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This year marks my fifth anniversary as the Carl V. Weller Professor and Chair of the Department of Pathology. The past five years have been eventful! We have established three new divisions in the department: Quality and Health Improvement, Molecular Pathology, and Experimental Pathology. In addition, our leadership structure was expanded to include two Vice Chair positions: Vice Chair for Academic Affairs and Vice Chair for Clinical Affairs. Perhaps the most important change we have experienced, however, is the relocation of our clinical laboratories, administration, and education units from various sites across Ann Arbor to newly renovated space occupying 140,000 sq. ft. in four buildings at the North Campus Research Complex (NCRC). More than 500 people transitioned to the NCRC over the summer of 2018. Our Pathology Relocation and Renovation (PRR) team ensured this move was a success and that patient care was uninterrupted. This team is now focused on renovations for our core laboratories and stat services at the University Hospital, which should be completed over the next 3 to 4 years. You will be reading more about the PRR project in this issue.

As we look to the coming five years, the Department’s focus will be to utilize our state-of-the-art facilities to increase collaboration and discovery, enhance our use of digital pathology and precision medicine for optimal patient care, and to provide the best training possible for our residents, fellows, graduate students, and postdocs. Together, we will forge the Pathology Department of the Future!

Charles A. Parkos, MD, PhD
Carl V. Weller Professor and Chair
Department of Pathology
Michigan Medicine
Navigating Change
A flurry of last-minute preparations and problem solving consumed much of 2018 as the Pathology Renovation and Relocation team and strategic move captains prepared for the relocation of faculty, staff, trainees, and all the implements of a modern clinical pathology facility to the North Campus Research Complex. Throughout, the move captains ensured their laboratories, faculty neighborhood groupings, trainees, and administrative staff transitioned smoothly to Pathology’s new home 2.8 miles from the University Hospital. Over a period of approximately 3 months, these teams converged from locations across Ann Arbor into a consolidated 140,000 sq. feet state-of-the art space designed for collaboration and to embrace the future. For the past year, the teams have been adjusting to the new space, adapting to new workflows, and taking advantage of the opportunities presented.

FIRST IMPRESSIONS
The first thing many noticed about the new space is the natural light! Instead of being in basements or in crowded, internal laboratories without any windows, the laboratories have floor-to-ceiling walls of windows looking out at the park-like setting of the North Campus Research Complex. The space is bright and inviting. The laboratory bench space is designed to be movable, so it can be easily reconfigured as future technologies require new workflows. The labs are equipped with many familiar pieces of equipment, but also many newly-acquired pieces to enhance the capacity of the labs. Each laboratory was carefully planned using Lean Facility Design for optimal workflows and to encourage mentor/trainee interactions and teaching. In addition, the nerve centers for each lab are housed within the laboratories with clear line-of-sight between managers and the bench staff.

Larger-than-life patient stories posted on walls in both laboratories and hallways remind all that excellent patient care is the focus of our work. Hallways and common spaces are enhanced with locally-created artwork. Conference rooms with glass walls line the exterior walls across from glass-walled offices, ensuring both offices and conference rooms are cheerfully lit. While not all offices are along this corridor, the majority are just steps away from natural light. Small offices make room for many common areas, conference rooms, and other work spaces to encourage collaboration among faculty and to enhance communication between faculty, trainees, and staff. A favorite common area to all is Central Park, complete with a long plank-wood dining table in a kitchenette adjoining high tables, soft seating, and a long fireplace, with natural greenery and artwork. This warm and welcoming space is shared by all of Pathology and is the heart of the new facility.

ADJUSTING TO CHANGE
The beautiful facilities provide the framework for success, yet they also require staff to adapt to the new environments. In the molecular pathology division, six laboratories...
that were scattered across Ann Arbor, each with separate cultures and norms, are now co-located in contiguous molecular laboratories. The new space provides an opportunity to have back-up equipment available in case of equipment failure.

“The move is a win for the Molecular Division,” stated Dr. Thomas Giordano, Director of the Division of Molecular Pathology. “We were in Traverwood (an off-site facility),” stated Dr. Lina Shao, Director of Cytogenetics, “which was isolating. Now we are at the NCRC and are more fully integrated. We feel like we are a real part of the Department. The move had a positive impact for our lab.”

The anatomic pathology laboratories now require patient specimens be transported between the UH and NCRC. This created an entirely new workflow, requiring additional staff, and a complex specimen tracking process. Pathology Informatics and the Division of Quality and Healthcare Improvement elegantly solved the tracking challenges with PathTrack™, which was featured in last year’s edition of *Inside Pathology* Magazine. “When we first moved in, PathTrack wasn’t able to keep up with the increased demand, so the application did not work efficiently as the number of users increased,” explained Dr. Ul Balis, Director of Pathology Informatics. “So the team stepped up, not only solving that architectural problem, but also extending certain features. Now we are deploying PathTrack to multiple clinical sites at the University Hospital and the Taubman clinic.” PathTrack has attracted significant attention from other organizations as well.

With the more open and collaborative environments, faculty and staff also faced adjustments. Administrative staff are located in close proximity to the faculty providing more opportunities for interaction and discussion, improved communication and engagement. Faculty are now part of multi-disciplinary neighborhoods, which has led to opportunities to reach out to neighbors for quick case conferences or for impromptu meetings at multi-headed microscopes. Residents and fellows are located in bright, modern space at the heart of the laboratories, adjacent to the sign-out areas and near the faculty suite. Robust educational experiences were built into the layout of the laboratories and sign out areas. While the overall environment for our trainees significantly improved, the relocation also meant that the residents and fellows needed to commute between the hospital and the laboratories for rotations in the stat labs and to attend some seminars and multi-disciplinary conferences. Digital signage prominently displayed throughout the space includes both inbound and outbound bus arrival times to assist in this commute. Pathology Informatics is located just down the hall from the faculty suite and administrative offices, which enhances service delivery and access for technical support. “Having MLabs right here with us makes it much easier to reach out to the outreach team themselves,” said Dr. David McClintock, Associate...
Professor of Pathology Informatics and Assistant CIO for Michigan Medicine. “We are close to the billing team and both AP and CP operations as well as Administration,” added Kathy Davis, Administrative Director of Pathology Informatics.

