Annual Report

2022

Department of **Pathology**

MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

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Message From the Chair

In considering the Michigan Medicine Department of Pathology over the past year, I can confidently say that our ongoing success is attributable to our faculty, staff, and trainees who have been exceptional in the face of constantly changing environments. In FY22, we transitioned from the tight COVID restrictions to a "new normal" where SARS CoV-2 requires vigilance and adaptability as it waxes and wanes while clinical, research, and education missions are returning to and even exceeding pre-pandemic levels. In addition, our ongoing Pathology Relocation and Renovation Project required significant flexibility as construction on our state-of-the-art core laboratories continued. Construction walls were erected and torn down, equipment was replaced, and work areas shifted as our new, updated facilities took shape.

I am so proud of every member of our team. While testing for the SARS CoV-2 virus decreased significantly, resulting in a 2.4% year-over-year decline in the total number of billed tests, other clinical workflows and testing continued to grow to pre-pandemic levels and beyond, with billed tests up 6% as compared to pre-pandemic levels and revenues up 1.5% over the prior year. In research, our faculty were extremely productive and were awarded 51 grants for a total of $32.4 million. During the pandemic shutdown, research in our labs was paused, and a record number of publications were written. With the reopening of our labs, our researchers resumed their experiments, and published their results in 393 journal articles.

Our education programs also experienced significant changes as the Director of Education Programs, Dr. Carol Farver, returned to the Cleveland Clinic and Dr. Kathleen Cho took on these responsibilities as the Interim Director. The residency program saw an expansion in their leadership ranks as Dr. Kristine Konopka stepped down as the Residency Program Director and Dr. Sean Li moved up from Associate Director to Director. With him were added Sara Abbott, MD, Associate Program Director for AP and David Manthei, MD, PhD, Associate Program Director for CP.

This year, we lost a much-loved member of our team when Marty Lawlor, Chief Department Administrator, unexpectedly passed away in September 2021. In the midst of their pain and loss, the staff of our Division of Finance and Administration pulled together with their resiliency on full display. David Golden, Director of Finance, ably stepped up to take on the role of interim CDA while other members of the team flexed their workloads to take on new responsibilities. David and his entire team has performed admirably! I want to thank each and every member of the team who took on expanded workloads and ensured the department continued to move forward.

FY22 caused each of us to stretch in new ways and the results are a testament to our faculty, staff, and trainees. We are continuing to grow personally, professionally, and as a department. As you read the pages of this report, and see the data, remember the faces behind the numbers who pulled together to make sure the best possible results were achieved.

Charles A. Parkos, MD, PhD

Carl V. Weller Professor and Chair

PEOPLE

160 Faculty

- **36** / Instructional
- **83** / Clinical
- **41** / Research
- **23** / Supplemental
- **67** / Student Temps

1,210 Staff

10 Direct Reports

3 Dotted Line Reports

CDA

COVID-19

Diagnostic Tests
Developed & Validated → **211,323** Tests Performed

Serology Test
Developed & Validated → **3,856** Tests Performed

OTHER

Partnerships

M-Labs – Primary Reference Lab, Mid-Michigan Metro Health and national presence in molecular/genetic testing, totaling $77.7 million in gross charges

MISSIONS / RESEARCH & CLINICAL

$85M
MS Annual Expense Budget

$181M
UMHS Annual Expense Budget

Ranked #8 In Funding
Received by NIH in 2021

Received 51 Awards from NIH in FY22

$36.4M
Sponsored Spending FY22

14.9% ↑
Growth in Billable Tests

Research Space Occupies
65,600SQFT
$375 DC/SF
$168 IDC/SF

- **25** / PhDs
- **18** / Fellows
- **44** / Post Doc Fellows
- **28** / Residents

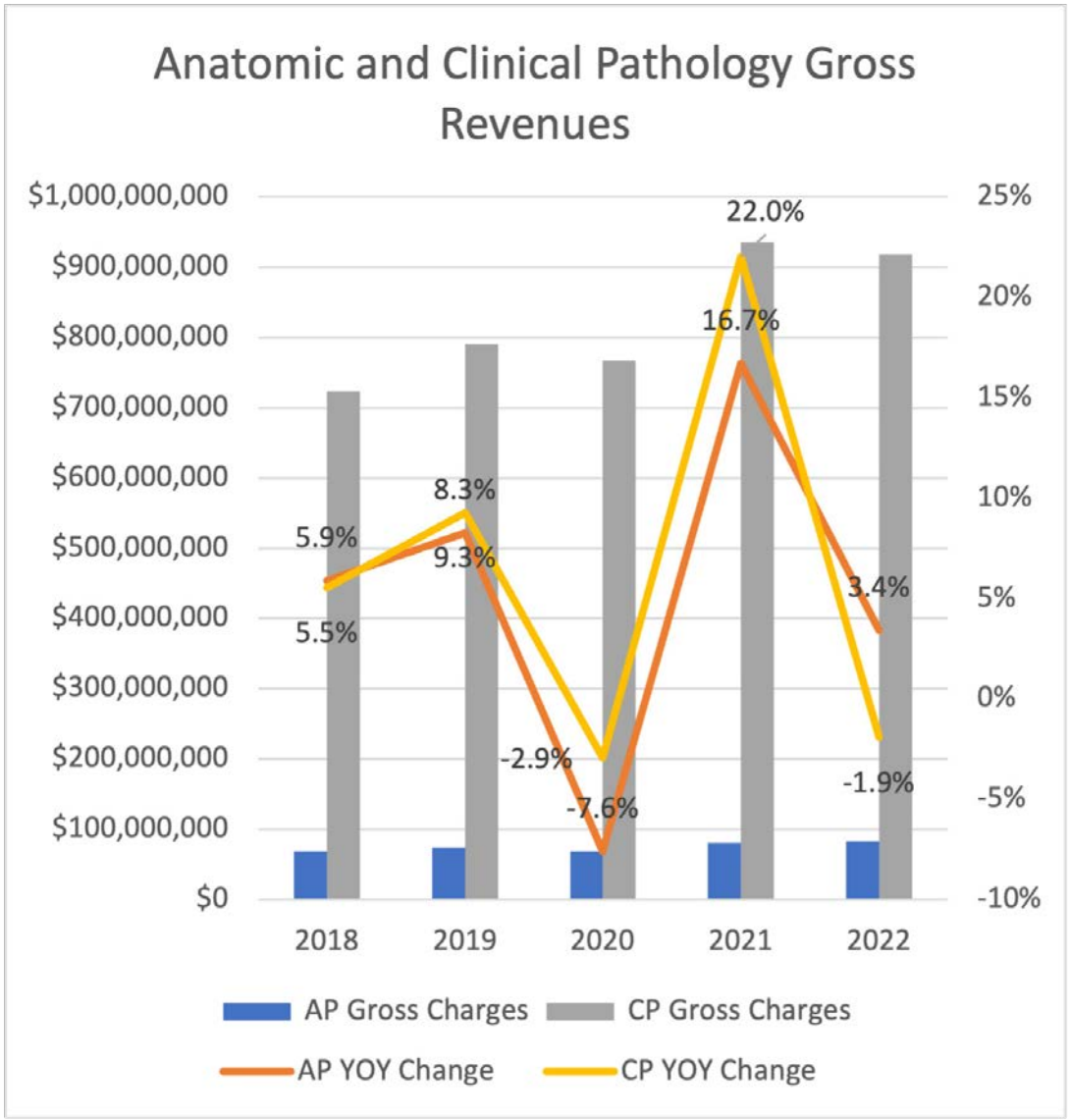
Clinical
Outpatient Phlebotomy in all Health Centers

Clinical Mission

The mission of the Department of Pathology is, "to create the future of our discipline by educating and nurturing the leaders and health providers who will care for us, unifying our common commitment to excellence across traditional barriers to collaboration and creativity, building solutions that leverage the power of data to solve real problems and create unique value, and leading the way for application of the right diagnostic tools, for the right patient, at the right time."

To accomplish this mission, our department has three primary foci: Clinical Care, Research, and Education. The clinical mission is committed to providing the best patient care, taking advantage of the strengths of our research and education expertise. To enhance our ability to provide optimal patient care, we built state-of-the-art clinical laboratories at the North Campus Research Complex and are currently renovating space at the University Hospital (UH) for modern core laboratories with automation lines and STAT services.

The clinical laboratory services are divided into four primary divisions: Anatomic Pathology, Clinical Pathology, Molecular Pathology, and Michigan Medicine Laboratories (MLabs). The following pages describe the activities of these four divisions.



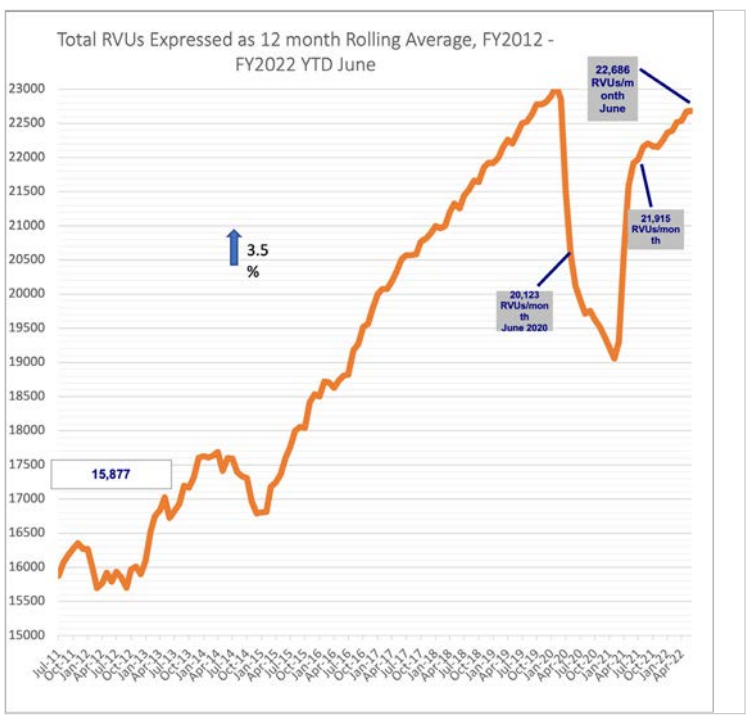
Anatomic Pathology

Liron Pantanowitz, MD, PhD, MHA
Director, Anatomic Pathology

Lakshmi Priya Kunju, MD
Director, Surgical Pathology
Director, Genitourinary Pathology
Director, General Surgical Pathology

David Lucas, MD
Director, Bone and Soft Tissue Pathology

Anatomic Pathology (AP) deals with testing of tissues, solid tumors, and cells as well as autopsies and forensics. AP experienced an increase in volume of 2.45% from a total of 151,065 cases from FY21 to 154,896 cases in FY22. The increase in specimens was likely attributed to a partial clinical service recovery from the COVID-19 pandemic. The AP clinical service is comprised of several sections including Surgical Pathology, Cytopathology, Dermatopathology, Ophthalmic Pathology, Renal Pathology, Neuropathology, Autopsy and Forensic Pathology, and Pediatric/Perinatal Pathology, each with its own section head. Surgical pathology includes multiple subspecialty services each with a designated service chief. Most of these services support weekly multidisciplinary tumor boards.



