who write the books," Dr. Park says."



Drs. Park (2004), Murray (2005) and Katabi (2006) (Fellowship)

#### **TEACHING HOW TO TEACH**

Excellence as a pathologist doesn't always translate to excellence as an educator. Kay Park, MD, aims to change that in her new role as Director of Education.

She is working to ensure that fellows at MSK are given more than just a top-notch education at one of the world's best cancer centers. She hopes to begin a series of faculty development lectures, working in conjunction with Monika Shah, MD, Chair of the Graduate Medical Education Committee at MSK, targeting areas like communication and feedback, burnout, wellness, and physician suicide.

"As physicians, we are taught the intricacies of medicine and disease, how to diagnose, how to cure and heal. Along this entire journey, we deal with people, not just patients but each other, trainees, colleagues. Nowhere along that path are we taught how to teach," Dr. Park says. "It is just assumed that doctors know how to communicate and teach effectively, and that is simply not the case. I am hoping to learn more about this topic and bring that knowledge to the wider GME community, as well as to my Pathology family."

#### A RECENT FELLOW'S JOURNEY

Matthew G. Hanna, MD. talks about his experience at MSK.

"I originally started at MSK as a medical student, which is unusual. They don't typically have a lot of medical students that rotate through the Pathology Department. I guess it was a stroke of luck that when I applied to a pathology elective, I was able to spend a month here. I rotated through the different subspecialties, interacted with different fellows, and felt comfortable and bonded with a lot of the faculty.

I was at Mount Sinai for my anatomic and clinical pathology residency, and Pittsburgh for my first fellowship, which was in informatics. Then I came here for the oncological surgical pathology fellowship. I recently completed it and am staying on as junior faculty, splitting my time between the Breast Pathology Team and informatics.

One of the things I say is that if you don't ask you won't find out, if you don't try you'll never know. I actually wanted to be a surgeon. My first experience with pathology was going to the lab to see what a specimen looks like downstream - because great surgeons are knowledgeable about that. It would have been a complete mistake if I hadn't ventured off to pathology and taken electives in it. The moral of the story: Put yourself out there and never knock something out of consideration unless you've experienced it yourself.

For anyone considering a Pathology fellowship, I would say the fellowship here will mold you into the best academic pathologist you could ever try to be."





My favorite part of the fellowship so far has been how humbling this experience is. Everyone is so knowledgeable, yet so friendly and grounded. They treat the fellows with respect and collegially and really care about our education. The amount of cutting-edge knowledge and experience the surgical pathology fellows will gain in one year is invaluable."

- Rami Alhassan, MD



My favorite thing about the fellowship here at MSK has been making new friendships and connections with people from around the country with different backgrounds and different experiences. Interacting with them, I feel as if they are able to impart some of their life experiences and wisdom to me, helping me to grow as both a pathologist and a person."

#### - Laurence Briski, MD



My favorite thing about the fellowship here is how passionate all the attendings are when teaching during sign-out. That passion is contagious and makes me want to learn as much as I can in each subspecialty."

- Nicholas Bercovici



This is a top-notch program in terms of clinical cases and faculty. The cases we see here, you will not see anywhere else with that frequency. The faculty are leaders in their field and are actively engaged in teaching and clinical research."

- Pavel Kopach



My favorite thing about my fellowship at MSK is the people with whom I get to work and knowing my patients are getting the best medical care available anywhere."

- Brie Kezlarian

#### VIEW FROM THE TOP: FELLOWSHIP PROS AND CONS

The Oncological Surgical Pathology fellowship is extremely valuable on its own, regardless of whether fellows go on to a subspecialty fellowship. Yet it's not always easy to recruit young doctors to the general surgical pathology fellowship.

"We have to get 17 really good people committed to coming here for a year and working really hard," Dr. Park says.

Other recruiting challenges, regardless of the type of Pathology fellowship: New York City is not an easy place to live, especially if you're from far away or have a young family. Also, Dr. Park says, the MSK Pathology fellowships are very rigorous and balancing work and life can be challenging.

Yet Dr. Park says there's no guestion that choosing a Pathology fellowship at MSK is worth every sleepless night, every diagnostic frustration.

"Every single fellow who graduates from here has always told me the same thing: What you learn here is beyond what you learn anywhere else." Dr. Park says. "They've also learned how to deal with all kinds of issues and problems. They've been through the trenches, and now nothing scares them. They can tackle anything that comes their way."

fellowship - related activities in the department as they pertain to regulatory and educational issues.

Prior to this role, Dr. Park spent around six years as Program Director for the fellowship. Breast pathologist Melissa Murray, The introduction of subspecialties is one of the most significant DO, stepped into the director role last year after serving as the shifts in recent memory, but other changes have also made the fellowship's associate director. Head and Neck pathologist Nora program stronger and even more appealing to prospective fellows. Katabi, MD, is now the associate program director. Together, they recruit and support fellows during an intensive, immersive period Less Time Grossing of training.