BUILDING ON SUCCESS
Now that we have been at the NCRC for one year, people are settling into their new space and routines and are beginning to look to how they can take full advantage of our facilities.

“The molecular laboratories have come together and the changes we have seen with the molecular lab and our work are significant,” stated Dr. Shao. “In cytogenetics, we were manually extracting DNA. The molecular lab, however, uses robots to do DNA extractions. Now we are able to use their resources. We validated DNA extraction by robots for both blood and bone marrow. That saves us a lot of work.” In addition, the new microarray laboratory layout allowed for other efficiencies. Rather than being in rooms on opposite ends of the hallway, the pre-PCR and post-PCR rooms are now in adjacent air-pressure-controlled environments to reduce contamination possibilities. Technologists simply move specimens a few steps rather than boxing them up and walking down the hall. Use of a new Thermotron eliminated the need for a cold room to process specimens, reducing exposure to caustic chemicals. Specimens are now safely processed in the contained, vented, box-like Thermotron.

“Now that we have the move done,” stated Dr. McClintock, “we are starting to work on new projects. We have some very good potential pathology solutions in the pipeline that this lab has enabled us to do. We have new, dedicated space for development for the future.” “This new space allowed us to be more productive with the precision medicine project,” agreed Dr. Balis. “One example of this is the whole slide-viewer technology developed by Dr. Jerome Chang, which has become the national standard now for the NCI/NIDDK for viewing whole slide images. That was a huge win!”

As Pathology continues to integrate within the new space and adjust to new possibilities, a new project has been initiated – the renovation of the STAT and core laboratories at the University Hospital. This four-year project will continue to both challenge us and help us improve patient care as we look to the future. The PRR team learned a great deal from the relocation of our laboratories to the NCRC. Many of these lessons learned are being applied to the University Hospital Project. We are looking forward to the possibilities for enhanced patient care that will emerge as a result of these renovations.

Photos (clock-wise): Top—residents work in the new, extensive, grossing lab; waiting area at the entrance of the department, building 35; the molecular pathology laboratory.
The Department of Pathology has been in its beautiful and efficient new space for ten months. Every day we learn more about the ways our work is improving due to the complex and well-thought-out design. That is the greatest success. As the clinical lead for the Pathology Renovation and Relocation (PRR) project, I have had the honor of helping to shape the future of Pathology at Michigan Medicine for the foreseeable future. Using Lean Facility Design techniques, the PRR project team facilitated the design and activation of 140,000 square feet of space at the North Campus Research Complex (NCRC), with all non-stat clinical laboratories, trainees, administration, and affiliated faculty and staff relocated over the summer of 2018. Along the way, the PRR team, of which I am a part, encountered many challenges and barriers, all of which were overcome through determination and a commitment to ensure the best possible outcomes for both patients and the department. This was a once-in-a-lifetime project for all of us and I think one of the things, in the midst of all of the challenges, that we tried to reinforce to people is that you will never have this opportunity again — to design space the way that is going to be best for the patients, the way it is going to be most efficient in accomplishing our jobs, and ultimately, provide the best level of care for our patients.

Would the building be finished on time? Would we be able to get the specimens here in a timely manner and be able to track them along the way? Is our courier plan sufficiently robust? These and a myriad of other issues were at the forefront of our minds as we worked to ensure a successful relocation of the pathology laboratories to the NCRC. We spent significant amounts of time and energy to make it happen. In the end, we efficiently and safely coordinated the moves and we continue to have a very robust courier system and specimen tracking system.

To accomplish these goals, there were extensive communications and interactions between the PRR project team, the department, the campus, architects, contractors, designers, and others. We were in constant communication with them. We had regular meetings, informal face-to-face discussions, phone calls, and texts to ensure that all were on the same page, and to closely coordinate and prioritize mitigation strategies when issues were
identified. In addition, the team worked closely with the department, laboratories, staff, administration, and faculty. Key to our success is that the labs were outstanding in this whole process, from leadership to staff, across the board. They excelled in organizing and articulating the validation timelines that they needed so that we could safely and efficiently coordinate the moves. The PRR team also worked closely with Metro Delivery (Ann Arbor, MI) to ensure the right schedule and the right kind of vehicles would be available to shuttle patient specimens between University Hospital and the new laboratories. Metro did a great job in accommodating all of our requests and needs. We had many unique requirements as a customer and they were very, very accommodating and helpful and made great suggestions to help us improve our processes.

Across the department, staff have done an exceptional job in developing workflows for packaging, transporting, and tracking specimens between UH and the NCRC. Everything is happening as smoothly as possible. Everyone has done an excellent job. The Division of Quality and Healthcare Improvement (DQHI) and Pathology Informatics (PI) played a major role in this success with the development of the PathTrack asset tracking system. This critical system enables us to know where specimens are during each point in our processes.

However, there still are challenges that have not yet been resolved. The things that have persisted are issues related to the building, and that has been a little frustrating. We are still working our way through some unanticipated issues—including adjustments and enhancements to heating and cooling as well as appropriate air-balancing and airflow. These issues were my greatest surprise in the project. The PRR Team worked hard to have success over the parts of the project for which we had direct control, but other aspects were more challenging. As it turns out, the coordination during design between the architects and engineers was not as strong as we were led to believe. This ended up causing rework and challenges during move in, some of which persist today. This was not something we anticipated or predicted, and presented a lesson the PRR team learned as we begin to tackle the next phase of the project – the UH renovation for the core labs.