Clinical Activities

RVU Trends in Anatomic Pathology

Total RVU's generated by AP in FY22 expressed as a 12-month rolling average were 22,686 RVU's/month. This represents a 3.52% increase over FY21 and reflects a steady recovery from the COVID-19 pandemic. RVU stands for relative value unit and is an incomplete payer-imposed measure of professional work that has become an industry standard for monitoring clinical productivity.

FTE Trends in Anatomic Pathology

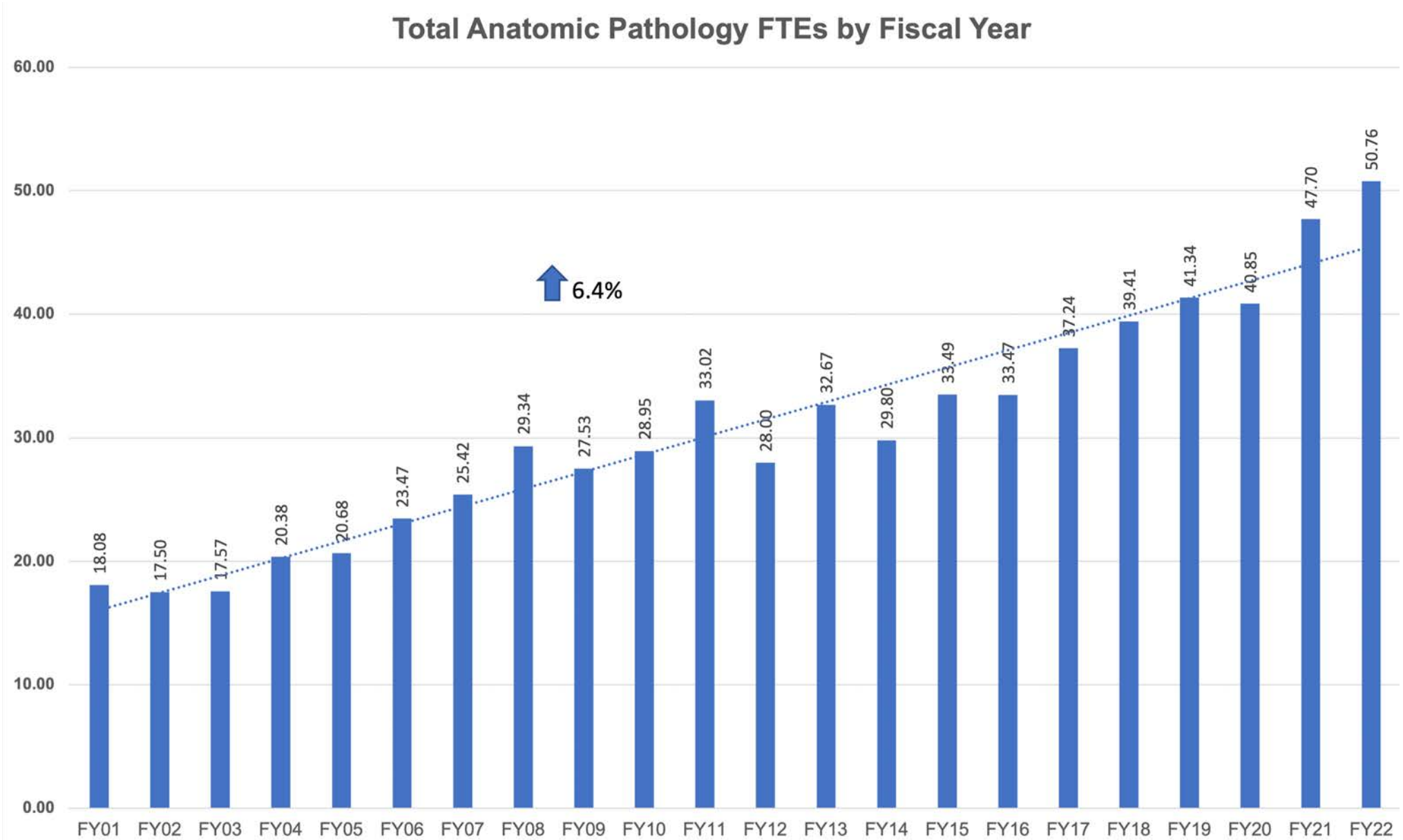
Total clinical FTEs for AP faculty was 50.76 in FY22 compared to 47.70 in FY21, representing 6.42% year-over-year increase. Over a five-year period, AP staffing has similarly increased by 28.80% from 39.41 FTEs to 50.76 FTEs due to hiring new faculty members each year to meet the demands of our constantly growing AP service workload and complexity. This included employing faculty with dual fellowships and hybrid skillsets in an AP subspeciality paired with molecular pathology, as well as hiring two new AP Hospitalists to primarily cover hospital-based services such as frozen sections.

RVU and FTE Trends in Anatomic Pathology

Total work RVUs/FTE in FY22 showed a 2.36% decrease. On average, each clinical FTE in AP generated 747.93 RVUs/month in FY22 compared to 766.03 in FY21. However, these data vary for different AP services and from month to month due to faculty hiring throughout the year.

Surgical Pathology

The Surgical Pathology section encompasses a general sign-out service and multiple subspecialty services, each with its own service chief. The clinical service provided by surgical pathology faculty includes frozen section coverage at University Hospital (UH), adult


Total Anatomic Pathology FTEs by Fiscal Year
60.00
50.00
40.00
30.00
20.00
10.00
0.00
6.4%
18.08
17.50
17.57
20.38
20.68
23.47
25.42
29.34
27.53
28.95
33.02
28.00
32.67
29.80
33.49
33.47
37.24
39.41
41.34
40.85
47.70
50.76
FY01
FY02
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FY04
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FY07
FY08
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FY16
FY17
FY18
FY19
FY20
FY21
FY22

Celina Kleer, MD
Co-Director, Breast Pathology

Andrew Sciallis, MD
Co-Director, Breast Pathology

David Gordon, MD
Director, Cardiac Pathology

Douglas Fullen, MD
Director, Dermatopathology

Thomas Giordano, MD, PhD
Director, Endocrine Pathology

Laura Lamps, MD
Director, Gastrointestinal Pathology

Kathleen Cho, MD
Director, Gynecologic Pathology

surgeries at C.S. Mott Children's and Von Voigtlander Women's Hospital, Frankel Cardiovascular Center, East Ann Arbor Medical Center, and Brighton Center for Subspecialty Care. Telepathology continued to be leveraged to remotely support our frozen section service. General Surgical Pathology (also known as "Room 1") service handles biopsies and surgical resection specimens not covered by other subspecialty areas. In FY22, 12,468 general specimens were processed, which represents a decrease of 0.98% from the prior year. Likewise, this service has experienced a 9.89% overall decrease when compared to specimen volumes from five years ago.

Bone and Soft Tissue Pathology

Bone and Soft Tissue Pathology is focused on the diagnosis and study of diseases of the bone and surrounding soft tissues. Bone & Soft Tissue consult cases, which include very challenging, unique, and rare lesions, increased by 14.5% with 1,830 cases received in FY22. This consult service has shown an overall 26% increase compared to specimen volumes from five years ago. There are accordingly now six dedicated faculty scheduled to cover this service.

Breast Pathology

Breast Pathology is a subspecialty of surgical pathology with expertise in the interpretation of breast lesions from various specimen types including needle core biopsy, lumpectomy, and mastectomy specimens. Our Breast Pathology service includes a unique dedicated frozen section laboratory for margin assessment and intraoperative consultation. The Breast Pathology division also features a consultation service that assists with diagnostically challenging cases. In FY22, the Breast Pathology service processed 3,575 cases which represents a 6.49% growth compared to FY21 and 44.21% growth compared to five years ago.

Endocrine Pathology

Endocrine Pathology is the study of diseases of the endocrine system including the thyroid, parathyroid, pituitary gland, endocrine pancreas, and adrenal glands. This service completed 510 challenging consult cases in FY22, which is a 24% increase from FY21 and represents a 25.3% increase compared to specimen volumes from five years ago.

Gastrointestinal/Hepatobiliary Pathology

Gastrointestinal Pathology (GI) is a subspecialty of surgical pathology that deals with the diagnosis and characterization of neoplastic and non-neoplastic diseases of the digestive tract and accessory organs such as the pancreas, gallbladder, and liver. The Gastrointestinal/Hepatobiliary service completed 22,000 in-house cases in FY22, which is similar to FY21. Case numbers show a 4.8% decrease compared to five years ago, which can be attributed to a revision in our workflow in 2017 where specimens accessioned as two cases (upper and lower gastrointestinal tract) were combined into one case. While case numbers decreased, specimen counts increased at the same rates shown in the past four years.

Genitourinary Pathology

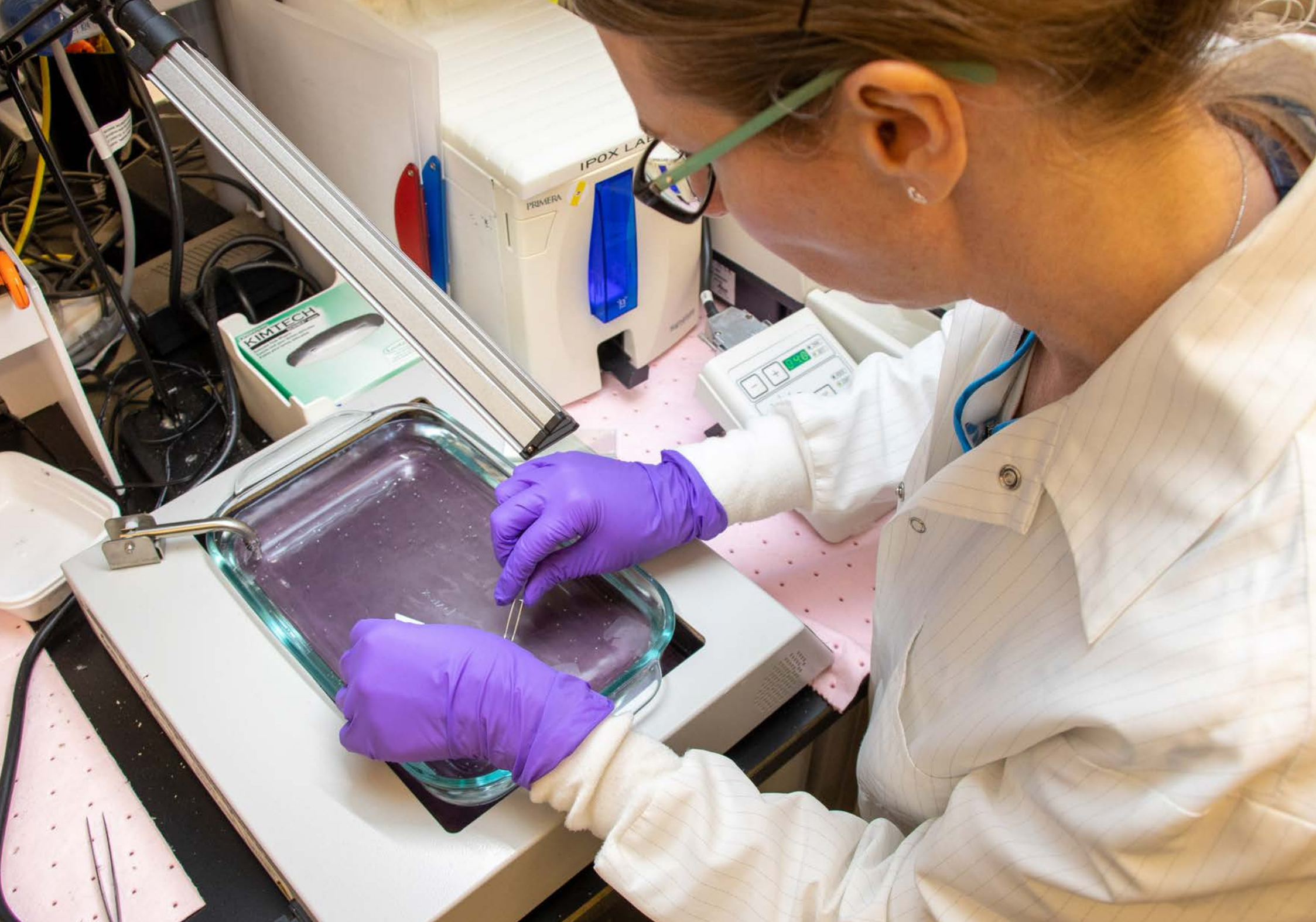
Genitourinary Pathology (GU) is a subspecialty of surgical pathology that deals with the diagnosis and characterization of neoplastic and non-neoplastic diseases of the urinary tract, excluding medical disorders of the kidneys, which fall under renal pathology. This includes diseases of the male genital tract and testes. The GU service processed 3,222 cases in FY22, which was down 12.4% from the prior year. Overall, GU specimen volumes are down 13.7% compared to specimen volumes from five years ago. The decrease of in-house GU specimens is partially due to Michigan Medicine urologists frequently operating at Chelsea Hospital (owned by Michigan Medicine), but pathology evaluation of these GU cases is performed at Trinity Health by contract. This service also completed 2,252 extramural consultations (transfer and private consults) in FY22, which is a 22% increase from FY21 and represents a 10.5% increase compared to volumes from five years ago.

