Pathways to Excellence

URMC DEPARTMENT OF PATHOLOGY AND LABORATORY MEDICINE WWW.PATHOLOGY.URMC.EDU VOL 3 | ISSUE 4 | APRIL 2018

WHEN IT COMES TO TARGETED TREATMENT, SPECIMEN QUALITY MATTERS

David Hicks, M.D.

More than 100,000 tissue specimens are tested each year in Surgical Pathology.

Dr. David Hicks has been a longtime advocate for standardizing the steps leading up to the moment when a tissue is tested.

"The problem for the community, and even many clinicians, is that the pathology laboratory is a black box," said Hicks, Director of the IHC and FISH Laboratory. "Tissue goes in, the answer comes out, and you assume it's right."

One factor that he and some peers see as a major obstacle to effective molecular testing is the lack of national standards for pre-analytic handling of tissue.

There are known, documented effects of leaving specimens sitting unattended after being cut off from a supply of blood and oxygen (cold ischemia time). Tissue can become hypoxic which triggers the activation of enzymes that cause things to change.

"The problem for the community, and even many clinicians, is that the pathology laboratory is a black box."
-Dr. David Hicks

Until it's placed into formalin, tissue can start degrading after just one hour.

More than a decade has passed since the College of American Pathologists (CAP) mandated certain guidelines for breast specimens when a slew of bad HER2 test results were traced back to inconsistencies in how the tissue was first handled. Those rules were implemented in 2007, but there are still no federal regulations for other types of AP specimens.

Hicks was on the panel that established the national protocols and has taken things a step further at URMC by applying strict handling protocols to all types of tissue being tested for cancer and other diseases.

Slide-based pathology tests involve lots of prep work. The tissue must be collected, fixed, stained, and given to the pathologist for diagnosis. Any weak link in that chain can compromise the final test results, so staff are trained to use a time log to track each step of the process.

Nicole Truax (left) of Accessioning assists pathologists' assistant, Lee Ann Kushner, as she adds formalin fixative to a tissue specimen.

Why is this important? Hicks says it all points back to the patient. For example, an ER-positive breast cancer specimen can produce an ER-negative result if the tissue sits for too long before being placed into formalin or is cut too thick, leading to improper fixation. This has dangerous implications for a patient who could be treated based on an incorrect diagnosis.

The emergence of molecular testing has added to the need for consistency in slide preparation. That's according to Dr. Yi Ding, associate director of the Molecular Genetic Pathology Unit. She has noticed a difference in quality between in-house specimens and those that may not have been as well prepared. Since URMC serves as a reference lab for outside hospitals that don't do molecular testing, there's no way of monitoring the way those particular slides are prepared before they arrive.

Ding says the lack of standardization has already posed a problem for certain genetic tests, for example, an unusually high number of false negatives for fluorescent in situ hybridization FISH testing in lung cancer specimens. *(continued on pg. 3)*

CHAIR'S COLUMN

Dr. Bruce Smoller

Greetings to all from the doldrums of winter! Despite the gray and the cold, nothing has slowed down here in the department. I must open the column with a few sad announcements. Two long-standing members of our department, Dr. Janet Sparks and Ms. Judy Miller passed away during the past few months. Their service and dedication to the department will be missed, but their legacies will be remembered and persist indefinitely. More information about each is included later in the newsletter.

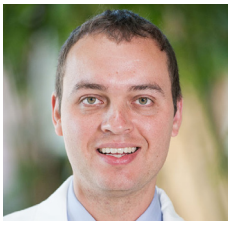
"The past few months have seen a flurry of activity on the part of our faculty."

I am very pleased to announce that Dr. Christa Whitney-Miller has agreed to take the position of Director of Surgical Pathology, following the decision of Dr. David Hicks to step down from that position after a 10-year stint. David will be serving as the Director of the Immunohistochemistry and FISH Laboratory, pursuing some clinical trials research work and beginning work on a new textbook of breast pathology. Dr. Whitney-Miller has been serving as the Associate Director of the Surgical Pathology division and as the Director of the GI Pathology section and has worked closely with David for several years in preparation for this transition. Dr. Jennifer Findeis-Hosey will step in to oversee the GI Pathology group.