Communicate often and broadly. The key takeaway from this project is that you cannot over communicate. People hear and interpret messages in various ways. People handle change differently and as such, the messages that go out need to take different approaches to adapt to different audiences. This was a major change that had significant cultural impacts on the department. We expected that there would be an impact to our culture, but it was much more significant than we anticipated.

We are working to learn from this and take that lesson into the renovation of UH, and address some of these cultural issues through communication. There is a concept from Taiichi Ohno, the father of the Toyota Production System, that states, “Having no problems is the biggest problem of all.” When “everything is fine” and remains “fine” throughout the planning process, that is an indicator that a group may not be digging deeply enough, and that more proactive communication is needed. Some groups are a little shyer or hesitant to share or to talk about how things are not working. So we need to be proactive in having those conversations and making sure that everyone is moving in the right direction.

As the UH renovation project moves forward, communication will be key to better understand challenges, to build better relationships, and to increase awareness, so that the team is not making any assumptions. That is a challenge, but also a tremendous opportunity. I appreciate the trust that the department put into me in allowing me to be in this position to help. I am proud of what we have been able to accomplish.
The newly-renovated workspace at NCRC afforded the opportunity for the department to purchase original artwork, supporting local artists. Working with Joy Naylor and Diane Bennett of Ann Arbor-based Distinct Design and U-M Interior Designer, Kate Stahl, an artwork committee chose pieces inspired by nature to complement the complex’s park-like setting.


Among the artists are Art Prize winners, including Lynda Cole, whose work in oil pigment stick, cold wax, and encaustic are featured outside the chair’s office and the Division of Quality and Health Improvement. Cole, along with several other of our featured artists, is a co-owner of the WSG Gallery on Main Street in downtown Ann Arbor.

Artist, Connie Cronenwett says that she feels most like herself while she is painting and that the process gives her the opportunity to really observe. “It’s like you lose a certain part of your ego that just takes a walk and you’re so engaged with that process and it’s very challenging and it’s freeing at the same time.”
Left Photo: Connie Cronenwett and Elizabeth Schwartz take in “Ives Creek” by Susan Morosky.

Top Photos (clock-wise): Connie Cronenwett’s series of oil on canvas hangs in the work café; Like many of the chosen artists, Lynda Cole is a co-owner of the WSG Gallery on Main Street in downtown Ann Arbor; Jill Stefani Wagner’s series of Ann Arbor landmarks is spread throughout the faculty suite.

Committee Members

Christine Baker

Kristina Martin

Duane Newton, PhD

Charles Parkos, MD, PhD

Christine Rigney

Kate Stahl

Elizabeth Walker
Artwork on display serves as a daily inspiration for all those who work in its midst and has inspired at least one NCRC tenant to become an artist himself, as Duane Newton has taken up watercolor lessons.

Jill Stefani Wagner uses her work as a way to document her community. “I like to capture what life is like now. Not idealized. I always put the telephone poles and everything in because I want it to be a record,” she says. She adds that the support she has had from hospitals purchasing her art has been much appreciated and it’s a way of keeping art alive, especially after the residential market basically disappeared back in 2008. Most of the artists featured in the new space are from Ann Arbor and all are from the Midwest.
New Frontiers in Pathology
Oct 31- Nov 2, 2019
Annual two-and-a-half day, state-of-the-art conference, designed to meet the educational needs of pathologists, residents, and fellows. AMA PRA Category 1 CME and SAMs credits offered.

17th Annual Pathology Research Symposium
Fall 2019
This Molecular and Cellular Pathology graduate student event showcases research within the department by faculty, postdoctoral fellows, and PhD students. Platform talks and posters are given and the day is highlighted with an invited keynote presentation.

Advances in Forensic Medicine & Pathology
May 6-7, 2020
Two-day symposium, held yearly, designed to meet the needs of practicing pathologists, medical examiners, law enforcement personnel, coroners, health care professionals, and district attorneys. CME and Mcoles credits offered.

CHAMPS Research Symposium
Spring 2020
One-day event showcasing scientific platform and poster presentations by department clinical faculty and trainees with open discussions for applying lessons learned to attendees’ areas of interest. The day culminates in a keynote speaker presentation.

Clinical Pathology Symposia
Spring 2020
This educational event for Pathology medical laboratory scientists and staff, geared towards a variety of lab topics, occurs on the first day of Medical Laboratory Week. A featured speaker delivers the Annual John G. Batsakis Lecture. CE credits are applied to the Certification of Maintenance Program (CMP).

Find More Events
Visit our website to find more upcoming events and symposiums: /conferences

Current Topics in Blood Banking
Spring 2020
Educational program for medical lab scientists, residents, fellows and faculty, designed to discuss topics related to blood banking, hemostasis, quality and management. CE credits offered for medical lab scientists.
Our faculty were very productive this year, publishing over 450 manuscripts in peer-reviewed journals! These publications represent successful research efforts undertaken. Some of the key highlights of particularly impactful research of late have included the following studies:

**New hydro-gel matrix holds promise for healing of intestinal mucosal injuries**

Dr. Asma Nusrat’s laboratory, in collaboration with Dr. An-dres Garcia (a bioengineer at Georgia Institute of Technology) and Dr. Jason Spence from the Department of Internal Medicine at Michigan Medicine, identified a synthetic engineered hydro-gel matrix for growth and differentiation of pluripotent stem-cell-derived human intestinal organoids that were successfully implanted into healing colonic mucosal wounds of mice, suggesting that this approach can be used to treat non-healing mucosal injuries in inflammatory disorders.