Gynecologic Pathology

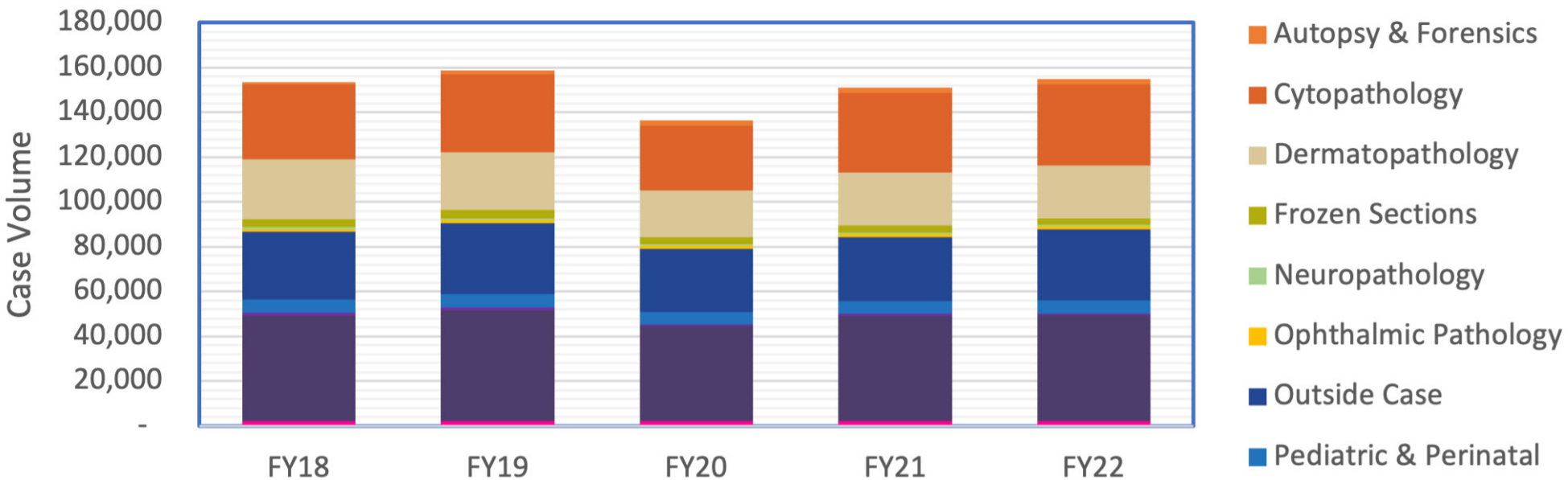
Gynecologic Pathology (GYN) is the subspecialty that deals with the study and diagnosis of disease involving the female genital tract. The GYN service processed 7,697 cases in FY22, which is a 1.3% increase over the prior year. This represents a 6.7% increase compared to specimen volumes from five years ago.

Head and Neck Pathology/Oral-Maxillofacial Pathology

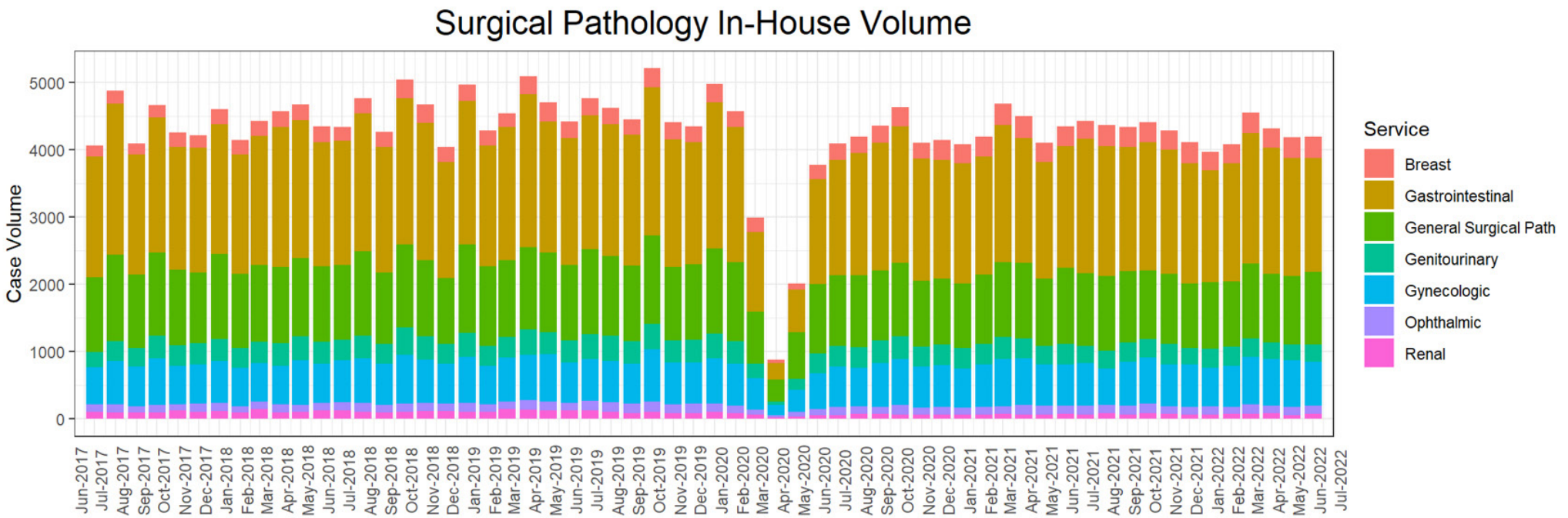
Head and Neck Pathology covers neoplastic diseases of the thyroid gland, salivary glands, and head and neck. Oral-Maxillofacial


KIMTECH
PRIMERA

Anatomic Pathology Annual Case Volume



AP Service	FY18	FY19	FY20	FY21	FY22	1-YR	5-YR
Autopsy & Forensics	1,202	1,722	2,472	2,499	2,534	1.40%	110.82%
Cytopathology	33,347	34,832	28,737	35,305	35,942	1.80%	7.78%
Dermatopathology	26,715	25,720	21,017	23,707	23,676	-0.13%	-11.38%
Frozen Sections	3,719	3,620	3,162	3,073	2,876	-6.41%	-22.67%
Neuropathology	782	789	682	710	753	6.06%	-3.71%
Ophthalmic Pathology	1,289	1,424	1,353	1,384	1,453	4.99%	12.72%
Outside Case	30,298	31,471	28,338	28,664	31,595	10.23%	4.28%
Pediatric & Perinatal	5,723	5,973	5,297	5,645	5,890	4.34%	2.92%
Renal Pathology	1,294	1,413	943	811	859	5.92%	-33.62%
Surgical Pathology	47,191	49,460	42,297	47,146	47,103	-0.09%	-0.19%
Technical Only	2,062	2,165	2,133	2,121	2,215	4.43%	7.42%
TOTAL	**153,622**	**158,589**	**136,431**	**151,065**	**154,896**	**2.54%**	**0.83%**



AP Service	FY18	FY19	FY20	FY21	FY22	1-YR	5-YR
Breast	2,479	2,927	2,578	3,358	3,575	6.46%	44.21%
Gastrointestinal	23,114	23,709	19,639	22,026	22,000	-0.12%	−4.82%
General Surgical Path[1]	13,842	14,134	12,581	13,037	12,468	-0.98%	−9.89%
Genitourinary	3,734	3,974	3,545	3,676	3,222	-12.35%	-13.71%
Gynecologic	7,212	7,739	6,611	7,599	7,697	1.29%	6.72%
Ophthalmic	1,311	1,455	1,367	1,397	1,462	4.65%	11.52%
Renal	1,239	1,281	877	807	858	5.80%	−33.69%
TOTAL	**52,931**	**55,219**	**47,198**	**51,900**	**51,282**	**-0.34%**	**−3.21%**

1 "General Surgical Path" is comprised of Endocrine, Bone, Soft Tissue, Head & Neck, and Pulmonary

Jonathan McHugh, MD
Director, Head and Neck / Oral-Maxillofacial Pathology

Jeffrey Myers, MD
Director, Pulmonary/Thoracic Pathology

Raja Rabah, MD
Director, Pediatric Pathology

Rajiv Patel, MD
Director, Dermatopathology

Pathology is concerned with the diagnosis and study of diseases affecting the oral and maxillofacial region and is sometimes considered to be a specialty of dentistry and pathology. Internally generated head and neck cases were included in the general Surgical Pathology service described above. Consult cases are handled by our head and neck service and amounted to 1,403 cases in FY22, which was a 7.67% increase over FY21 and represents a 7.92% increase compared to specimen volumes from five years ago.

Pulmonary/Thoracic Pathology

Pulmonary Pathology is a subspecialty of surgical pathology that deals with the diagnosis and characterization of neoplastic and non-neoplastic diseases of the lungs, pleura, and mediastinum. In-house cases are not tracked separately from other Surgical Pathology cases. However, the Pulmonary Pathology service evaluated 2,962 complex consultation cases, which represents a 15.52% increase over FY21 and a 0.3% decrease compared to specimen volumes from five years ago.

Case Volumes

Case volume for all Surgical Pathology services in FY22 includes all in-house specimens and extramural consultations (transfer and private consults). This case volume for Surgical Pathology was 51,282, which represents a varied year-over-year change for different subspecialties, with an overall 0.34% decrease from the prior year.