Any Pathology fellowship at MSK is incredibly challenging. Drs. Park and Murray share how the program has evolved to Dr. Park has never made light of that when communicating with keep up with high demands of the field as well as the Pathology prospective fellows. "I tell them how hard they'll be working. It took department itself, which generates more than 160,000 diagnostic me a full year after my fellowship to catch up on my sleep," she says. reports each year. Fellows also have incredible access to the department's resources, from its prominent pathologists to the tools they use. Introducing Subspecialization from MSK-IMPACT data to countless interesting clinical cases. Drs. Murray and Park are both former MSK fellows - in 2005 and "By the time they graduate this fellowship, they may have seen

2004. respectively. These were the first years of subspecialization more cases of a specific type of specimen or tumor than practicing sign out in the department, which impacted the general surgical community pathologists have seen in five years," says Dr. Murray. pathology fellowship. Instead of seeing vastly different cases every Unfortunately, MSK used to have a bit of a shadow over its day, these fellows could focus on one organ system at a time during hard work-high reward reputation. It was once a grossing-heavy three-week rotations. fellowship, which became a deterrent to some fellowship candidates. "As a fellow during each subspecialty rotation, you are learning The department made a concerted effort to change that.

from the best of the best, thought leaders in their fields, those who write the books," Dr. Park says.

If you were a fellow here in 2002, for example, the kinds of cases that came across your desk on any given day were different. How you were taught was different, too, says Dr. Park. "You were signing out all different types of cases with attendings who may not have been experts in certain types of cancers."

She uses the example of signing out cases, pre-subspecialization, with Victor E. Reuter, MD. He is currently the Vice Chair for the Pathology Department and Director of Genitourinary Pathology, the Genitourinary Pathology Fellowship, and the Pathology Core Facility.

"Dr. Reuter is a GU specialist, but you'd be signing out thyroid "With all the molecular technology that's ramping up at and breast cases with him. Don't get me wrong, he is a great general lightspeed, that's become an important part of fellowship education. pathologist and I would trust him with anything, but those areas We are trying to incorporate it more and more," Dr. Park says. are not his main research interests," Dr. Park says. "You would still The discussions at sign out have been moving toward

С	be learning a lot, but probably not at the same level as if you were
	signing out breast cases with a breast pathologist, like fellows do
1	now."

One solution was to hire more Pathologist Assistants (PAs) to do most of the grossing. Prior to 2012, there were about seven PAs. Today there are 14 PAs who cover three sites: Main Campus, MSK Monmouth, and the Josie Robertson Surgery Center.

Further, the grossing that fellows do today is more interesting and less onerous than in the past. "The fellows only gross about three weeks out of the year, and maybe five or six specimens during the day. They're usually large, complex specimens, as opposed to all the lymph node dissections and lumpectomies that are often rote and not particularly educational," Dr. Park says.

#### More Molecular Training

#### **MEET THE FELLOWSHIP DIRECTORS**



Kay Park, MD Director of Education, Department of Pathology



Melissa Murray, DO Director, Oncologic Surgical Pathology Fellowship Program



Nora Katabi, MD Associate Program Director, Oncologic Surgical Pathology Fellowship Program



**Darren Buonocore, MD** Associate Director, Cytopathology Fellowship Program



Diana Mandelker, MD, PhD Associate Director, Molecular Genetic Pathology Fellowship Program



Filiz Sen. MD Director, Hematopathology Fellowship Program



Hannah Yong Wen, MD, PhD Director, Breast Pathology Fellowhsip Program



Jean-Marc Cohen, MD Director, Cytopathology Fellowship Program



Jinru Shia, MD Director, Gastrointestinal Pathology Fellowship Program



Klaus Busam, MD Director, Dermatopathology Fellowship Program



Marc Ladanyi, MD Director, Genomic Pathology Research Fellowship Program



William Travis, MD Director, Thoracic Pathology Fellowship Program



The art of giving feedback is a key to leadership that may be underappreciated in the larger context of training Pathology fellows. In a recent presentation to fellows. Dr. Park offered these pearls of communication wisdom:

- Good feedback should be objective, timely, brief, and based on direct observation.
- While giving constructive criticism, stay neutral/non-judgmental. Use nouns and verbs, not adjectives and adverbs.
- Allow the recipient of your feedback time to reflect.
- Be specific with praise. Don't use vague terms such as "great job" and "pleasure to work with," which learners may come to expect regardless of work performed.
- Schedule follow-up and review to ensure your message was received and the fellow, or other learner, has had an opportunity to improve performance.

Contact Dr. Park for more information on effective communication strategies, including giving and receiving feedback. Dr. Park also has important information on how to recognize and avoid physician burnout. Email parkk@mskcc.org.

understanding the molecular underpinnings of cancer, and knowledge from The Cancer Genome Atlas (TCGA) and MSK-IMPACT are being incorporated in diagnoses. "This information is becoming increasingly more important in classifying tumors, as well as prognosticating and guiding therapy," Dr. Park says.