**L3MBTL3 is a novel modulator of Notch signaling**

Dr. Jean-Francois (Jeff) Rual’s laboratory, in collaboration with Drs. Yali Dou, Venkatesha Basrur, Alexey Nesvizhskii, and others, published a study in *EMBO Journal* demonstrating that methyl-lysine reader, L3MBTL3, switches the Notch coactivator RBPJ to a transcriptional repressor by mediating removal of activating histone marks at Notch target genes in mammalian cells, including brain and breast cancer cell lines. In *vivo* analyses of the homolog of L3MBTL3 in reductionistic models that include *Drosophila melanogaster* and *Caenorhabditis elegans* demonstrate that the functional link between RBPJ and L3MBTL3 is evolutionarily conserved, thus identifying L3MBTL3 as a universal modulator of Notch signaling in metazoans. *EMBO J* published online October 13, 2017:

DOI:10.15252/embj.201796525

**Available Funds**

Pathology Faculty Research Fund - 324557
victors.us/pathologyfaculty

Pathology Resident Research Fund - 324555
victors.us/pathologyresident

Pathology Fellowship Fund - 324556
victors.us/pathologyfellowship

**A new immunogenic class of metastatic prostate cancer**

The Chinnaiyan laboratory also identified a new subtype of prostate cancer that occurs in about 7 percent of patients with advanced disease. The subtype is characterized by loss of the gene CDK12 and it was found to be more

**Research Highlights**

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Dr. Arul Chinnaiyan and the MCTP team identified lncRNA that provides insight into a key driver of prostate cancer – and a potential target for future therapy. This group identified a novel gene they named ARNLC1, which controls signals from the androgen receptor. Inhibition of ARNLC1 in cell lines expressing androgen receptor led to cancer cell death and prevents tumor growth. Conversely, in mouse models, elevating ARNLC1 resulted in large tumors. This study was published in:

*Nature Genetics* 2018 June, 50(6):814-824

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**Our Mission**

The Department of Pathology is advancing the future of health care through education, patient care, and research missions. We are committed to achieving the highest standard of service excellence to ensure an ideal experience for our patients and their families.

**Support Leaders & Best**

In the pursuit of continued excellence in our educational training, clinical care and scientific discovery, the Department of Pathology has always been grateful for private support. Gifts from individuals, foundations, corporations, and associations play a key role in medicine at Michigan.

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**Research Highlights**

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**A new immunogenic class of metastatic prostate cancer**

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common in metastatic prostate cancer compared with early stage tumors that had not spread. CDK12 mutant cases were associated with elevated neoantigen burden ensuing from fusion-induced chimeric open reading frames and increased tumor T-cell infiltration/clonal expansion and thereby defines a distinct class of metastatic prostate cancers that may benefit from immune checkpoint immunotherapy.

Published in Science Immunology (19 Apr 2019; 4(34), eaaw4341), Caruso et. al. report a new mouse model where they can recapitulate multiple hallmarks of intestinal inflammation seen in patients with Crohn's Disease. Crohn's Disease is associated with bacterial dysbiosis (imbalance) and chronic intestinal inflammation. It has been unclear whether the imbalance is a consequence of intestinal inflammation or whether specific bacteria trigger the disease in people with Crohn's Disease susceptibility gene mutations. In this study, Caruso et al. report that in mice with NOD2 and CYBB gene deficiencies, marked accumulation of Mucispirillum (a gram negative mucus-dwelling anaerobe bacterium) occurred, which was also associated with impaired neutrophil recruitment and killing of the bacterium by luminal neutrophils.

Maternal immunoglobulins against Mucispirillum protected mutant mice from disease during breastfeeding. These results indicate that a specific intestinal microbe triggers CD-like disease in the presence of impaired clearance of the bacterium by innate immunity and also illustrates the protective mechanisms of breast feeding.

Specific microbes trigger Crohn’s-like Disease in genetically susceptible mice

Dr. Gabriel Nuñez's laboratory, in collaboration with the Nusrat Laboratory, identified a specific bacterium that interacts with the NOD2 gene, driving the development of Crohn’s disease-like colitis in mice.

Sixteen patents/innovations were filed or issued to our faculty in FY 2018.

UI Balis, MD, developed VIPER: Validated Identification of Prescreened Exemplar Regions, a high-performance image-segmentation and annotation tool based on a proprietary GPU-based, massively parallel segmentation library designed to run on the Cuda architecture.

Noah Brown, MD, and Bryan Betz, PhD, created a Next-Generation Sequencing, Data Analysis and Visualization Tool to aid in the interpretation of sequencing results.

Arul Chinnaiyan, MD, PhD, has a patent pending on the Detection of CDK12 alterations to predict prostate cancer therapeutic sensitivity.

Jolanta Grembecka, PhD, and Tomasz Cierpicki, PhD, received three patents for small molecules to treat Leukemia. They have licensed their menin inhibitors to Kura Oncology and these will be tested in a Phase 1 clinical trial for the treatment of Leukemia beginning in FY 19.

David Keren, MD, and Lee Schroeder, MD, PhD, filed their invention of the InheRET, Inherited Risk Evaluation Tool.

Sean Li, MD, PhD, developed and licensed to the University of Michigan the Plasminogen activator inhibitor-1 (PAI-1), inhibitor and method of use.

David Lombard, MD, PhD, is the co-inventor on two patents that include the potential use of inhibitors of sirtuins and PAPP-A as anti-aging drugs.

Zaneta Nikolovska-Coleska, PhD, received a patent for the design of compounds to hinder DOT1L recruitment by MLL-fusion proteins.

James Varani, PhD, patented a compound that focuses on the use of biologically active moieties, such as alltrans retinoic acid, for the treatment of acne.
An avid tennis player, Johanna Silver Gordon was incredibly dynamic and outgoing. She taught high school English and humanities and worked at being healthy. She ate a heart-healthy diet and exercised regularly, hoping to fend off heart disease, high blood pressure, and stroke, all of which were known family health issues. In many ways, her sister Sheryl Silver recalls, she was the glue that held her family together. “She was my best friend, confidante, and supporter.”