Frozen Sections

The frozen section case volume for FY22 was 2,876, representing a decrease of -6.41% compared to FY21.

Turnaround Time

Turnaround time, defined from when a specimen is received in pathology until the case is signed out, increased an average of 12.2% compared to one year ago. This turnaround time is 55.24% faster compared to 5 years ago. This can be attributed to several measures including leveraging informatics for better tracking of turnaround time and delayed cases, as well as immediate notification of faculty about late cases.

Cardiovascular Pathology

Cardiovascular Pathology examines the heart and major blood vessels to determine the diseases of these organs, whether congenital or acquired in life. Cases include surgical specimens from living patients or autopsy specimens from deceased patients as well as heart biopsies. A formal cardiovascular pathology service was created in February 2022 in Anatomical Pathology.

Case Volume

The cardiovascular surgical pathology case volume of 555 for FY22 reflects a 24.7% increase compared to the previous year.

Turnaround Time

Average turnaround time for cardiovascular surgical pathology cases was 2.76 days in FY22, which decreased by 7.2% in the last year.

Pediatric and Perinatal Pathology

This medical subspecialty is focused on childhood diseases as well as perinatal conditions affecting the placenta and fetus. The work includes pediatric surgical pathology cases as well as autopsies and placental examinations.

Case Volume

The pediatric surgical pathology case volume of 6,504 for FY22 reflects a 5.07% increase compared to FY21 and a 2.93% increase compared to specimen volumes from five years ago. Placental exams increased by 17.75% to 2,149 cases in FY22 and shows a 3.77% increase over five years. Pediatric fetal exams had no change from FY22 with 257 cases performed, where pediatric autopsies had 27 cases, which is a 12.5% increase from FY21.

Turnaround Time

Average turnaround time for pediatric surgical pathology cases was 2.36 days in FY22, which increased by 8.67% in the last year. These turnaround times also demonstrate that cases in FY22 were signed out 19.42% faster compared to five years ago.

Dermatopathology

Dermatopathology focuses on the study of cutaneous diseases at

a microscopic and molecular level. The dermatopathology service utilizes light microscopy, immunofluorescence, and molecular testing.

Case Volume
The Dermatopathology service experienced an overall 1.14% increase in FY22 and handled a total of 30,438 cases. This included a 4.42% decrease in specimens from Michigan Medicine patients ("in house" cases) which accounted for 51% of the cases seen. Cases from patients outside of Michigan Medicine ("MLabs cases") were also up 8.33% in FY22.

Turnaround Time
Overall turnaround time for dermatopathology cases averaged 3.59 days, showing on average 7.03% increase over FY21.

Neuropathology
Neuropathology is that branch of pathology that focuses on the diagnosis of diseases of the central and peripheral nervous systems and incorporates non-neoplastic conditions targeting skeletal muscle.

Case Volume
For FY22 there were a total of 2,205 cases signed out compared to 1,952 cases in FY21, representing a 12.96% increase. Over a five-year period, this service has witnessed a 36.9% increase in neuropathology cases.

Turnaround Time
Turnaround time for neuropathology cases decreased on average to 5.21 days, showing a 5.61% improvement from FY21 and a 7.5% improvement compared to five years ago.

Ophthalmic Pathology
Ophthalmic Pathology focuses on diseases of the eye and unique periorbital structures. These cases are predominantly signed out at the W.K. Kellogg Eye Center in Ann Arbor.

Case Volume
This service accounted for 1,545 cases in FY22, representing a 4.96% increase over the prior year and a 13% increase over the past five years.

Turnaround Time
Ophthalmic Pathology turnaround-time averaged 3.68 days showing an increase of 12.4% in FY21 and a 47.3% improvement over five years.

Renal Pathology
The Renal Pathology service focuses on the diagnosis and characterization of medical diseases (non-tumor) of the kidneys.

Case Volume
Medical renal biopsy case volume increased to 911 in FY22, representing 7.8% increase and 32.5% decrease in one- and five-year-over-year changes, respectively. The decline was driven in part by a FY20 kidney transplantation hold and changes in transplantation surveillance biopsy practices, both related to COVID-19.

Turnaround Time
For medical renal biopsies the overall turnaround time was 5.65 days in FY22, representing a marked (56.8%) improvement compared to last year and even greater (97.4%) decrease compared to five years ago.

Cytopathology
Cytopathology is a branch of pathology that performs diagnostic testing on samples consisting of mostly individual cells, such as Pap tests, body fluids, brushings, and fine needle aspirations (FNA). Our cytopathologists perform rapid on-site evaluations (ROSE) at multiple clinics and procedure rooms throughout Michigan Medicine. Telecytology is frequently employed to support this service. ROSE enables rapid specimen triage and diagnostics for patients while they are still at the medical center, eliminating the need for follow-up visits due to inadequate sampling. Our cytopathology team are also skilled at performing palpation-guided and ultrasound-guided FNA themselves.

Andrew Lieberman, MD, PhD
Director, Neuropathology

Victor Elner, MD, PhD
Professor, Ophthalmology

Evan Farkash, MD, PhD
Director, Renal Pathology Service

Judy Pang, MD
Director, Cytopathology

Allecia Wilson, MD
Director, Autopsy & Forensic Pathology

Case Volume / UH, Washtenaw, and Livingston Counties							
	FY18	FY19	FY20	FY21	FY22	1-YR	5-YR
Brain Cases	52	70	52	42	44	4.76%	−15.38%
Livingston Autopsies	80	99	123	137	120	-12.41%	50.00%
Livingston Exams	3	9	26	28	32	14.29%	966.67%
UH (Adult) Autopsies	152	167	164	128	114	−10.24%	−25.00%
UH (Peds) Autopsies	37	27	24	24	28	16.67%	−24.32%
Washtenaw Autopsies	330	351	344	378	336	-11.11%	−1.82%
Washtenaw Exams	70	62	67	104	100	-3.85%	42.86%
TOTAL	**724**	**785**	**800**	**841**	**774**	**-7.86%**	**6.91%**

Table: *Autopsy and Forensics Total Examinations at UH, Washtenaw and Livingston Counties.*

Wayne County ME Office Case Volume							
	FY18	FY19	FY20	FY21	FY22	1-YR	5-YR
Full Autopsies	2,417	2,318	2,116	2,901	2,647	-8.76%	9.52%
Externals	855	865	891	562	979	74.20%	14.50%
TOTAL	**3,272**	**3,183**	**3,007**	**3,463**	**3,626**	**4.71%**	**10.82%**

Table: *Wayne County ME Office Case Volumes.*

Case Volume

Our cytopathology service processed 35,942 cases in FY22 which was up 1.8% from FY21 and up 7.8% compared to five years ago. Gynecologic pap tests represented the bulk of these cytopathology cases. There were 8,118 non-gynecologic cytopathology cases in FY22 in addition to 3,194 FNAs, which included percutaneous and endoscopic aspirations.

Turnaround Time

Turnaround times in cytopathology have remained excellent. The average turnaround time for all cytology cases was 1.59 days in FY22, which is approximately a 4% decrease from previous years.

Autopsy and Forensic Pathology

Hospital and forensic autopsies and examinations represent major activities within Anatomic Pathology. Our fellowship-trained forensic pathologists handle forensic cases from Wayne, Monroe, Washtenaw, and Livingston Counties. All Michigan Medicine adult and pediatric autopsies as well as all forensic cases from Washtenaw and Livingston Counties are performed in the University Hospital (UH) morgue. Wayne and Monroe County forensic cases are performed at the Wayne County Medical Examiner's Office (WCMEO) in Detroit.

Case Volume

Case volumes of autopsies performed in the UH morgue were down 7.86% from FY21 and showed a 6.91% increase over the past five years. Case volumes of autopsies performed at the Wayne County Medical Examiner's Office increased by 4.7% from the previous year and increased by 10.8% over the past five years.

Turnaround Time

Autopsy and Forensic turnaround times demonstrated an average of 47.07 days to finalize an autopsy, representing a 27.8% overall decrease compared to last year, but a 37.5% increase compared to FY18.

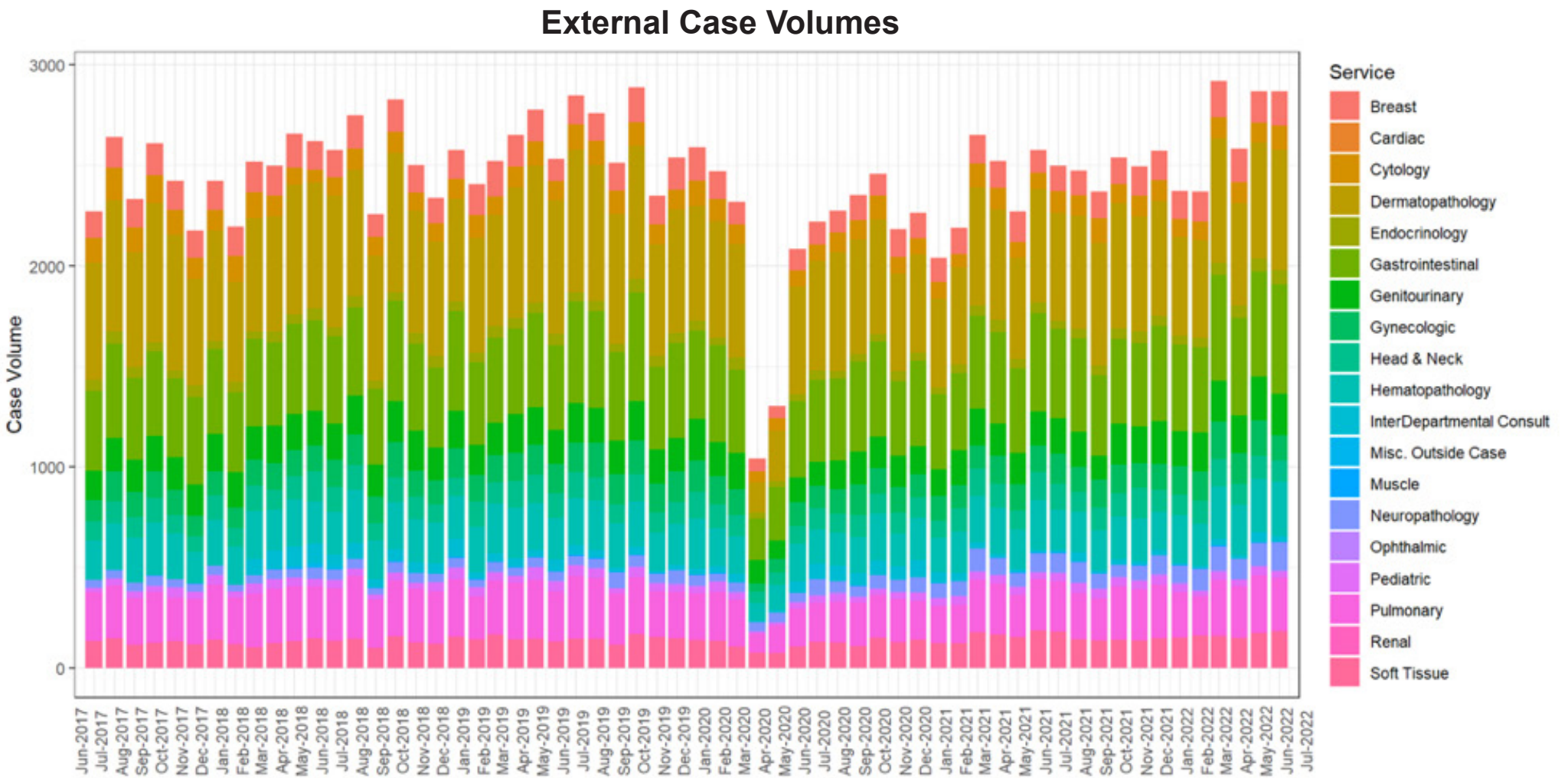


Chart: *External Case Volumes. For figures table, see Appendix* ***pg. 66****.*

Consultation Service

Our extramural consultation practice is an important component of our practice. The rare and difficult cases encountered with this service challenge our faculty to continue to deepen their expertise and expose our trainees to cases otherwise rarely seen. This practice strengthens our brand at regional and national levels, leads to research opportunities in rare diseases, is fundamental to the success of subspecialty fellowships, drives revenue, and enhances patient recruitment to Michigan Medicine.