While all fellows will gain knowledge about molecular diagnostic pathology, a few will subspecialize in it. The Molecular Diagnostic Service (MDS) offers five Molecular Genetic Pathology Fellowship positions, and more will likely be added in the future. This is not only an effort to train future molecular pathologists, but also to keep up with the pace of demand of MDS.

#### What Hasn't Changed

Whether graduating fellows stay at MSK, join the world of academia, go into community practice, or pursue other Pathologyrelated paths, graduates of this fellowship are uniquely prepared.



**Robert Soslow, MD** Director, Gynecologic Pathology Fellowship Program



Snjezana Dogan, MD

Director, Molecular Genetic Pathology Fellowship Program



Victor Reuter, MD Director, Genitourinary Pathology Fellowship Program

"We've made tweaks to the program and improved the scheduling, but the philosophy of all our specimens going through the fellows' hands first hasn't changed in a long time," Dr. Murray says.

Another treasured aspect of the fellowship is the strong sense of community, forged by both the intensity of the fellowship experience and the attendings' dedication to the fellows' education. There's a reason that at the annual, hospital-wide, MSK alumni meeting, the second day is reserved for Pathology alumni. "We have hundreds of alumni coming back for it. That's how loyal they are because of the relationships that are forged here," Dr. Park says.

#### **MEET THE COORDINATORS:**

For additional information on our fellowship programs, please contact our Graduate Medical Education (GME) Coordinators, Nadia Tilden and Arisleyda Infante. (pthfellows@mskcc.org)



# CYTOLOGY **EDUCATION** AT MSK

## A legacy training program

By Hope Cristol

Nearly two hundred people have graduated from the cytotechnology training program at MSK since its official launch in 1961. Mary Ann Friedlander, the Pathology Department's Quality and Regulatory Manager, is a graduate, instructor, and former program director for the school (which is now the Hunter College Advanced Certificate Cytotechnology Program). She sat down with MSK Pathology Review to talk about the education, experience, and opportunities it provides.

#### What can a prospective student expect from the program?

The program feels like an internship or a year of on-the-job training. Students are embedded in the day-to-day operations of the laboratory from the very beginning and get a good sense of the work of a cytotechnologist at MSK.

Our students are exposed to rare and unusual tumors that they may not otherwise see in other programs or clinical laboratory environments. Students also benefit from the MSK cytotechnologists, cytopreparatory technicians, and cytopathologists who all play a role in the educational program.

From left to right: Mary Ann Friedlander, Handy Oen, Lu Wang, Rusmir Feratovic, Silvia Babore, Mihaela Kracun and Dorota Rudomina Not pictured: Tanzeer Chowdhury

#### Tell me about the career possibilities for graduates.

MSK graduates have historically obtained employment before or soon after graduation from the program. Most graduates obtain positions as staff cytotechnologists in either a hospital or commercial cytology laboratory. Over time, some cytotechnologists decide to further their careers as a laboratory supervisor/ manager. Some decide to work in private industry for companies that develop

technologies in cytopathology. Many cytotechnologists go back to school for an advanced degree or additional certification as a specialist cytotechnologist.

În some laboratories, cytotechnologists are also "physician extenders." They have been trained to assist pathologists in other areas including: morphologic assessment of FISH/CISH; pre-screening of AFB stains performed on tissue preparations; quantitation of HER-2, Ki-67, ER and PR IHC performed on histologic preparations via manual

## **1940'**s

Dr. George

TIMELINE Cytotechnology Training at MSK

Papanicolaou, inventor of the Pap smear test, visits MSK several times a week to provide cytology consultation and training.

### 1961 1964

MSK establishes

cytotechnology

program with

three available

a six-month

training

slots

Maximum enrollment in the program doubles to six students.

Program length doubles to 12 months.

The School of Cytology is formally established.

1968 1969

# 2005

NYSED passes a law requiring licensure of all clinical laboratory practitioners including cytotechnologists. Specific requirements for cytotechnology training programs are defined, including registration as a creditbearing program.

## 2012-2014 2015 2018

Collaboration begins between MSK and Hunter College to continue the operation of the only cytotechnology training program in metropolitan New York



or digital image analysis; and estimation of tumor volume and purity in tissue samples submitted for molecular testing. Involvement in these additional areas is dependent on the needs and training resources of the institution or laboratory.

#### Looking back on your time in the program, what stands out in your memory?

The training at MSK was memorable. Students studied alongside pathologists who were at the forefront of cytology

Affiliation agreement is established and approved between MSK and Hunter College.

Program enrolls 6 students-highest enrollment experienced since 1995.



From left to right: Sean McNair, Priscila Andrade, Rusmir Feratovic and Dr. Steven Einheber (Hunter College) Not pictured: Dr. Raj Murali and Dorota Rudomina

practice. The articles we were reading to learn cytology were often written by the same pathologists with whom we would sign out cases. I remember vividly being asked what I thought the diagnosis was on a case during a conference. You could not say you did not know, even though you were only a student. In front of the entire service, you had to be prepared with an educated guess and a descriptive explanation as to why you decided upon a particular diagnosis. While

intimidating, it was a lesson that reinforced our use of cytomorphologic criteria.