The entire family was stunned when, in January of 1997, Johanna was diagnosed with late-stage ovarian cancer. “I remember time stopping,” Sheryl recalls. “I thought, ‘This can’t be happening. We’re in deep trouble here.’”

Ovarian cancer hadn’t been on Johanna’s radar. She had complained of persistent bloating at her annual gynecological exam, but her doctor shook it off as a symptom of perimenopause. The bloating intensified and she developed heartburn, so she made an appointment with a gastroenterologist but, as a new patient, it would be a few months before the scheduled appointment. As her symptoms worsened, she decided to follow up with her gynecologist, who finally ordered a CA125 blood test and a transvaginal ultrasound.

A week later, Johanna was in surgery to have cancer removed. She was referred to purchase a wig and started chemotherapy. “Her face just registered this terrible shock. She said she felt very betrayed. She’d always been able to rely on her body,” Sheryl says. “If she thought her symptoms were life-threatening, she would have done more sooner.”

Sheryl began attending national ovarian cancer conferences in Washington, DC, and later, a Gilda’s Club support group in Michigan with Johanna. Along with her sister, Sheryl immersed herself in research, looking for anything that might save Johanna’s life. It turned out that Johanna’s case was textbook. She was a woman over 50 who had not had multiple pregnancies or used hormonal birth control. She was Ashkenazi Jewish. She had nothing that would lower her risk of ovarian cancer and everything that would increase it. Even not starting menopause by age 54 added to her risk; late menopause is a risk factor for ovarian cancer. Sheryl and Johanna were daughters of a doctor and had always put their faith in medicine. They were appalled at the lack of information on, and monitoring for, ovarian cancer.

Johanna briefly went into remission after her first surgery and chemotherapy, but her cancer returned. Three more major surgeries and chemotherapies followed along with her efforts to enter clinical trials. Nothing worked and, on August 29, 2000, she died. Within a few months, Sheryl realized that just grieving for her sister was not the way to honor her life. “I’d gone looking for research information that I thought would save
her. What I learned, instead, was that her story was tragically common.”

Sheryl, who was a freelance writer and editor at the time, approached The Washington Post about running a special advocacy section on ovarian cancer to educate women about the disease. She reached out to the Gynecologic Cancer Foundation (now known as the Foundation for Women’s Cancer) and secured them as a sponsor. When articles for the section began arriving via email, Sheryl recalls, “I would sit there with tears rolling down my face because it meant so much to me to know that she hadn't died in vain.” Her idea of educating the public about ovarian cancer was becoming reality.

It didn’t stop there. A similar special section on gynecologic cancers which Sheryl edited and for which she also wrote articles followed in the New York Times. Then, knowing that newspaper articles wouldn’t reach everyone who needed the information, Sheryl was inspired to propose a federal law that created a national gynecologic cancer education program. First introduced in the House of Representatives by Michigan Congressman Sander Levin in 2003, Johanna’s Law: The Gynecologic Education and Awareness Act, gained the support of more than 300 bi-partisan co-sponsors and passed both the U.S. House and Senate unanimously on December 8th and 9th, 2006. Signed into law by President George W. Bush in January of 2007, it directed the Centers for Disease Control to create a national education campaign. Sheryl says that working on the law was very healing. “It consumed my life for a few years, but otherwise I would just have had this gigantic hole where my sister had been. Instead, she’s on my mind a lot. I know that she made a difference.”

In 2009, Sheryl established the Dr. I. Walter and Anne Silver Family Foundation for Ovarian Cancer Research in memory of her parents. Last fall, at the suggestion of a friend in the ovarian cancer community, Sheryl was referred to the Department of Pathology’s Dr. Analisa DiFeo as a potential recipient of funding. DiFeo, who joined the department in the summer of 2018, focuses on identifying novel biomarkers of ovarian cancer therapeutic response and generating novel targeted molecular therapies. These therapies can work with current treatment options or on their own.

Prior to arriving to Ann Arbor, Dr. DiFeo was the Director of the Gynecologic Oncology Translational Research Program at Case Western Reserve University. Through this program, she developed an extensive gynecologic tumor biobank which includes novel primary cancer cell lines and patient-derived mouse models which she was able to transfer to her new laboratory at The University of Michigan. She has now expanded this program to Ann Arbor. Through the Ovarian Cancer Initiative, she will be able to continue her efforts in growing the tumor biobank and utilize this robust and clinically-relevant resource to uncover molecular factors that are involved in ovarian cancer and the development of novel drugs to treat the disease.

Sheryl called DiFeo and was impressed by her passion, compassion, knowledge, and commitment to patient-centered care. “Her clear focus on strategies that could improve patient survival and treatment plans was incredibly compelling and inspiring,” Sheryl says. “She’s a star and the University of Michigan is lucky to have her.”

DiFeo is extremely grateful for the gift explaining that it will allow her lab to pursue projects that are a bit more high-risk-high-reward than funding from more traditional funding agencies, such as the National Institutes of Health, will allow. “Sheryl and her family will now be intimately involved in our scientific endeavors. I am honored that the Silver Family Foundation was able to see that our passions align and we can only make a true impact if we work together.”

“Any health care professional who has ovarian cancer patients needs to keep fighting for them and keep trying. It’s why we love doctors like Dr. DiFeo who have chosen this specialty,” Sheryl says. “We deeply appreciate the commitment to research.”
A Fundamental Passion
The son of a physician-scientist, a young Bryan Betz was fascinated by the field. After enrolling at the University of Michigan for his undergraduate degree, he took the usual courses to put himself on track for medical school. In his junior year, he took a course that would cement his future. That class? The Biology of Cancer. “It is a bit cliché, but I’ll never forget the tremendous impact that class had on me,” he recalls. Betz became immersed in everything about the disease and knew he would dedicate his career to cancer.