Case Volume

In FY22 the extramural AP consultation practice total case volume was 30,926 which represents a 10.5% increase from FY21 and a 5.3% increase from 5 years ago.

Turnaround Time

Our consultation service showed continuous improvement with regard to turnaround time, remaining excellent at an average of 3.08 days per case. This represents a 4.3% improvement over last year and 21% quicker turnaround time compared to five years ago.

Technical-Only Histological Service

Our histology laboratory offers outside laboratories access to our test menu including immunohistochemical and in situ hybridization stains, which are handled by our highly skilled technologists. For a limited menu, we also perform both technical stains and pathologist interpretation.

Case Volume

Technical only cases were up 4.43% compared to FY21 and have increased by 7.42% from five years ago.

Turnaround Time

The turnaround time for Technical Only cases decreased by 23% from FY21 to 1.51 days and demonstrated a 52.8% decrease from FY18.

Personnel

In AP there are 66 faculty members that sign out, including many world-renowned pathologists. This does not include pathologists who are part of leadership or other divisions, and it also does not include active emeritus faculty. Since July 2021, 9 new faculty were hired. The service also involves 8 fellows.

Academic Activities

AP faculty excelled at fulfilling our research mission. AP pathologists collectively published 326 peer-reviewed articles in prestigious journals. Our faculty collectively delivered 142 presentations at regional, national, and international meetings and other institutions.

Education

Medical School Teaching/Graduate School Teaching

Under the organizational leadership of Dr. Lew, nearly 40 AP faculty participated in medical school teaching (M1-M4 students) including lectures, labs, and experiential learning. Several AP faculty members also participated in teaching and mentoring our graduate students.

Residency Program/Fellowship Program

AP faculty across disciplines dedicated many hours to teaching our residents and fellows. Residents in AP were exposed to excellent learning opportunities in surgical pathology, cytopathology, and autopsy/forensic pathology. AP fellows were exposed to challenging cases from our extensive consultation practice and participated in many multidisciplinary conferences and tumor boards.

Riccardo Valdez, MD
Director, Clinical Pathology

Clinical Pathology

The Division of Clinical Pathology (CP) encompasses the medical laboratories within the Department of Pathology. These CLIA-certified and CAP-accredited laboratories, like the clinical laboratories within the Anatomic Pathology Division, support the diagnosis and management of human disease through automated and/or manual testing of blood, body fluids, bone marrow, and fresh or fixed tissue specimens.

The clinical laboratory disciplines and support services administered within the CP Division include Clinical Chemistry, Toxicology, Drug Analysis, Hematology, Coagulation (Clinical Core Laboratory Service); Blood Bank, Apheresis, Cell Therapy (Transfusion Medicine Service); Special Chemistry, Clinical Immunology; Clinical Microbiology; Morphology and Flow Cytometry (Hematopathology Service); Clinical Cytogenetics; Molecular Diagnostics; Histocompatibility; Point-of-Care Testing; Phlebotomy; Specimen Processing. The Michigan Medicine Genetics Laboratories share infrastructure and CLIA resources with CP.

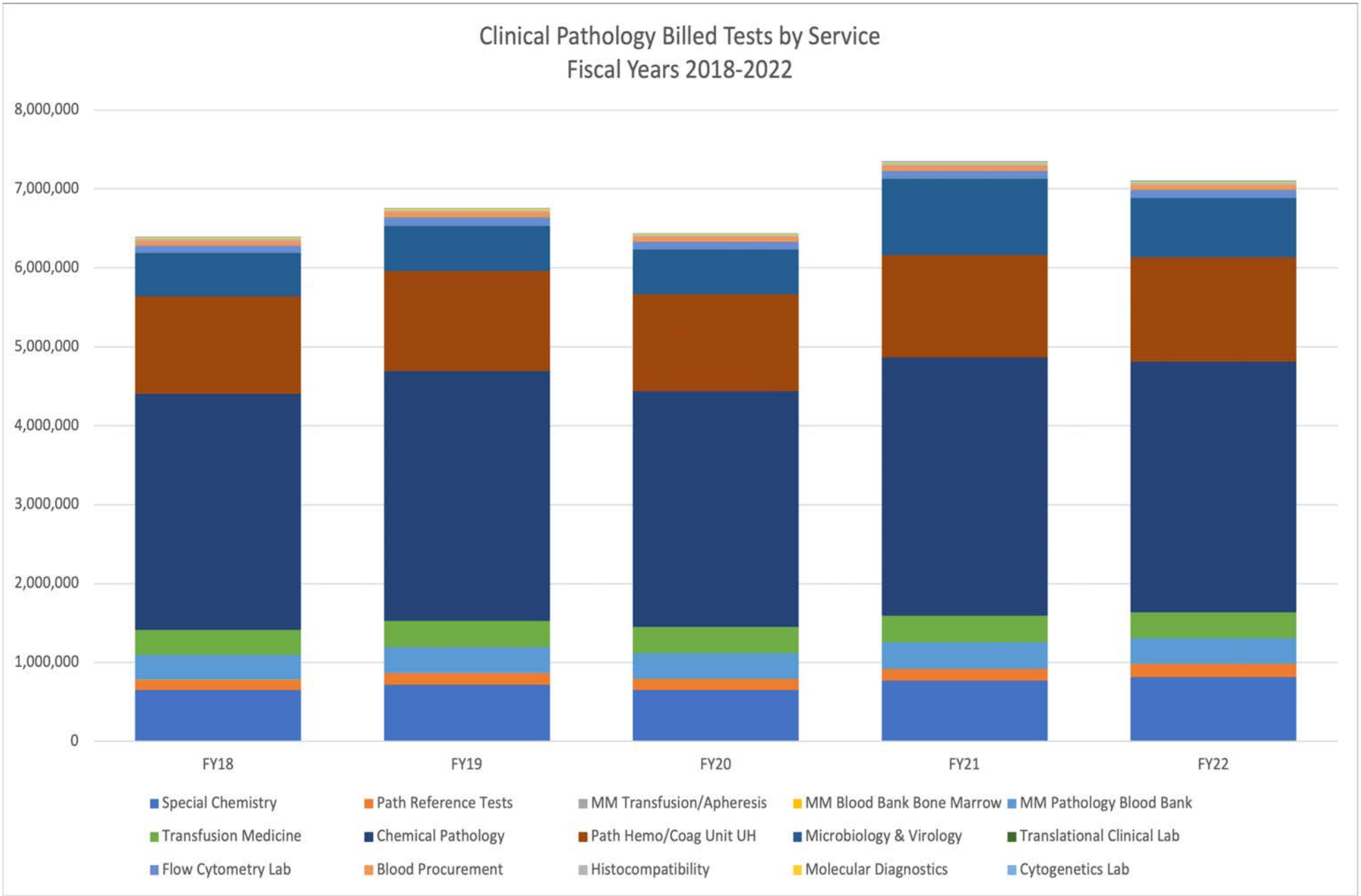
The CP Division has twenty-eight active clinical faculty and approximately 831 allied health staff. The clinical effort of the CP faculty is equivalent to 12 FTEs, and the RVU/FTE is unchanged from last year. Three new faculty were added to the Division in FY22: Aiko Otsubo, PhD joined in April as a Clinical Cytogeneticist and Molecular Geneticist. Dr. Robert Bell was recruited as Clinical Informatician supporting the molecular testing databases in various labs of the Division, also serving as a diagnostic hematopathologist and molecular pathologist. Virginia Pierce, MD was also recruited to join the physician leadership in the Clinical Microbiology Laboratory. Both Drs. Bell and Pierce joined the Department in July 2022.

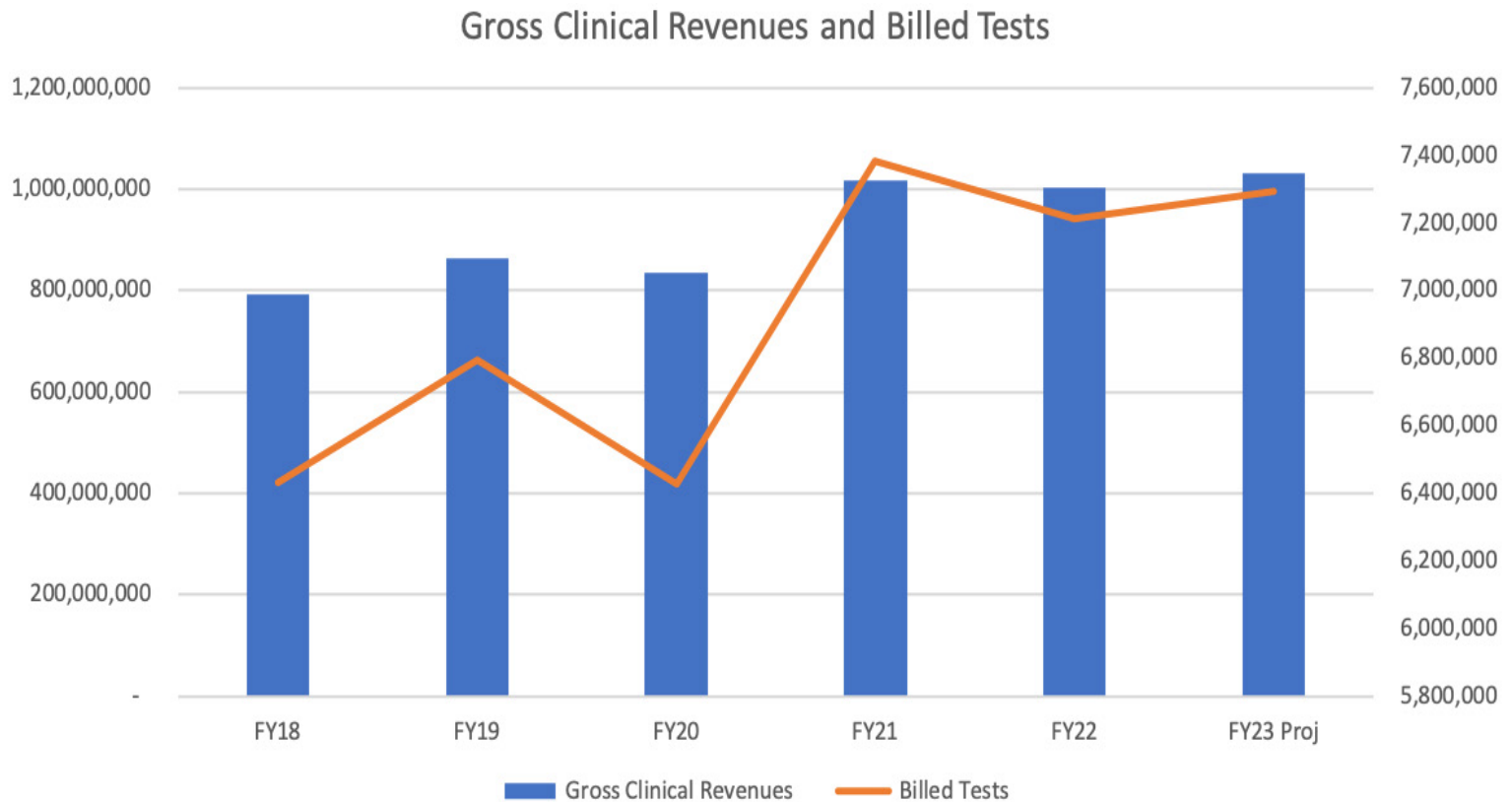
The clinical laboratories in the CP Division achieved 7,211,107 billed tests and $918,236,636 in gross charges in FY22, representing decreases of 2.4% and 1.9% year over year, but with overall increases of 14.7% and 34.1% respectively, over the past five years.