The past few months have seen a flurry of activity on the part of our faculty. Several of our current faculty members have opted to relocate, for a variety of professional and familial reasons. Dr. David Zhou has already departed for Washington University in St. Louis, primarily to participate in a huge multi-centered grant regarding esophageal carcinoma. Dr. Jan Czyzyk will be moving to the University of Minnesota to pursue further work in diabetic kidney disease. Dr. Raul Gonzalez is headed to Boston's Beth Israel/Deaconess Hospital and Dr. Shobha Parajuli is leaving to re-join with her husband. Her next stop is not yet determined as of this writing. Finally, Dr. Yi Ding will be leaving to assume a position as Geisinger Clinic's Director of Molecular Pathology. We are sad to see them leave, but wish them all the very best with the next phases of their careers.







We have had a very exciting and productive recruiting season this year, in part based upon the unexpected departures of our colleagues and in part based upon the enormous rate of growth within the department. Dr. Dongwei Zhang will be joining our GI Pathology section upon completion of his fellowship at the University of Florida, as will Dr. Mark Ettel upon completing his fellowship at University of Michigan. Dr. Xiaoyan Liao will also join the GI team after finishing her training at Mt. Sinai Hospital in NYC.

Dr. Diana Agostini-Vulaj, one of our own recent graduates, will also join that rapidly expanding section. Dr. Zhiming Yang, coming from Los Angeles, will join the GU Pathology section in July and Dr. Huina Zhang is completing a breast/gyn pathology fellowship in Pittsburgh and joining that team in July. All come highly recommended and there is much excitement in the department about the influx of new faculty members with new ideas.

The enterprise development work continues apace as we move to consolidate anatomic and clinical laboratory testing across the network of affiliated hospitals. This provides URMC great opportunity for increase in volumes, along with generating not insignificant growing pains. We are temporarily increasing our footprint in surgical pathology at SMH to accommodate the increased workload, while at the same time busily planning for the move to the new laboratory facility at Bailey Road.

The critical statewide shortage in laboratory technical personnel has forced an accelerated pace for the consolidation efforts amongst our smaller affiliated hospitals and we are all struggling to keep up with the increasing volumes and decreasing workforce. Our Strategic Enterprise Committee has developed a process that is ensuring smoother transitions and ultimately, better performance as we evolve into a completely new practice model.

I remain optimistic that there is a bright future ahead for our department as we strive to adapt to a new world of medical economics. We continue to thrive in terms of clinical output, academic productivity and our fiscal state, based entirely on the hard work of our faculty and staff. I want to publicly thank the group for their dedication and perseverance during difficult times.

Pictured clockwise from top left: Christa Whitney-Miller, Diana Agostini-Vulaj, Dongwei Zhang, Huina Zhang, Mark Ettel, Xiaoyan Liao, and Zhiming Yang

WHEN IT COMES TO TARGETED TREATMENT, SPECIMEN QUALITY MATTERS (CONT.)

Our Surgical Pathology division implemented internal guidelines for how specimens of all types are timestamped during pre-analytic handling.

Quality control is important not only for pre-analytic slide prep, but also tissue block storage. This is especially vital for patients who have recurring cancer. If tissue from their original tumor was not well preserved, it can become difficult, or even impossible, to compare DNA sequencing of the new biopsy to what was tested prior. Without comparable results, the patient can't know early on if their new tumor has a different genetic makeup (i.e. high grade versus low grade). Add into the equation that the patient is from a different country, and the results become even more variable.

These are known obstacles to getting targeted treatment to patients early on.

"This kind of information really helps people make clinical decisions, and if we don't have high quality in previous specimens, it's kind of useless," said Ding.

Ding would like to see pre-analytic standards implemented on not just a national scale, but internationally. She believes this would improve the reliability of different genetic tests (i.e. FISH, Next Generation Sequencing) by producing results that are both reliable and comparable.

"They may look the same," she said. "They are all tissues on a piece of glass, but they are not the same. It's the procedure that can change it permanently and from a molecular perspective, if damage happened at an earlier stage, we may not recover enough information that can help."