Convinced he wanted to pursue a career in research, he entered a molecular and cellular pathology graduate program at the University of North Carolina. In the laboratory of Dr. Bernard Weissman at the Lineberger Comprehensive Cancer Center, his work focused on identifying the genetic basis of malignant rhabdoid tumors, a rare and aggressive childhood cancer. “I performed some of the first work demonstrating that mutations in a gene called SMARCB1 (INI1) occurred in almost all cases of this tumor,” Betz says.

He was also able to demonstrate that replacing the defective SMARCB1 gene back into rhabdoid tumor cells resulted in a rapid block in tumor cell growth. Collectively his work helped shed light on previously unknown molecular pathways driving this disease.

It was during this time that Betz also met his wife, Sharon, whom he discovered he not only shared a bus route with but also a graduate program and an apartment complex. An invitation to celebrate Cinco de Mayo with a group of her friends led to more, and the couple married after completing their PhDs in 2002.

Pursuing a clinical career path, Sharon entered dual fellowship training in clinical cytogenetics and molecular genetics, while Betz began a post-doctoral research fellowship at the National Institutes of Health. There, he identified a new mouse model of gastrointestinal stromal tumors – a soft tissue tumor of the gastrointestinal tract – that helped define the mechanisms of that disease. “It was through the collective experiences during my time in research that I was able to develop a deep understanding of cancer pathogenesis and hone my technical skills in molecular genetic techniques and technologies. Those skills are what laid the foundation for my career today.”

Yet, despite his research discoveries he was drawn to Sharon’s work in the clinical genetics laboratory. He found himself envious of her work in the clinical setting and yearning to apply his technical skills and knowledge to more directly impact the care of cancer patients. So, the duo decided to co-apply for jobs in a clinical department and, in July of 2007, they joined the Department of Pathology at the University of Michigan as Clinical Assistant Professors. Sharon was hired as an assistant director of both the cytogenetics and molecular diagnostics laboratories while Betz was hired as the technical director of the molecular diagnostics laboratory.

Betz, who was raised in Ann Arbor, was excited about giving his two young children a similar childhood. “I knew this was a great place to raise a family but also the environment here in the department was really set up to allow us to succeed.” The future was bright for the husband-wife team and they began to work collaboratively to coordinate the activities between the Cytogenetics and Molecular labs. Under the leadership of Dr. Kojo Elenitoba-Johnson who was director of the Molecular laboratory, Betz also made it a priority to work collaboratively with the division of Anatomic Pathology to meet the needs of our own pathologists by building infrastructure and workflows to make tissue-based molecular tests available in-house. In doing so this helped to bridge activities between the Anatomic and Clinical Pathology divisions. Then, their world came crashing down when Sharon was diagnosed with a rare variant of cervical cancer in December of 2007. She received intensive therapy, but the cancer was difficult to treat, and she died in July of 2008. The blow was devastating.

“Going through that gave me new perspective on the significance of my work. It was particularly motivating for me to enhance our clinical service so that we could offer our cancer patients access to the best, and most cutting-edge molecular tests,” Betz says.

Together with the Molecular Diagnostics team,
Betz honed his energy on placing a high priority on customer service for the clinical teams and clients and expanding the test menu and technical capabilities of the molecular laboratory. The result? A 3-fold increase (19 tests to 66) in the number of molecular diagnostic tests offered over the next 10 years. This growth and the patient/client-first focus helped to enhance recognition of the laboratory which today is a leading national provider of molecular diagnostics testing for cancer care.

When it came time for the move to the North Campus Research Complex, Betz and his team embraced the opportunity to co-locate with 6 different molecular labs into a single space. The individual teams had done very little collaborating previously, so a variety of forums were created to bring the groups together. First were a series of team-building exercises for the lab groups to get to know one another. From there, working groups were formed so the teams could get familiar with shared workflows and there were staff shadowing exchanges between labs. These activities helped ease the transition to a shared laboratory and set them up for success in actually designing the space. “The fundamental approach we took was design the space around technologies and workflows rather than the preexisting organizational structures,” Betz says. “You hear the word lean and people roll their eyes and I have to be honest I did that as well. But actually after going through the process and learning how it can influence and impact efficiencies in your lab it’s tremendous.” In fact, the lab implemented changes to help with inefficiencies even before the move.

Now that the labs are all in one location, work has begun to combine efforts for shared resources. DNA extraction is a fundamental first step in most molecular tests so, a DNA extraction core was the first to be implemented. The plan is for more resources to be combined as it’s beneficial and naturally evolves.

There are still numerous challenges to be faced in the field of cancer molecular diagnostics. Rapidly changing technologies, the accelerating pace of discovery and application of cancer biomarkers, and continued barriers to reimbursement of molecular testing. However, Betz is optimistic about the future given the combined and collective efforts of his groups, the support of the department and hospital, and the opportunities provided by the new well-designed space. He says it’s the fundamental passion for helping patients that makes his team so amazing.

“A recurrent theme I find myself saying is that our ability to provide top-tier molecular testing is a direct result of our collective laboratory team. Our people are what make us great and I credit them for our accomplishments.”

“A recurrent theme I find myself saying is that our ability to provide top-tier molecular testing is a direct result of our collective laboratory team. Our people are what make us great and I credit them for our accomplishments.”