Intermittent laboratory supplies and blood product shortages continued to negatively impact the clinical laboratories during the past year, but overall, the clinical labs experienced less volatility compared to FY21. Laboratory and phlebotomy staffing steadily improved over the year due to concerted departmental and institutional efforts to include increased resources towards recruiting and hiring laboratory personnel.

The UH Clinical Laboratory portion of the Pathology Relocation and Renovation Project (PRR) proceeded as planned with successful activation of the Chemistry/Drug Analysis/Toxicology laboratory areas, the Biochemical Genetics laboratory (MMGL), Specimen Processing, and the Blood Bank lab portion of the Transfusion Medicine section. This major milestone of the PRR included implementation of an automation line connecting the clinical chemistry, hematology, and coagulation parts of the Clinical Core Laboratory, with improved efficiency and better throughput for high volume and frequently ordered lab tests.

The required interim CAP inspection of all the Clinical Laboratories (CP and AP; on- and offsite lab locations) was completed by an internal team composed of twenty-eight individuals from the various lab areas, including pathology trainees and faculty. The findings validated correction of deficiencies found during the external inspection of 2021 and helped to identify other opportunities for improvement.


Clinical Pathology Billed Tests by Service
Fiscal Years 2018-2022
8,000,000
7,000,000
6,000,000
5,000,000
4,000,000
3,000,000
2,000,000
1,000,000
0
FY18
FY19
FY20
FY21
FY22
Special Chemistry
Path Reference Tests
MM Transfusion/Apheresis
MM Blood Bank Bone Marrow
MM Pathology Blood Bank
Transfusion Medicine
Chemical Pathology
Path Hemo/Coag Unit UH
Microbiology & Virology
Translational Clinical Lab
Flow Cytometry Lab
Blood Procurement
Histocompatibility
Molecular Diagnostics
Cytogenetics Lab



Clinical Core Laboratory

The Clinical Core Laboratory (CCL) is located on the University Hospital main campus and provides 24/7/365 clinical testing for hundreds of different health- and disease-related analytes in blood, urine, or body fluids. The around-the-clock staff support the inpatient, outpatient, and emergency service practices for both adult and pediatric patients. In addition, the CCL performs testing for patients seen at our offsite laboratory and medical practice locations (e.g., West Ann Arbor, Northville, Canton, East Ann Arbor, Brighton Specialty), as well as from our MLabs patients. The CCL is medically supported by Drs. Carmen Gherasim, Sean Li, David Manthei, Steven Pipe, Riccardo Valdez, and Jeffrey Warren. Eric Vasbinder was selected to serve as the CCL Administrative Manager in June 2022, succeeding Janette Todd. A major milestone for the CCL was completion of the automation portion of the chemistry and hematology lab renovation project in March 2022. With the renovation complete, the CCL will continue to work toward finding new workflows and internal organization to include cross training and development of standard best practices. This will allow for an improved ability to respond to staffing shortages, improved TAT where needed, and test menu expansion.

Clinical Chemistry, Drug Analysis, and Toxicology

This subsection of the CCL performs STAT and routine testing in

the areas of general chemistry, endocrinology, drug analysis, and toxicology. The test menu includes routine chemistries (electrolytes, creatinine, liver function, glucose, and proteins), lipids, vitamin testing, cardiac markers, tumor markers, reproductive hormones, hepatitis serology testing, metals testing (e.g., lead), therapeutic drug monitoring, drug-of-abuse testing, and intraoperative parathyroid hormone testing. The area is equipped with state-of-the-art automated analyzers utilizing spectrophotometry, immunoassays, mass spectrometry, and other methods for a full range of diagnostic testing. The clinical labs in the Adult and Children's Emergency Services areas are administered by the chemistry section of the CCL. The AES and CES laboratories played a critical role in our COVID response in FY22, helping to alleviate diagnostic COVID testing TAT through implementation and use of the Abbott ID NOW COVID test.

In FY22, this area performed 3,177,933 tests with a 3.5% increase in outpatient tests and a 10% decrease in inpatient testing compared to FY21 (total tests 3,277,102), reaching similar volumes to those seen pre-pandemic (FY19). Toxicology lab performed 95,278 tests; a 9.8% increase compared to FY21 (total tests 84,714) and back to the pre-pandemic test volumes (FY19). CES labs expanded access to COVID-19 diagnostic testing to all procedural units which increased the testing volume by 87% compared to FY21.

Additional highlights from this area include:

- Installation of a new Aptio automation line and new analyzers in Chemistry Automation area
- Re-validation/verification of over 100 FDA-approved and FDA-modified tests performed on nine new Siemens Atellica analyzers (6 CH + 3 IM)
- Validation and implementation of selenium testing by ICP-MS, useful in monitoring selenium replacement therapy in patients without a functional bowel, and selenium deficiency or toxicity
- Implementation of the new race-free equation (CKD-EPI 2021) for estimating glomerular filtration rate to remove bias in diagnosis of kidney diseases (among the first laboratories to adopt the new race-free equation)

Hematology and Coagulation

This subsection of the CCL performs testing on blood and urine specimens to measure the various blood components (e.g., red blood cells, white blood cells, and platelets), assess clotting factor levels, determine the impact of medications on blood clotting processes, and help diagnose diseases of kidneys and urinary tract. Quantitative flow cytometry supports the apheresis unit of Transfusion Medicine as well as the institutional stem cell transplant program. In addition, the hematology lab also remains involved in the bone marrow biopsy process, providing lab techs to attend and assist these bedside clinical procedures.

The hematology and coagulation labs performed 1,319,143 billed tests in FY22, a 2% increase over last year. These lab areas have experienced a 7.7% increase in billed tests and 12% increase in gross charges over the past five years.

The hematology and coagulation lab areas benefited from completion of the core chemistry automation line project and worked closely with the chemistry area and specimen processing to modify pre-analytical workflows to align with the new lab capabilities. While the Sysmex hematology analyzers were connected to the auto line last year, the coagulation instruments were put on the line this year with completion of the Aptio line in the automated chemistry area.

The hematology lab transitioned from the Work Area Manager (WAM) middleware to a new middleware product called Care sphere (CWS) in 2021, but considerable time and effort went towards stabilizing and optimizing CWS in FY22.

Additional highlights from this area include:

- Initiated planning process to replace the Arkray urinalysis instruments to include researching options and prepared a Request for Proposal (RFP)
- Performed in-lab evaluation of new flow cytometry sample prep instrument and flow cytometry with an aim to replace existing equipment in FY23.
- Began quality improvement project in conjunction with NCRC hematopathology lab with a goal of finding better ways to

Daniel Boyer, MD, PhD
Director, Clinical Flow Cytometry Laboratory

Jeffrey Warren, MD
Director, Clinical Immunology

Robertson Davenport, MD
Director, Blood Bank and Transfusion Service

Chisa Yamada, MD
Director, Apheresis Services

Laura Cooling, MD
Director, Cellular Therapy Laboratory

schedule bone marrow biopsy procedures (ongoing).

- Reviewed and updated quantitative flow cytometry standard operating procedures, with emphasis on QA/QC practices.

Clinical Immunology & Special Chemistry

The Clinical Immunology and Special Chemistry labs perform testing to assess immune responses in patients with autoimmune, infectious, and other similar conditions; testing for patients with protein disorders such as those seen in multiple myeloma and related disorders; and hemoglobin evaluations in patients with suspected red blood cell disorders.

In combination, these laboratories performed approximately 290,000 tests in FY22, representing a 7% increase over the approximately 270,000 tests performed in FY21. Longitudinal year-over-year comparisons for these two areas has been complicated by the historical organization of these labs within the clinical chemistry section, but both areas have shown consistent growth.

Highlights from this section include:

- Transition of Section Directorship to Dr. David Manthei from Dr. Jeffrey Warren, who will continue to consult on clinical matters.
- Continued integration of laboratory staff and duties, with examples including work in the LIS and late-in-shift tasks before the following day.
- Validation and implementation of serum tryptase, useful in the evaluation of mast cell disorders and allergic conditions.
- Validation and implementation of testing for anti-phospholipase A2 receptor antibodies, frequently observed in primary membranous nephropathy.
- Coordination with clinical counterparts for improvement of test ordering and appropriateness for fecal immunochemical tests (FIT).

Transfusion Medicine

Blood Bank, Immunohematology Reference Lab, Apheresis Procedure Unit, Cellular Therapy

The Transfusion Medicine Section consists of the multiple areas noted above. The section is supported by the following faculty: Drs. Laura Cooling, Robertson Davenport, Kristina Davis, and Chisa Yamada. Dr. Sean Li continues to provide clinical service as needed.

Overall blood product utilization decreased slightly in FY22 (See Appendix, pg. 76). This reflects overall clinical activity and the efforts of the medical staff in appropriate use of blood components. The platelet inventory was transitioned completely to pathogen-reduced or LVDS apheresis platelets, which advanced transfusion safety. Due to national blood donation and supply constraints, intermittent component shortages occurred throughout the year. These were successfully managed in accordance with the institutional blood allocation and utilization strategy with minimal impact on patient care. In addition, alternative suppliers to the primary vendor, the American Red Cross, were utilized when available and appropriate. Activity in the Immunohematology Reference Laboratory decreased slightly in FY22; however, test volume does not reflect the complexity of problem resolution, which has increased due to the patient population and the increasing use of therapeutic biologics that interfere with pretransfusion compatibility testing. Activity also decreased slightly in the Cellular Therapies Laboratory reflecting changing referral and eligibility patterns for transplantation and cellular therapies. Overall activity in the Apheresis Procedure Unit increased 3.0% over the prior year and 9.8% over the past five years. Clinical investigation activities were strong with Transfusion Medicine faculty serving as Principal Investigators on two randomized clinical trials, and the section supporting multiple BMT and cellular therapies clinical trials, including novel initiatives in chronic kidney disease, renal transplantation, congenital heart disease, and sarcomas.