#### How is the program different now?

The cytology landscape has changed. The Pap test used to be the most common specimen type evaluated in cytotechnology labs, but this has now shifted to nongynecologic samples, particularly fine needle aspirates and touch preparations of core biopsy specimens.

Students are trained to evaluate all types of specimens and be knowledgeable about the essential ancillary tests that are now used to support the cytodiagnostic process.

Students are also exposed to the experience of on-site adequacy assessments of cytologic specimens, as well as on-site assessments provided via telecytology.

Students shadow cytotechnologists during FNA/biopsy procedures. They learn how to prepare and stain a FNA smear preparation and microscopically determine if a sample is adequate. With this experience, students get out from behind the microscope, interact with other healthcare professionals, and see the impact of cytology within the healthcare system.

**66** Our students are exposed to rare and unusual tumors that they may not otherwise see in other programs or clinical laboratory, environments."





From left to right: Leopold Koss M.D., Wanda Wolinska (CT), George Papanicolaou M.D., Grace Durfee (CT) and Andrew Ricci (CT)

# Hunter College?

In 2005, Education Law Article 165 was passed in New York State (NYS). The law requires licensure of cytotechnologists and stipulates requirements for cytotechnology training programs, including requisite coursework and registration with NYS Department of Education (NYSED) as an academic credit-bearing training program. In response to these new requirements, our School of Cytotechnology reached out to the City University of New York - Hunter College Medical Laboratory Sciences

#### **PROGRAM OVERVIEW**

The post-baccalaureate Hunter College Advanced Certificate in Cytotechnology program is an extensive 1-year program taught entirely at MSK. The current curriculum of didactic and microscopic instruction includes:

#### GYNECOLOGIC CYTOPATHOLOGY

Students are introduced to the principles of normal and abnormal gynecologic cytopathology.

#### **MICROSCOPIC EVALUATION 1, 2 AND 3**

Students become proficient at microscopic screening and correlating microscopic findings with clinical information, history, and concurrent histologic specimens.

#### **EXFOLIATIVE CYTOPATHOLOGY 1 AND 2**

Students learn non-gynecologic exfoliative cytopathology including anatomy, embryology, histology, and physiology.

#### RESEARCH METHODS 1, 2 AND 3

Teaches principles of experimental design, lab techniques, and data collection and interpretation.

#### CYTOPREPARATORY TECHNIQUES 1, 2 & 3

Students master smear preparation, cytocentrifugation, pipetting, liquid-based processing, staining, and coverslipping.

### How and when did the program become a collaboration with

Department to explore a collaborative training program. With perseverance, the affiliation and collaborative agreements were developed and signed between these two institutions. NYSED approved the new Hunter College Advanced Certificate in Cytotechnology Program in June 2014. Although now a Hunter College program, it remains a post-baccalaureate certificate program that is taught on-site at MSK, by MSK staff.

#### FINE NEEDLE ASPIRATION (FNA) CYTOLOGY 1 & 2

Students assess FNA specimens from numerous sites, including lung, breast, thyroid, salivary gland, liver, and pancreas.

#### CYTOLOGY LABORATORY MANAGEMENT AND **OPERATIONS**

Exposes students to regulatory and accreditation requirements that impact cytology practice, laboratory safety, guality assurance, digital pathology, billing/coding practices, and more.

# MOLECULAR DIAGNOSTICS: 9 Facts and Firsts

By Hope Cristol

The Molecular Diagnostic Service (MDS) is crucial to clinical and research efforts at MSK. It was established in 2006 through the consolidation of three pre-existing clinical laboratories: the Laboratory of Diagnostic Molecular Pathology (DMP), for tumor genetic testing; the Laboratory of Diagnostic Molecular Genetics (DMG), for germline genetic testing; and the Laboratory of Clinical Cytogenetics; with Marc Ladanyi, MD, as its chief. While the activities of the three components (especially DMP and DMG) have become more highly integrated, the old designations have persisted as a useful shorthand for these different activities of MDS.

Pathologists far and wide know about MSK-IMPACT, a groundbreaking, tumor-profiling multiplex panel that looks for abnormalities in hundreds of cancer-related genes. However, there's so much more to MDS – some of which may surprise those in the rest of the Pathology department, from fellows to other service chiefs. Dr. Ladanyi, along with Maria Arcila, MD, Director of DMP, recently shared some of these facts and firsts with *MSK Pathology Review*.



#### DR. MARC LADANYI'S EARLY DAYS IN MEDICINE

Dr. Ladanyi is, after all, one of the longest- serving pathologists in our Department. Here are some fun facts about his earliest days in medicine that even his oldest colleagues might not know.