From start to finish, URMC is leading the way in quality control for tissue specimens. It takes extra time, staffing, and resources to make a rapid tissue acquisition (R-TAP) program successful. Because of the extra fuss, other institutions aren't likely to follow suit despite the evidence of its importance. That's why Hicks is pushing for national protocols to be implemented in the near future.

"Until you mandate this and say you have to do this as part of your lab accreditation, people aren't likely to do it," said Hicks. "It has to have some teeth."

HISTOTECHNOLOGY PROFESSIONALS DAY

The URMC Histotechnology team observed Histotechnology Professionals Day on March 10 by wearing matching t-shirts that read, "Saving Lives One Slide at a Time."

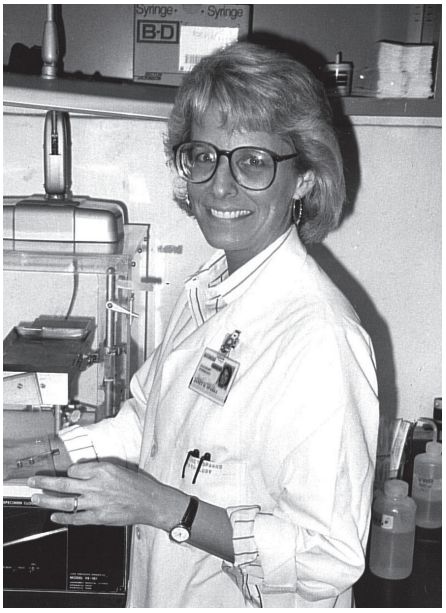
WEAR BLUE DAY

From left, Bethany Bushen, Drs. Aaron Huber (Pathology), Danielle Marino (Gastroenterology & Hepatology), and Jennifer Findeis-Hosey at the "Wear Blue" event to promote colon cancer awareness on March 2.

SINGING OUT

Mike Norton of Autopsy performed with his band, The League of Extraordinary Uncles, at a New Wave tribute concert at Strong Theater on Feb. 17. Photo by Keith Bullis.

JANET SPARKS, PH.D. WAS A MODEL SCIENTIST AND MENTOR TO MANY



Dr. Janet Sparks in her research lab.

Her colleagues have described her as a hidden gem, a well-kept secret, and even "human dynamite." Dr. Janet Sparks, whose life ended suddenly in December 2017, had a career at URMC spanning more than three decades. Her accomplishments and legacy as both a researcher and mentor continue to impact those who had the chance to work alongside her.

Janet began her career as a medical technologist at the University of Pennsylvania, where she earned bachelor's degrees in medical technology and biology and, later, her Ph.D. While she ultimately pursued basic research, having a background in the clinical labs helped shape her perspective and understanding of disease. Janet met her future husband, Dr. Charles ("Charlie") Sparks, while she was working as a med tech at U. Penn. They were married in 1977, starting a longstanding personal and professional partnership. Both were hired onto the Pathology faculty at URMC where he worked primarily as a clinical pathologist and she ran the Sparks research lab. The two collaborated on projects related primarily to cardiovascular diabetes. Their working relationship was built on mutual respect, explained Charlie, who says Janet was a devoted mother to their three children in addition to taking her work very seriously. Having the opportunity to work as a husband-wife team was, as he says, a privilege.

"When two people work together that closely, it could be good or bad," said Charlie. "We would only argue about science so that by the time we got home, there was no time to argue about anything else."

They continued this work after moving to Florida and split time between living there and at their longtime Pittsford home. At the time of her death (related to complications related to a myocardial infarction) the pair had a research collaboration with the University of South Florida. Janet had submitted an NIH grant that, at the time of this writing, was still awaiting approval. Charlie says he hopes to continue the work in her honor.

"I felt very good about the research we were doing and I would like to see it completed," he said.

Across the University, many former colleagues and trainees have shared their memories of Janet – describing her as kind, driven, and a dedicated scientist.

One of her many mentees over the years was Dr. Jim Corsetti. He first crossed paths with her as a resident. When she saw that he was scrambling to find time to complete research experiments, she gladly jumped in to help, volunteering her time and lab space to run experiments for him.

"There wasn't an awful lot in it for her except the satisfaction of helping somebody and getting them to a place where their career was more established," said Corsetti, who credits her with teaching him the many nuances of lipids and lipoproteins, which he continued to explore during his career.