Other notable initiatives in FY22 included:

- Completion and occupation of the newly renovated blood bank as part of PRR

- Implementation of new workflow changes to streamline test and order processing
- Active participation on the Blood Allocation and Utilization Task Force
- Revision of the Massive Transfusion Protocol and migration to PolicyStat
- Revision of the Blood Transfusion Policies Manual
- Revised Transfusion Record Form with nursing instructions for form management and compatibility table
- Active enrollment in the ReCePI trial
- Initiation of the CHIPS trial

Hematopathology

Flow Cytometry and Morphology Laboratory and Diagnostic Service

The Hematopathology service focuses on the evaluation and diagnosis of blood, bone marrow, and lymph nodes disorders, both reactive and neoplastic, using a variety of techniques including routine microscopy (morphology), flow cytometry, and immunohistochemistry with incorporation of data from cytogenetic and molecular diagnostic testing in a vast majority of cases.

This section is supported by eight hematopathologists (Drs. Daniel Boyer, Noah Brown, Winston Lee, Anamarija Perry, Charles Ross, Russell Ryan, Lauren Smith, and Riccardo Valdez) who variably participate on each of three clinical services (in-house biopsies, flow cytometry/blood and body fluid smear interpretation, and transfer and consult case interpretation). Two of the primary hematopathology section faculty participated in the interpretation of myeloid next-generation sequencing test interpretation in FY22 with more faculty expected to provide those diagnostic services in the coming years. Case volumes continued to increase to at or above pre-COVID numbers in FY22.

In FY22, 2,784 bone marrow and other tissue biopsies collected from Michigan Medicine patients were diagnosed and signed out by the hematopathology team, compared to 2,060, in the previous year. The diagnostic service also managed 1,304 cases from external healthcare systems associated with patients seeking care at Michigan Medicine and 1,486 external cases sent by other pathologists for primary diagnosis or expert opinion. The flow cytometry lab performed 101,563 billed tests in FY22 compared to 101,981 in FY21. Of note, the test volume in flow cytometry specifically includes 5,901 leukemia and lymphoma immunophenotyping panels. Over the past five years, flow cytometry lab test volume has increased by 29.6% (based on billed tests). Notable FY22 achievements in this section include:

- Implementation of new combined bone marrow schedule between hematopathology and hematology for daily tracking and quality indicator monitoring
- Completion of four new laboratory developed flow cytometry panels (BML, TBASIC, CTCL, and TTOX) leading to increased specificity and consistency for identifying abnormal population in clinical samples
- Planning and preparation for the next set of revised panels to include new Myeloid+T, Myeloid+B, Myeloid+P, and Monocytic panels
- Redesign of the plasma cell panel to allow for more diagnostic markers in a single tube and reduction of reflex testing
- Quality Month Poster presentation on redesigned plasma cell flow cytometry panel by Conor Daining, MT, on behalf of the hematopathology lab staff.

Clinical Microbiology and Virology

The Clinical Microbiology Laboratory consists of multiple subspecialty areas (bacteriology, mycology, parasitology, antimicrobial susceptibility, molecular microbiology, and virology). These lab areas focus on identifying bacterial, fungal, and viral pathogens to aid in the diagnosis and treatment of patients.

Lauren Smith, MD
Service Director, Hematopathology

Michael Bachman, MD, PhD
Associate Director, Clinical Microbiology Laboratory

Paul Lephart, PhD
Associate Director, Clinical Microbiology Laboratory

In FY22, the Clinical Microbiology Laboratory (including virology) performed 752,331 total billed tests compared to a total of 963,936 the previous year, representing a 22% decrease year-over-year. The decrease in test volume reflects changes in diagnostic COVID test volume and practices.

The lab continued to be significantly impacted by the COVID pandemic in FY22. Like last year, FY22 was notable for continued supply chain issues affecting not only COVID testing, but also other testing platforms, such as the primary one used for sexually transmitted infection testing. Despite record rates of infection during the Omicron surge, the laboratory met its quality goal and supported hospital operations by maintaining <24h turnaround time on pre-procedural COVID testing. At the same time, notable advancements were achieved, including:

- Inventory Project Management – implemented 5-S for each of the Microbiology Lab Benches and aligned the inventory with testing usages to reduce supply waste (urgent shipping charges, expiration dates/over ordering)
- *Candida auris* PCR implementation – supports infection prevention screening for this urgent antibiotic resistance threat
- Revised *Clostridioides difficile* testing algorithm – optimizes patient management and definitions of hospital-acquired infection
- Improvements in laboratory operations including increased diagnostic testing on the third shift, protected offline time for area leaders to revise and improve procedures, decentralized scheduling, standardized huddle format, and numerous activities to boost morale and staff engagement

To restore faculty levels after Dr. Newton's departure, a search committee led by Dr. Valdez successfully recruited Virginia Pierce, MD as Associate Director. She is board certified in Pediatric Infectious Diseases and Medical Microbiology, and a national leader in antimicrobial susceptibility testing.

Thomas Giordano, MD, PhD
Director, Molecular and Genomic Pathology

Noah Brown, MD
Director, Molecular Diagnostics Laboratory

Molecular & Genomic Pathology

Molecular diagnostics is the science of analyzing biological markers in the genome and proteome, an individual's genetic code, to determine how cells express their genes as proteins. Specialized laboratory techniques are utilized to diagnose and monitor disease, determine response to therapy, assess risk of relapse, and help determine which therapies will work best for individual patients. Year-over-year, the Division of Molecular and Genomic Pathology has made considerable progress toward realizing its overarching goals of facilitating a coordinated strategy for the various clinical laboratories performing molecular tests within the Department of Pathology, and interfacing with Michigan Molecular Genetics Laboratory (MMGL) administered by the Department of Pediatrics.

Molecular Diagnostics Laboratory

The Molecular Diagnostics Laboratory (MDL) performed 19,098 billed tests in FY22, unchanged from FY21 (19,169).

The MDL again remained an active area of new test development, test maintenance, and continuous improvement. The selected items below represent notable highlights from another productive year:

Completed Test Development:

- POLE Mutation (10/6/2021) – Detection of mutations in endometrial carcinoma associated with an 'ultra mutated' signature
- FGFR2 Rearrangement by FISH (3/2/2022) – Detection of targetable rearrangements in cholangiocarcinoma and other cancers
- Specimen Source Identification (3/23/2022) – Identity testing for anatomic pathology quality control
- USP6 Rearrangement by FISH (6/22/2022) – Detection of rearrangements to aid in the diagnosis of aneurysmal bone cyst and nodular fasciitis
- Consolidation of Cystic Fibrosis Carrier Screening into

Diagnostic Testing performed by the Medical Genetics Laboratory (MMGL)

Ongoing Test Development Activities:

- Neuropathology Methylation Array – Methylation profiling to aid in the diagnosis and classification of neurological neoplasms
- Solid Tumor Fusion Panel – Detection of a broad range of diagnostic and targetable fusions in solid tumors including bone and soft tissue, neuro-oncology, head and neck, dermatological, gastrointestinal, genitourinary, and gynecological
- Validation of cell-free DNA from fluids including cerebrospinal fluid, vitreous humor, and aqueous humor for MYD88 L265P mutation and IGH and IGK B-cell clonality testing
- Evaluation of alternative, EDTA-based decalcification method for improved molecular and immunohistochemical testing

Cost Savings Initiatives:

- Validation of bulk reagents for FISH testing (rather than kits) resulting in cost savings of $108.84 per test corresponding to a cost savings of $152,376 per year.

Clinical Cytogenetics

Cytogenetic testing involves analysis of bone marrow, blood, or fresh tissue specimens to look for changes in chromosomes, including rearrangements, additions, deletions, or insertions of genetic material. Changes in chromosome number or structure may be a sign of a genetic disease or condition and may help diagnose types of cancer.

The primary tests performed in the Clinical Cytogenetics lab are the karyotype, fluorescence in-situ hybridization (FISH; fresh and paraffin embedded tissue), and genomic microarray. Enhancements to increase sensitivity are performed including pre-analytical cell separation and mitogen stimulation of cultures.

The Clinical Cytogenetics Laboratory performed 16,315 billed tests in FY22, compared to 14,249 in FY21, an increase of 14.5%. Dr. Aiko Otsubo joined the faculty in cytogenetics as well as the molecular genetics laboratory in MMGL. Laboratory staffing numbers remained stable in FY22.

The Clinical Cytogenetics Laboratory continued to improve patient testing and workflow during the past year. These improvements included:

- Compared genomic array results and karyotype results in the pediatric solid tumor samples received in the past two years and found karyotype had limited additional value when genomic array results were available, especially when copy number aberrations instead of gene fusions are clinically significant biomarkers.
- Implemented practice change based on internal study noted above to include not performing karyotype analysis in pediatric solid tumors such as neuroblastoma, Wilms tumor, teratoma, etc. (59% of pediatric solid tumors, 2/1/22 - 9/30/22) when genomic array was also requested.
- Continued optimizing the plasma cell enrichment processes to improve the plasma cell yield and to reduce the percentage of samples with insufficient quantity (QNS). The QNS rate has decreased from 34% prior to June 2020 to 8.3% in 2022.

Lastly, the Clinical Cytogenetics Laboratory has its first Laboratory Genetics & Genomics (LGG) fellow starting July 2022. The LGG training is a 2-year ACGME accredited program that will lead to the eligibility for certification by the American Board of Medical Genetics and Genomics.

Lina Shao, PhD
Director, Cytogenetics

Histocompatibility Laboratory

The Histocompatibility (HLA) Laboratory performs an array of clinical tests used to help determine compatibility between donors and recipients and to assess immunologic risks associated with solid organ and stem cell transplantation. Lastly, the lab performs histocompatibility testing for other clinical purposes such as disease association. In addition to CAP accreditation, the HLA

Matthew Cusick, PhD
Service Director, Histocompatibility Laboratory

laboratory also maintains accreditation by the American Society for Histocompatibility and Immunogenetics (ASHI).

The Histocompatibility Laboratory performed 25,917 billable tests in FY22, an increase of 16.6% from FY21. In FY22, 1,688 high resolution typing were completed, as compared to 1,477 in FY21, a 14.3% increase. In FY22, 1,674 low resolution typing were completed, as compared to 1,245 in FY21, a 34.5% increase. Antibody specificity testing increased 6.4% from 10,801 in FY21 to 11,488 in FY22. Antibody screening testing decreased 35.3% from 3,687 in FY21 to 2,382 in FY22. A total of 392 flow cytometric crossmatches were performed in FY22, representing a 25.5% decrease compared to FY21. Disease association testing decreased in FY22 with 1,580 completed tests compared to 1,739 in FY21, a 9.1% decrease.

The laboratory validated and implemented next-generation sequencing for high resolution typing in FY22. Next-generation sequencing for transplant compatibility applications has advantages to the clinical laboratory and patient, including elimination of additional typing tests needed to resolve patient HLA ambiguities. The latter improves workflow and conserves supply and personnel resources. This resulted in improved turnaround times, lowered costs, and higher quality test results.