- He completed three fellowships at MSK: surgical pathology, cytogenetics and research.
- He graduated medical school at 23, courtesy of an accelerated program at McGill University in Canada.
- The original roots of the MDS evolved from his early work overseeing clinical molecular testing in the lab of then Cytogenetics Service Chief Raju S. K. Chaganti, PhD.
- As a medical student, he earned the award for being the top student in his pharmacology class. "It might seem paradoxical for somebody who ended up going into pathology, but now what we do is so central to deciding which drug the patient gets," Dr. Ladanyi says.

With five fellowship positions, MDS has the largest Molecular Genetic Pathology (MGP) Fellowship program in the country led by Drs. Snjezana Dogan and Diana Mandelker. It has also become one of the most competitive.





**2** Of all the Services within Pathology, MDS has the highest proportion of female attendings. "There was no agenda behind it: we just had several excellent female MGP fellows who stayed on and have been successful in recruiting outstanding outside candidates who also happened to be women." Dr. Ladanyi says.

Fellows are strongly encouraged to write papers, given their access to MSK-IMPACT data and other clinical test data. For instance, last year, fellow Sounak Gupta, MBBS, PhD, mined MSK-IMPACT data with assistant attending pathologist Dara Ross, MD, to write a paper on amplification of PD-L1 in breast cancer. It will soon be published in the *Journal of Molecular Diagnostics*.



**4** In 2004, the precursor of MDS, the DMP Laboratory, was the first lab in New York State, and one of the first in the country, to have a clinical assay for EGFR mutations in lung cancer.

**5** In 2014, DMP was the first lab in New York State to get approval for a large-panel NGS assay: MSK-IMPACT.



6 In 2017, DMP was the first academic lab to have a laboratorydeveloped tumor profiling assay (again, MSK-IMPACT) cleared by the U.S. Food and Drug Administration.

The world-class clinical bioinformatics group of MDS, led by Ahmet Zehir, PhD, has implemented a bioinformatic algorithm called MSIsensor. It identifies patients with microsatellite instability using MSK-IMPACT data, which can be routinely checked across all cancers. The work was led by MSK computational biologist Sumit Middha, PhD, and molecular and gastrointestinal pathologist Jaclyn Hechtman, MD. This new capability of the MSK-IMPACT test has already become clinically very important, identifying patients eligible for immunotherapy.



**8** DMP was the first lab to obtain New York State Department of Health approval for HER2 status assessment by NGS (via MSK-IMPACT) in breast and gastric cancer. The effort, led by Drs. Ross and Arcila, enables routine screening of all cancer patients for potentially targetable HER2 amplification. **9** DMP was also the first lab in New York State to validate NGS-based clonality testing for clonal characterization, somatic hypermutation, and MRD assessment, an effort led by Dr. Arcila and molecular geneticist Khedoudja Nafa, PharmD, PhD.



### **Research** Overview MICHAEL H. A. ROEHRL, MD, PHD Inside the Lab of Michael H. A. Roehrl, MD. PhD

By Hope Cristol

Gastrointestinal pathologist Michael H. A. Roehrl, M.D., Ph.D., plays a central role in several initiatives that are bringing us closer to the future of precision healthcare. Dr. Roehrl, who joined the Pathology department in November 2015, is the Director of the Precision Pathology Biobanking Center, an MSK collaborative research center that obtained College of American Pathologists accreditation in 2018, and that includes efforts in big data analytics, development of new pathology technologies, and clinical trials.

He is also Principal Investigator of a research laboratory on the role of proteins in cancer using quantitative biophysical approaches. Dr. Roehrl traces his love for biophysics and protein chemistry back to his days as Ph.D. student at Harvard and MIT where he "spent fun years doing quantum mechanical nuclear spin gymnastics" with proteins and small molecule drug leads. That, of course, is a very simple description for his highly complex research in proteomics, which includes identifying proteomic biomarkers of solid tumors. But Dr. Roehrl can distill his laboratory's work in a way that just about

#### **EYES ON THE FUTURE**

The unique opportunity we have in pathology as a discipline is that we can take new technologies and approaches and change the way we diagnose, treat, and monitor disease. I can see that the next generation of tests and assays are going to be much more functional, meaning they will study the biology as it happens: looking at protein modifications, enzyme activity, signaling cascade states, or metabolite levels. We are not currently doing these things, but there's good precedent. For example, in microbiology we are testing how bacteria respond to drugs functionally. Something similar can happen in many diseases, including cancer. The fundamental technology is there, and it's really to up to us, to pathology, to develop approaches that use protein-based assays to functionally characterize disease. -Michael H. A. Roehrl, MD, PhD



anyone with an interest in pathology can understand - and get excited about.

He and his research team use a variety of technologies, such as biophysical, biochemical, molecular, and computer science tools, to measure, quantify, and characterize thousands of proteins in parallel. "We are studying various solid tumors, including colon cancer, pancreatic cancer, and a variety of other cancers," says Dr. Roehrl.