"To degree that I've gotten good in those areas, it certainly was she that brought me there," he said. "She was so good in the lab and very generous with her time."

Janet also mentored Dr. Linda Schiffhauer during a teaching fellowship. In addition to being a role model, Schiffhauer was happy to call her a friend.

"She was a great mentor and advocate for me in so many ways when, in my career, I probably needed it the most," said Schiffhauer. "She was all that you could ever want in a mentor."

Those who knew her remember Janet's enthusiasm for nutrition and exercise. She would get up before dawn to make coffee and hit the gym before heading into work. Her energy was contagious.

> "She was so good in the lab and very generous with her time."
> -Dr. Jim Corsetti

"She was most passionate about her research," said Joanne Cianci, who worked in the Sparks lab for more than 20 years. "Her work was a huge part of what she was, but she cared about people and established a culture of complete trust."

Janet was very well known internationally, being listed in both *Who's Who in America* and the world. There will be a memorial tribute in *The Journal of Lipid Research*. She sat on numerous review committees, including for the NIH. She was quiet and humble which is one reason why she was better known internationally than locally.

In spite of her own skill and accomplishments, those who worked alongside Janet in the lab say she was a very hands-on instructor; a daily coach who always sought to encourage and elevate her trainees.

This quality left an impression on many, including Dr. Thuy Phung who had Janet as her PhD thesis advisor and worked in Sparks lab for four years.

Phung had never heard of Janet until she was sitting in the office of the MD/PhD director at the time. He suggested working with Janet because she was a well-hidden secret. What did he mean by that?

"He said that she was highly valuable and skillful, but not well known," said Phung. "She was talented and humble as well, which to me is a virtue."

In this way, she modeled what it meant to be a good scientist, fueled by constant curiosity, Phung explained.

"She was doing experiments even until the last days."

IN MEMORY: JUDY MILLER (1953-2017)

Few people in our department had as much experience or influence working in the lab at URMC as Judy Miller. She died unexpectedly in December 2017 just months after retiring from the Flow Cytometry Laboratory – a lab that she helped build from the ground up.

Judy came to the University in the 1970s after graduating from University of Buffalo with her medical technology degree. She and her family lived in the Buffalo suburb of Tonawanda, but there were more job opportunities in Rochester for med techs. This ultimately brought her, and her younger brother, Bob Miller, now chief supervisor of Chemistry and Hematology, to URMC. He says she was the reason he chose this career from day 1.

Judy started working as a med tech in the Hematology Lab, which at the time included bone marrow testing. She eventually became the morphology expert and trainer for reading blood smears, teaching many of the techs who worked in the lab over the years.

Rosemary Ziemba-Ball, now director of Finance, first became friends with Judy while both worked in Hematology. In 1979, they were part of a core team that implemented the medical center's first computer-based lab information system, called Meditech. This was a huge task that required lots of overtime, so they used the money to pay for a trip to Hawaii.

In the 1980s, the Bone Marrow Lab was broken off of Hematology and moved onto the second floor. It was combined with Flow Cytometry, a novel new testing method that was first used for research but later applied to clinical use. Judy moved to the new lab and oversaw bone marrow and special stains there for many years. She was later promoted to tech specialist and, ultimately, supervisor of the Bone Marrow/Flow Cytometry Lab.

Her influence as an instructor and colleague continues to be felt by many who had the opportunity to work with her.

"Judy always advanced in her role and was a source of knowledge in training techs and residents," said Ziemba-Ball. "Her opinion was also very valued by the attendings."

While dedicated to her job, Judy's family was always her first priority. She was the proud mother of one grown son, Eric, who now lives and works overseas in Germany. She loved to travel and the two had recently toured Europe together.

Judy Miller, shown at right, started her career in the Hematology Lab at URMC.

Melissa Allen, now director of Operations, first met Judy while she was a med tech training in Flow. She describes Judy as a patient teacher who enjoyed taking people under her wing during the learning process.

"She was very much a people person and had an even keel about her," said Allen. "She really wanted to make sure people got the fundamentals of what we do and why we do it."