Above: Noah Brown (left) and Bryan Betz (right) work in the Molecular Diagnostics laboratory at NCRC.
Jiaying Tan began her journey at the University of Michigan as an international student from China, entering via the Program in Biomedical Sciences (PIBS) in 2007. This was at a time when the Molecular and Cellular Pathology Graduate Program was not available for international students. However, two of her mentors were members of Pathology and she was “adopted” into the MCP family, which she describes as supportive, friendly, and encouraging. As an international student, Jiaying was not able to attend one of the on-site open houses and didn’t know anyone on campus when she arrived. Tan was not deterred. She reviewed the rotation mentors and selected three laboratories in which to perform her rotations based on their disease-relevant research. Following her rotations, she chose to remain in the laboratory of Dr. Jay Hess, the former Chair of Pathology. “I enjoyed his [lab management] style very much, and everyone in the lab was super supportive,” said Tan. “I also very much appreciated his perspective coming from his medical training background and practice, which turned out to be influential for shaping my own perspective in many years to come.”

When Tan entered the graduate program, she fully intended to become an academic researcher/principal investigator. As she pursued her PhD, however, her goals changed. “The training I got at the MCP program prepared me very well for all of the gear-changing explorations,” she recalled. The course requirements allowed her the flexibility to tailor her educational program to her research interests and needs. “I was exposed to a variety of scientific topics through the department seminar series, which sparked a lot of intellectual exercises that I took on topics not particularly relevant to my thesis,” she said. The exposure Tan received at these seminars helped shape her career goal, which transitioned from academic research to an editorial career. “The high-quality presentations from experts across various research fields brought me a very broad perspective on biological/biomedical sciences. In retrospect, I probably started forming my ‘scientific gut feeling’ from those seminars.”

After graduating from the MCP, Tan completed a 1-year postdoctoral fellowship at Novartis Institutes for BioMedical Research in Shanghai before joining the Cell Journal editorial team in 2013. She has been a scientific editor there ever since.

In looking back over her experience with the MCP, Tan advises future graduate students to seriously consider the breadth of scientific topics and the level of collaboration present. These are two of the most important elements in choosing a program. She also advises that students think carefully when selecting a mentor to ensure that your style fits well with that of the mentor. “If you prefer hands-on training and step-by-step mentoring in experimental designs/progress, generally junior faculty may be more appropriate,” she guides. “If you prefer independent thinking and exploration for your thesis projects and big-picture communication with your mentor, more established faculty may be what you are looking for.”

Tan is grateful for her experience in the MCP program and its collaborative environment, “The supportive and friendly environment was very encouraging to me.”

— Jiaying Tan, PhD

by Lynn McCain
COMMUNITY OUTREACH

High School students have many opportunities to learn about careers through career days at their schools, brochures, videos they find on-line, etc., but what if they had a chance to actually experience careers? A chance to see what it is really like, day to day? Wouldn’t that be the best way to open their eyes to new possibilities?

Faculty at the University of Michigan Department of Pathology believe that high school students who have the chance to learn about Pathology from the inside are more likely to choose a career in pathology, medicine or one of the other sciences, than just by hearing about it through other channels. With the average age of pathologists increasing and the number of students entering pathology decreasing, there is a greater need to expose more students to the field than ever before.

Dr. Arul Chinnaiyan, Professor of Pathology and the Director of the Michigan Center for Translational Pathology, has been hosting high school student volunteers in his lab since 2002. Over the past 16 years, 31 high school students have been mentored in his laboratory. Generally, students volunteer to work in the lab throughout the summer, with a few staying on through the school year.

One who stayed on was Aparna (Ghosh) Kachoria, who joined the lab in 2008 from Pioneer High School, Ann Arbor. She became engaged in the research and contributed to the discovery that the TMPRSS-ERG fusion protein binds to the ERG locus, which is tied to prostate cancer. This resulted in two publications, one in Science, a very prestigious scientific journal. She is now at the University of Massachusetts Medical School working as a Project Analyst in research. Sahr Yazdani joined the lab in 2013 from Huron High School and, following the research she conducted in the lab, has gone on to the Stritch School of Medicine at Loyola. In 2014, Caleb Chang also joined the lab from Huron High School. Chinnaiyan indicated that he is one of the brightest young researchers he has ever had in his lab. Cheng is now being considered for the University of Michigan Medical Scientist Training Program where he plans to pursue a career in
academic medicine and research.

For the past 10 years, Dr. David Keren, Professor of Pathology and former Director of Clinical Pathology, has been mentoring Pathways to Success High School students through the STRIVE (Students Taking Renewed Interest in the Value of Education) program, sponsored by the Ann Arbor Rotary Club. Students meet with mentors twice per month and have an opportunity to earn a scholarship to Washtenaw Community College upon graduation. Keren has engaged with these students, bringing them to Michigan Medicine where they shadow healthcare professionals and learn more about nursing, medicine, and other fields. Many of these students, who were previously in danger of being left behind, have gone on to college and even graduate school due to the mentorship efforts of Keren and his STRIVE colleagues.

A newcomer to Michigan Pathology is Dr. Analisa DiFeo. Dr. DiFeo was introduced to the benefit of mentoring high school students in the laboratory when she was a graduate student. “They ask questions we don’t consider. Sometimes it is the simplest questions that we forget to ask. These questions can change the trajectory of a research project and lead to discoveries that would have otherwise been missed,” explains DiFeo. However, many students need to work over the summer to help pay family expenses and cannot volunteer in labs. To overcome this barrier, DiFeo established the Young Scientists Foundation (YSF.org) with her husband, Dr. Goutham Narla, while working at Mt. Sinai in New York. Their foundation traveled with them to Cleveland, Ohio, when they transferred to Case Western and now they hope to expand it here in Ann Arbor. YFS supported 15 students in New York and 20 in Cleveland. In the latest move, however, they lost much of their funding support for the foundation and are seeking new sources of support. DiFeo shared one story of how YSF changes the lives of students. Olga Kovalenko is the daughter of an immigrant mother who spoke very little English. Olga was a bright high school student, but very shy and timid. DiFeo suggested she apply to YSF. The day she was about to take a job at the Botanical Gardens, Olga applied to YSF. She joined the DiFeo lab the summer prior to her senior year in high school, stayed throughout her senior year and was accepted to Case Western University. Olga continued working in the DiFeo lab throughout her undergraduate education and is now a 3rd year medical student on track to become an Ob/Gyn.