#### Increasing Knowledge of the Cancer "Antigen-Ome"

One focus of Dr. Roehrl's lab is the antigen-ome, or "the totality of all proteins that have become visible to the immune system," he explains. "My lab's research in this area began in autoimmune disease (like lupus and arthritis), but we soon discovered that the same mechanisms hold for many cancers." Dr. Roehrl has focused on the mechanisms by which a person's humoral immune system recognizes various proteins expressed in different cancers. The research could pave the way for using serological of markers of immune induction in diagnosis, treatment monitoring, and identification of new drug targets.

In a paper published in Oncotarget this year, Dr. Roehrl used proteomic profiling of antibody-inducing immunogens in colorectal cancer. He and his colleagues discovered that PSMA1, LAP3, ANXA3, and maspin are highly immunogenic proteins and may have a role in colon cancer pathogenesis and aggressiveness.

Dr. Roehrl employed a similar approach for research published in 2017 in the Journal of Proteomics. The focus was also on colorectal cancer, in this case advanced disease with liver metastasis, which has poor prognosis and a lack of known biomarkers. His lab discovered that the proteins OLFM4, CD11b, and ITGA2 are overexpressed in both primary colon tumors and liver metastases, and thus may have a

**66** I have postdocs in my laboratory who are highly motivated and scientists in their own right, and they do a lot of work that is very labor intensive and sophisticated - protein extractions, running mass spec, etc.,"

potential role in opportunities for colon cancer diagnosis, molecular classification, and therapy. Most recently, they have found that colon cancers can become immunologically "invisible" by switching off the immunoproteasome (showing that PSB7 protein levels can be used as an outcome-predictive parameter) and that OLFM4 may be clinically useful in predicting who may benefit from adjuvant chemotherapy and who may not.

Dr. Roehrl is also part of a multinational consortium that investigates the role of immune cell infiltration into cancers (Lancet, May 2018).



#### **Towards Proteogenomics**

Other areas of his laboratory's research include:

- Directly calling cancer mutations at protein level by informing "proteogenomic" mass spectrometry with next gen DNA/RNA sequencing
- · Developing an integrated epigenetic genome enhancerproteomic approach to cancer subtyping (with Mark Ptashne's group at SKI)
- · Deciphering mechanisms by which cancer cells vary widely in exosome secretion
- Developing tools and analytics for the large-scale international NIH/NCI-sponsored Clinical Proteome Tumor Analysis Consortium (CPTAC)

Excitingly, the field is moving forward at fast pace: On Oct. 1, 2018, Dr. Roehrl helped launch the brand new Human Proteome Project Pathology Pillar at the HUPO (Human Proteome Organization) World Congress in Orlando.

Dr. Roehrl makes a point of acknowledging his team, which he says are integral to successful outcomes on many levels - including the essential work of identifying and fixing any mechanical problems with the mass spectrometer, which is crucial to proteomics research. "I am honored to have postdocs in my laboratory who are highly skilled scientists in their own right, and they do a lot of work that is

very labor intensive and sophisticated - protein extraction, mass spec, computing/coding, etc.," Dr. Roehrl says.







Memorial Sloan Kettering Cancer Center is renowned as a leader in cancer care and research, but the institution's excellence is reflected by staff at all levels. Surgical Pathology Laboratory Manager Peter Ntiamoah, PhD, MPH, is no exception.

This year, Ntiamoah completed his PhD in epidemiology; he completed his MPH in 2011. He earned both degrees online, carving out study time in the small hours of the morning – after his three children were in bed, before his alarm went off at 5:30 a.m.

"I was born and raised in Ghana, where academic rigor is part of the system," Ntiamoah says. "You stay up late, you wake up early, you hit your books."

Back in Ghana, he studied hard to just to make it through high school, where you can't advance to the next grade level, much less graduate, without a test. Now Ntiamoah is driven by a commitment to patient care and a desire to play a role in reducing cancer rates.

# How did you become a laboratory manager in Pathology?

After I finished my undergraduate degree in biology in New York at Baruch College, I went on to teach at Baruch College High School. One of my mentors, who was a teacher, recommended me for a job in a reference lab. That was about 18 years ago. I've worked in a few different labs since then. I became a supervisor in one of them, then a manager at Quest Diagnostics. I joined MSK as a laboratory manager in 2013.

## What does being a laboratory manager involve?

Even though I don't come into contact with patients during my daily activities, they depend on what we do in Pathology. Specimen integrity must be maintained to ensure we are giving an accurate diagnosis to the patient. That is what I do as a lab manager – and part of that involves bringing the most current technology available in the industry to MSK. I also manage 79 employees.

## What are some things you enjoy about your role?

What I enjoy most is the ability to contribute to patient care. I also look forward to employee engagement. As a manager, I need to motivate my staff and get them highly engaged. That makes them more productive, motivates them to take more responsibility, and helps them enjoy what they're doing.

## What are some of your engagement strategies?

Engagement is twofold. One: You want to help your team achieve certain goals, so feedback is important. Two: You have to take interest in their professional development. I have an open-door policy, so if people want to talk about career development, their routine, work they do for patients, to understand certain concepts or how we do certain things, I'm always there to help them.