Many describe her as easygoing, and someone who instantly made others feel comfortable. This served her well when she had the chance to be at patients' bedsides for bone marrow draws. It often meant comforting pediatric or leukemia patients during an uncomfortable procedure.

Outside of work, Judy volunteered at CURE Childhood Cancer Center, educating others about bone marrow testing and the role of the lab in patient care. She also volunteered with Take-Your-Child-to-Work-Day on several occasions.

Her brother, Bob, says she will be remembered not only for her skill and experience, but the way she made people feel. "People will remember how friendly and easygoing she was. How easy it was to get along with her," he said. "She could talk to anybody and relate well to people. That, her knowledge base, and her ability to teach are things that people remember her for."

FOCUS ON FACULTY: VICTORIA ZHANG, PH.D., MBA (CONT.)

Zhang spearheaded the effort to create a new national division: Mass Spectrometry and Separation Sciences. She represented the AACC in delivering public comments on laboratory developed test oversight issues to the FDA. She was invited to be the sole clinical chemist representative on the "Cancer Moonshot" APOLLO Project Technology Working Group. In addition, Zhang is the founding faculty chair of the Asian Pacific Working group, a global lab quality initiative.

These experiences have helped equip her to take on the challenge of spurring growth and integration in her current role. As she explains, teams within the clinical enterprise have complementary skills: Pathologists and medical directors at affiliated hospitals use their broad knowledge to serve the specific needs of their local communities. Meanwhile, the flagship medical center has experts whose specializations can provide in-depth insights into focused areas. By providing access to these experts and resources from the medical center, Zhang envisions a wide-reaching service that is mutually beneficial to the institution and its affiliates.

"The ultimate goal of the lab enterprise is to have an integrated and synergistic system to serve our patients and enable UR Medicine to become the care of choice in this region," she said.

Outside of work, Victoria is experienced in mixed martial arts and ballroom dance. She collects stuffed animals from conferences she attends around the world. Her partner, Kirk, is a vice president executive veteran of the video game and high tech industry. Together, they enjoy watching historical biographies, animated movies and "nerdy" TV shows like "The Big Bang Theory." Her personal motto is, "For whatever you do in life, do it like you mean it!" She lives in Brighton.

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FOCUS ON FACULTY: VICTORIA ZHANG, PH.D., MBA

In her daily work, Dr. Victoria Zhang has one foot planted in strategic planning and the other in what she calls the "real world" trenches of clinical lab operations.

Her role as vice chair for clinical enterprise is focused on developing a vision and strategies for standardization and efficiency in the UR Medicine Labs network. This includes an ever-evolving plan to broaden and support growth within the network.

"I think people in this region deserve, and should have access to the same quality of care and clinical expertise as we have in Rochester," she said. "That's the vision of the enterprise."

While actively seeking opportunities to make this vision a reality, her other foot is planted firmly in the lab itself as director of the Clinical Mass Spectrometry and Toxicology Lab, and Associate Director of Clinical Chemistry. Staying involved with daily clinical work and front line staff has helped her appreciate the daily challenges of clinical operations and inform her long-term vision for the enterprise.

Zhang first came to the U.S. for graduate school after studying microbiology and engineering in China. She earned her Ph.D. in biochemistry and bioinformatics from the University of Minnesota specializing in proteomics and biomarker discovery. She then completed a clinical chemistry fellowship at Harvard Medical School, combining her interests in healthcare and translational research. She later earned her M.B.A. from the Wharton School at the University of Pennsylvania.

Since joining the URMC faculty in 2011, she has taken on key leadership responsibilities both within the department and in national and international organizations. She is the past chair and treasurer of the American Association for Clinical Chemistry (AACC) regional section and the past president and advisor of the North American Chinese Clinical Chemists Association (NACCCA). *(continued on pg. 5)*

THANK YOU FOR YOUR SUPPORT!

We have been fortunate to receive philanthropic support from many individuals, allowing us to maintain and accelerate vital clinical, educational, and research initiatives. If you are interested in making a tax-deductible gift today, or as part of your estate plans, please visit www.pathology.urmc.edu and look for the "Make a Gift" button, or contact Matt Haag at 585-276-3638 or matthew.haag@rochester.edu.