These are just a few examples of the way Pathology is investing in the community to help high school students consider rewarding careers in medicine and the sciences. Their efforts are making a difference, one student at a time. If students wish to volunteer in a pathology research laboratory, they need to be at least 16 years old, apply through Volunteer Services at Michigan Medicine (www.med.umich.edu/volunteer), and make a commitment to regular hours for the entire summer.
In January, the Department of Pathology lost Dennis Serras, a dear member of our Patient and Family Advisory Council (PFAC). With his warm smile and easy laugh, Dennis’ positive energy permeated the room. As his wife Ellie said, he always lived big. “He was never one to hold back on living his life.”

Dennis entered what he called a “cancer world” when he was diagnosed with esophageal cancer in May of 2011. He woke up from his esophagectomy to the realization that his cancer had broken the margins and he’d need chemo and radiation. His surgeon, Dr. Mark Orringer, thought he might be of help to other patients in similar situations and Dennis began visiting patients in their rooms post-surgery. Dennis explained that the patients he visited were always skeptical as to what he wanted and why he was there, but when they learned he was an esophageal cancer survivor, their eyes got big. “I’ve never gone into a room and have them not ask, ‘can we talk?’” he said at his home last December. “I don’t see living in a cancer world as a burden. I just see it as life for me today. That’s why I enjoy working with people so much. If it can help them, it helps me.” He hopes that other patients will hear his story and learn that there are opportunities for them on patient advisory councils like Pathology’s PFAC.

When Dennis learned of the Department of Pathology’s PFAC, he knew he had to join. He was already volunteering with the departments of oncology and radiology, but pathology quickly became his pet. “I had never met a pathologist and that was probably the most significant part of my recovery,” he said. “Every slide that they view, it’s someone’s life. And it affected my life tremendously.”

He was an active member of the council, traveling to a San Antonio patient-centered care conference and participating on panels. At the time he was diagnosed with a recurrence of esophageal cancer, the council was just starting work on a project exploring how to best-deliver difficult news to patients.

When Dennis began experiencing pain in his chest last July, he followed up with his doctor. His cancer had returned. Yet Dennis continued living big as usual, starting bongo lessons, planning fishing trips, and making special Christmas plans with family.

He wanted those in medicine to know that the stories without happy endings are as important to be told and heard as the success stories. “There’s just nothing better than having people recognize how important pathology is.”
[1] **Classification of endocrine tumors in the age of integrated genomics**, by Thomas Giordano, MD, is published in *Endocrine-Related Cancer* to celebrate 65 years of the double helix.

[2] Faculty and staff, including Drs. David Lucas and Jeffrey Myers, work on plans inside a sign-out room on the NCRC campus.

[3] Second-year resident, Lori Griesinger, works at a grossing station in the new facilities at NCRC.


[6] Leon Friesen works in the lab of Dr. Chang Kim. The lab’s work, RARα supports the development of Langerhans cells and langerin-expressing conventional dendritic cells, was featured in *Nature Communications*.

[7] Linda Lapsley works on the new BD Kiestra™ automated line in the clinical microbiology lab.
Residents

Laurence Briski, MD
Surgical Pathology Fellowship
Memorial Sloan Kettering
New York, NY

Sara Hall (Hawes), MD
Surgical Pathology Fellowship
Michigan Medicine

Sameer Khatri, MD
Hematopathology Fellowship
Brigham & Women’s Hospital
Boston, MA

David Manthei, MD, PhD
Molecular Genetic Pathology Fellowship
Michigan Medicine

Jonathan Mowers, MD, PhD
Gastrointestinal Fellowship
Michigan Medicine

Sarah Rooney, MD
Breast/Gynecologic Pathology Fellowship
University of Washington
Seattle, WA

Stephanie Skala MD
Gynecologic Pathology Fellowship
Michigan Medicine

Grace Wang, MD
Dermatopathology Fellowship
Michigan Medicine

Milad Webb, MD
Forensic Pathology Fellowship
Michigan Medicine

ACGME Fellows

Ellen East, MD
Breast Fellowship
Michigan Medicine

Mark Ettel, MD
Gastrointestinal Pathology
University of Rochester
Rochester, NY

Kenneth Hughes, MD
Surgical Pathology Fellowship
Michigan Medicine

Zaid Mahdi, MD, PhD
Gastrointestinal Fellowship
Beth Israel Deaconess Medical Center
Boston, MA

Tanmay Shah, DO
Surgical Pathology Fellowship
Michigan Medicine

Reena Singh, MD
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Osman Yilmaz, MD
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Tufts Medical Center
Boston, MA

Clinical Lecturers

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Bone & Soft Tissue Fellowship
Michigan Medicine

Stacy Arnold, MD
Pathology
Tucson, AZ

Sarah Avedschmidt, MD
Forensic Pathology
Medical Examiner’s Office
Wayne County, MI

Michael Carter, MD, PhD
Molecular Genetic Pathology
Dalhousie University
Halifax, Nova Scotia
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<td>Yulei Shen, MD, PhD</td>
<td>Molecular Genetic Pathology Fellowship</td>
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<td>St. Joseph Mercy Health</td>
<td>Ann Arbor, MI</td>
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**FLASH FROM THE PAST**

Can you guess who these individuals are? They are all currently working in the Department of Pathology here at Michigan Medicine.