## Why did you choose to pursue graduate work in public health?

In 2008, I saw an ad in a journal (*CAP Today*) that was looking for laboratory technologists to volunteer their time in developing countries. I responded and went to Ghana. When I got there, I realized there were a lot of advanced cancer cases that we don't see in the United States. I asked the U.S. pathologists I was there with, "What can we do?" They told me there needed to be epidemiological studies to understand more about the environmental factors. That is how I decided to pursue public health.

Now that I have my PhD in epidemiology, I look forward to contributing to research about what we can do to help prevent certain cancers. We don't exactly know what triggers a gene to turn into cancer, and I am interested in data analysis to look into factors that may initiate carcinogenesis.

# New FACULTY





Matthew Hanna, MD

M. Gabriela Kuba, MD Assistant Attending Pathologist



Jamal Benhamida, MD Assistant Attending Pathologist











# Follow us on TWITTER @MSKPathology

3rd Quarter 2018 | 23



# **THE RISE OF MSK PATHOLOGY ON** SOCI@L MEDIA

By Hope Cristol

Many senior pathologists regard social media engagement as low on their priority list – if it makes the list at all. After all, their schedules are already packed,

even overburdened, with clinical work, research, teaching, conferences, and committees.

Nonetheless, social media platforms are becoming increasingly valuable to the field. Pathologists far and wide post images of deidentified cases to crowdsource diagnostic opinions. Early-career pathologists, for whom social media use is second nature, rely on social platforms to connect with others, learn about opportunities and institutions, and stay abreast of current research.

The trend toward social media use in pathology has not gone unnoticed, as evidenced by numerous papers on the subject over the years. Back in 2014, one headline in the *Archives of Pathology* & Laboratory Medicine read: "Social Media: Pathologists' Force Multiplier." In 2018, *The American Journal of Dermatopathology* published "Enhanced Worldwide Dermatology-Pathology Interaction via Facebook, Twitter, and Other Social Media Platforms."

Here at MSK, Pathology's Education and Communications Coordinator, Sarah Virgo, feels it's important for the department to have an active social media presence – even if many of our most accomplished physicians are far too busy for it. In May 2017 Virgo launched Twitter and Instagram accounts for the department.

"I've devoted 13 years to the Department of Pathology and wholeheartedly believe that we are the leaders of this field. However,

to maintain that status we need to be willing to evolve in all areas. Establishing a social media presence is part of that, especially because it helps our recruiting efforts," Virgo says. "We need to meet the next generation of top pathologists where they are today, and that's on social media."

Virgo manages the Twitter and Instagram accounts on her own, but she says faculty members are helpful in her efforts. "I often



receive tweets or ideas for tweets from staff," Virgo says. She adds that urologic pathologist Samson W. Fine, MD, has been especially supportive of efforts to build a Twitter presence for the department. Active on the platform himself (@rovingatuscap), he tweets about USCAP meetings, his colleagues' work, and MSK Pathology.

While the Instagram presence is small, @MSKPathology on Twitter has nearly 750 followers and counting. Virgo tweets regularly, highlighting MSK pathologists and their various achievements. Sometimes she'll tweet about an article from the *MSK Pathology Review*, as she did in August:

#FunFactFriday During research for the #MSKPathologyReview we uncovered volume stats dating back to year 1! Specimens: 5 in 1888 and 145.412 in 2017! Autopsies: 5 in 1888 and 34 in 2017 (with a peak of 518 in 1960). Find out more in our "History of Pathology" article out now.

Other times, Virgo tweets out information that's relevant to caregivers and cancer patients, as she did in September:

It's a team effort @sloan\_kettering and @ MSKPathology is proud to serve our patients! Even if you are not able to travel to New York City for an appointment, you can still receive the medical opinion of one of MSK's world-class pathologists. Visit https://www.mskcc.org/experience/become-patient/ appointment/pathology-consultation-request

Often, she will retweet the few MSK pathologists who are actively using Twitter, including Drs. Mark Ladanyi, Jennifer Sauter, Samson Fine, Edi Brogi and Kay Park. They are among the large and growing number of healthcare professionals using social media for workrelated matters - which has numerous potential benefits. As was highlighted in a paper in *Pharmacy and Therapeutics*, these benefits include: developing a professional network, increasing awareness of news and discoveries, motivating patients, and providing health information to the community. Physicians on social media can share and get instant feedback to their cases and ideas, discuss practice

# TWITTER FOLLOWERS **VOLUME GROWTH (2017-CURRENT)**



- management challenges, disseminate their research, and more. For @MSKPathology,
- Virgo's goal is to keep a wide, diverse audience in the loop on Pathology experts and research advances. Recent statistics show that 35% of our Twitter followers are pathologists, 18% are former fellows and alumni, 15% are medical students/non-MSK fellows, and 12% are non-Pathology faculty at MSK. (For more details, see pie chart.)
  - "I'm trying hard to highlight the impressive accomplishments of our faculty and staff and educate our patients about the diagnostic aspects of their care. Social media provides additional opportunities to do that," Virgo says. "I think that over the next decade, social media platforms will become even more important to connecting pathologists, educating people about pathology, and recruiting future fellows, staff, and faculty."



#### @MSKPATHOLOGY

#### Pathology @ MSKCC @MSKPathology

#FunFactFriday Are you interested in learning more about some of our #MSKPathologyLegends ? Check out the latest issue of the #MSKPathologyReview for the "History of Pathology at @sloan\_kettering" mskcc.org/departm





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#### Pathology @ MSKCC @MSKPathology

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#### Pathology @ MSKCC

Congratulations to our Surgical Pathology Manager, Dr. Peter Ntiamoah who recently earned his PhD in epidemiology. Peter is a dedicated and valuable member of the @MSKPathology team and we're very proud of this impressive achievement! #PeopleOfMSK



Pathology @ MSKCC

"Nothing in life is to be feared, it is only to be understood." - Marie Curie Congratulations to our graduating class of 2018! May your future endeavors always align

with the ideals of #MoreScienceLessFear Best wishes and well done! #MSKPathology #CO2018 #MSKPathologyAlumni



### Pathology @ MSKCC

#BreakingNews The CAP has awarded accreditation to the PPBC (Precision Pathology Biobanking Center) of @MSKPathology. Congratulations to Dr. Michael Roehrl and his entire team! Well donel



#### Pathology @ MSKCC @MSKPathology

#FunFactFriday Did you know that @MSKPathology 's first Chairman, Dr. James Ewing was born on Christmas Day and diagnosed his own bladder cancer in 1943? Learn more about the "History of Pathology at @sloan\_kettering " in the 2Q18 issue of the #MSKPathologyReview



thology @ MSKCC @ ted by Drs. Vaucher, Travis and @JL\_Sauter of : A 55 yo woman presented with pneumonia. Chest CT shows n in the right lower lobe.



hology @ MSKCC @MSKPathology - Sep 17 gratulations to Drs. Victor Reuter and Marc Rosenblum who walked through oors of @sloan ke ng together on their first day of surgical pathology ouv would not be the same without you



Pathology @ MSKCC @MSKPathology

Pathology @ MSKCC

Pathology @ MSKCC @MSKPathology

#### #FunFactFriday The founding editor of the journal Cancer, which debuted in 1948 as the first periodical devoted solely to pathology was @MSKPathology's Dr. Fred Stewart. Learn more about the "History of Pathology at @sloan\_kettering" in the 2Q18 issue of the #MSKPathologyReviev



Congratulations to @sirints ! His recently

Directions" in JCO Clinical Cancer Informatics

was among the most -read in 2018! Find the

Happy Lab Week from @MSKPathology! Our

celebration this week will include a wide

showcase the impressive and vital work

preformed by our dedicated lab staff here

variety of activities, events and educational lectures and will serve as a platform to

article here: ascopubs.org/doi/abs/10.120..

published article "Synoptic Reporting:

Evidence- Based Review and Future

### Pathology @ MSKCC

Exceptional study led by Drs. Xiao and Yabe from #MSKHemePath in collaboration with the Leukemia Service on the clonal evolution of core-binding factor AML. Find the article here: bloodadyances.org/content/2/13/1



### Pathology @ MSKCC

![](_page_13_Picture_36.jpeg)

![](_page_13_Picture_37.jpeg)

# Pathology @ MSKCC

our full feature in 1Q2019!

![](_page_13_Picture_40.jpeg)

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The first clinical laboratory of cytology, established at the Strang Cancer Prevention Clinic by Dr. Elise Strang L'Esperance, subsequently became the Cytology Service of @MSKPathology. Learn more in the latest #MSKPathologyReview and stay tuned for

![](_page_13_Picture_50.jpeg)

It was an exciting day here at MSK as our #ComputationalPathology Team at @MSKPathology unwrapped our new high performance computing cluster for our deep learning initiatives and applications in digital and computational pathology under the direction of @ThomasFuchsAI

![](_page_13_Picture_53.jpeg)

"Sarcomas make up only about 1% of all cancers, yet there are more than 50 different types." Learn more about sarcoma research being done with @MSKPathology 's Dr. Cristina Antonescu

Memorial Sloan Kettering Cancer Center 
© @sloan, kettering
"This is an exciting time to be doing sarcoma research. We are able to take discoveries
that we make about gene fusions & other mutations & immediately translate them
into new test that can guide treatments." Pathologist Cristina Antonescu

![](_page_13_Picture_57.jpeg)

@MSKPathology celebrates the first day of the #WordCup2018 by wearing their colors! #teamworkmakesthedream

![](_page_13_Picture_59.jpeg)

![](_page_13_Picture_60.jpeg)

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#### Inquiries about the MSK Pathology *Review* should be addressed to:

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

Phone: 212-639-5696

cooks@mskcc.org www.mskcc.org/departments/ pathology

Twitter & Instagram: @MSKPathology

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