Additional notable highlights for FY22 include:

- Validation of Real-Time PCR for STAT HLA typing
- Collaboration with EPIC-Phoenix and the transplant team to provide discrete test results in EPIC/MiChart which will allow providers to visualize test results, allowing for better patient care
- Streamlined orders between MiChart (Phoenix), Soft, HistoTrac, and improved process for how results flow back to the electronic medical record

Lee F. Schroeder, MD, PhD
Director, Point-of-Care Testing

Point-of-Care Testing

Point-of-Care Testing (POCT) is clinical laboratory testing performed at or near the patient bedside by thousands of operators throughout Michigan Medicine in both the inpatient and ambulatory settings. The operators include nurses and other non-traditional laboratory trained personnel. Testing ranges from the simpler (waived) glucometer and urine pregnancy tests to more complicated (non-waived) blood gas and viscoelastic testing to assess coagulation status in places such as the operating rooms.

The POCT team, led by Dr. Lee Schoeder (Section Director) and Andrew Szczembara (Administrative Manager), supports clinical units with laboratory instruments, reagents, operator training, quality assurance, and regulatory guidance. Their mission is to improve patient health by providing access to safe and efficient laboratory testing at the point of care, through technology, service, and education. Notable achievements for FY22 include the following selected items:

COVID Response
POCT continued to support institutional symptomatic and asymptomatic SARS-CoV-2 testing through the addition of devices at existing sites to provide surge capacity, the addition of testing locations at Brighton Center for Specialty Care & UH Labor and Delivery, and transition to the newest assay versions.

Training/Quality Assurance
A significant component of POCT services is provision of training and quality assurance throughout the enterprise. In FY22, this consisted of:

- Training hundreds of operators to perform point-of-care testing in blitzes as well as targeted educational sessions to several groups: Nursing, Anesthesia, Radiology, Labor and Delivery, Survival Flight, ECMO, physician offices, ambulatory health centers, surgery and procedure centers, Wolverine Street and Regional Alliance of Healthy Schools program
- Maintaining the glucometer program, which includes over six hundred glucometers, over 11,000 operators, and 530,000 patient tests in FY22
- Managing over twenty different test systems and over eight hundred instruments for point-of-care testing.
- Performing over four hundred quality assurance rounds and

troubleshooting visits at the various supported sites.

- Implementing the latest versions of POCT middleware applications RALS and GemWeb Plus.
- Harmonizing blood gas values throughout Michigan and updating glucose reference intervals and critical values.

Laboratory Accreditation
The POCT team facilitated laboratory accreditation biennial inspections at Domino's Farms Metabolism, Endocrinology, and Diabetes clinic and triennial Joint Commission Survey at the Main Campus. A sampling of test volumes for tests performed at the point-of-care is shown below.

Test Name	Number of Patient Tests Uploaded in FY2022
POC Glucose (Glucometer)	530,749
POC Hemoglobin A1C	23,056
POC Blood Gas/Electrolytes (GEM)	36,580
POC UA	52,582
POC COVID	12,203

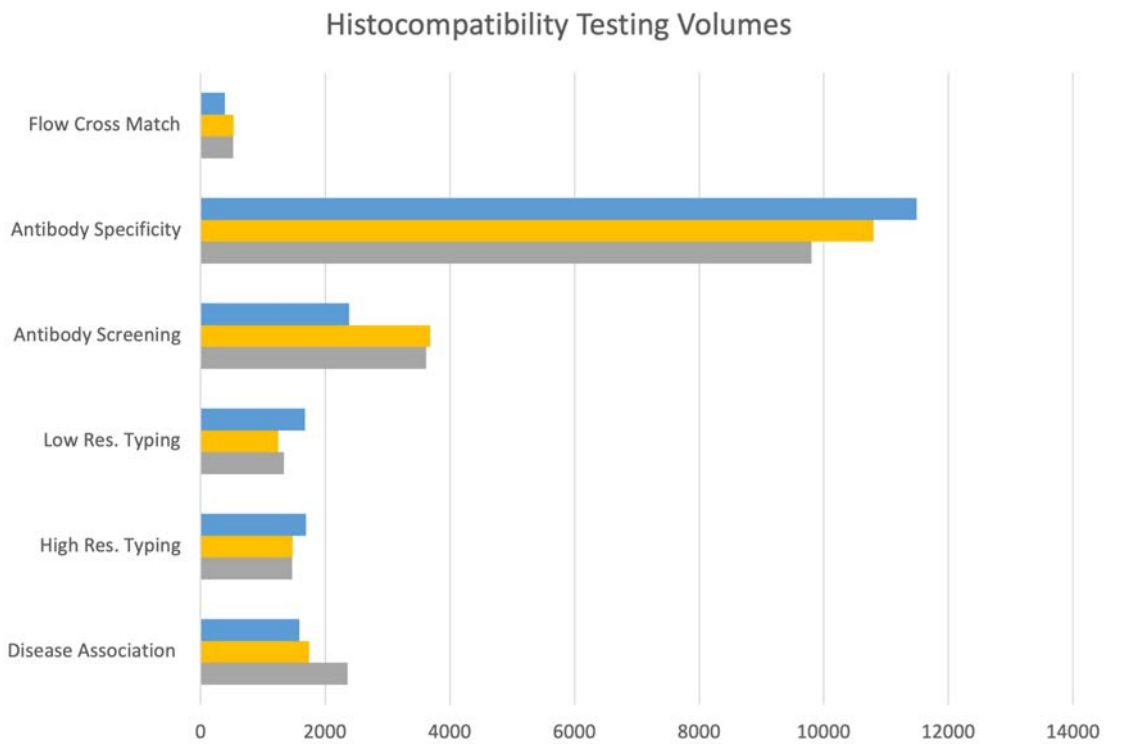


Table (Above): Disease association testing, mentioned on pg. 26.

Arul M. Chinnaiyan, MD, PhD
Director, Michigan Center for Translational Pathology

Michigan Center for Translational Pathology

The research in MCTP focused on functional genomic, proteomic, and bioinformatic approaches to study cancer for the purposes of understanding cancer biology as well as to discover clinical biomarkers, continues to progress, resulting in high-impact discoveries. Summaries from a few of the major published studies over the past year are provided below:

The Genetic Heterogeneity and Drug Resistance Mechanisms of Relapsed Refractory Multiple Myeloma

In partnership with the Multiple Myeloma Research Foundation's molecular profiling initiative (NCT02884102) that included 22 academic medical centers, we carried out clinical-grade targeted sequencing (tumor/normal) and whole transcriptome sequencing of 511 relapsed, refractory multiple myeloma (RRMM) patients and reanalyzed equivalent data from 965 patients enrolled in the CoMMpass Study to systematically compare alterations in RRMM with newly diagnosed multiple myeloma (NDMM). Our uniform integrative analyses uncovered a wide range of genetic alterations, implicates known oncogenic MM pathways, often at a much higher prevalence than previously known, and provides a comprehensive genetic basis for drug resistance mechanisms in RRMM. The NF-κB and RAS/MAPK pathways are more commonly altered than previously reported, with a prevalence of 45–65% each. In the RAS/MAPK pathway, there is a long tail of variants associated with the RASopathies. By comparing our RRMM cases with untreated patients, we identify a diverse set of alterations conferring resistance to three main classes of targeted therapy in 22% of our cohort. Activating mutations in IL6ST are also enriched in RRMM. Taken together, our study serves as a resource for future investigations of RRMM biology and potentially informs clinical management. (*Nat Commun*. 2022 Jun 29;13(1):3750).

Targeting SWI/SNF ATPases in enhancer-addicted prostate cancer

The switch/sucrose non-fermentable (SWI/SNF) complex has a crucial role in chromatin remodeling and is altered in over 20% of cancers. Here we developed a proteolysis-targeting chimera (PROTAC) degrader of the SWI/SNF ATPase subunits, SMARCA2 and SMARCA4, called AU-15330. Androgen receptor (AR)+ forkhead box A1 (FOXA1)+ prostate cancer cells are exquisitely sensitive to dual SMARCA2 and SMARCA4 degradation relative to normal and other cancer cell lines. SWI/SNF ATPase degradation rapidly compacts cis-regulatory elements bound by transcription factors that drive prostate cancer cell proliferation, namely AR, FOXA1, ERG, and MYC, which dislodges them from chromatin, disables their core enhancer circuitry, and abolishes the downstream oncogenic gene programs. SWI/SNF ATPase degradation also disrupts super-enhancer and promoter looping interactions that wire supra-physiologic expression of the AR, FOXA1, and MYC oncogenes themselves. AU-15330 induces potent inhibition of tumor growth in xenograft models of prostate cancer and synergizes with the AR antagonist enzalutamide, even inducing disease remission in castration-resistant prostate cancer (CRPC) models without toxicity. Thus, impeding SWI/SNF-mediated enhancer accessibility represents a promising therapeutic approach for enhancer-addicted cancers. (*Nature*. 2022 Jan;601(7893):434-439).

Autophagy Inhibition by Targeting PIKfyve Potentiates Response to Immune Checkpoint Blockade in Prostate Cancer

Multi-tyrosine kinase inhibitors (MTKIs) have thus far had limited success in the treatment of castration-resistant prostate cancer (CRPC). We reported on a phase I-cleared orally bioavailable MTKI, ESK981, with a novel autophagy inhibitory property that decreased tumor growth in diverse preclinical models of CRPC. The anti-

tumor activity of ESK981 was maximized in immunocompetent tumor environments where it upregulated CXCL10 expression through the interferon gamma pathway and promoted functional T cell infiltration, which resulted in enhanced therapeutic response to immune checkpoint blockade. Mechanistically, we identified the lipid kinase PIKfyve as the direct target of ESK981. PIKfyve-knockdown recapitulated ESK981's anti-tumor activity and enhanced the therapeutic benefit of immune checkpoint blockade. Our study revealed that targeting PIKfyve via ESK981 turns tumors from cold to hot through inhibition of autophagy, which may prime the tumor immune microenvironment in advanced prostate cancer patients and be an effective treatment strategy alone or in combination with immunotherapies. (*Nat Cancer*. 2021 Sep;2:978-993).

TRIM63 as a sensitive and specific biomarker for MiT family aberration-associated renal cell carcinoma

Microphthalmia-associated transcription factor (MiT) family aberration-associated renal cell carcinoma (MiTF-RCC) is a subtype of renal cell carcinoma harboring recurrent chromosomal rearrangements involving TFE3 or TFEB genes. MiTF-RCC is morphologically diverse, can histologically resemble common RCC subtypes like clear cell RCC and papillary RCC, and often poses a diagnostic challenge in genitourinary clinical and pathology practice. To characterize the MiTF-RCC at the molecular level and identify biomarker signatures associated with MiTF-RCC, we analyzed RNAseq data from MiTF-RCC, other RCC subtypes and benign kidney. Upon identifying TRIM63 as a cancer-specific biomarker in MiTF-RCC, we evaluated its expression independently by RNA in situ hybridization (RNA-ISH) in whole tissue sections from 177 RCC cases. We specifically included 31 cytogenetically confirmed MiTF-RCC cases and 70 RCC cases suspicious for MiTF-RCC in terms of clinical and morphological features, to evaluate and compare TRIM63 RNA-ISH results with the results from TFE3/TFEB fluorescence in situ hybridization (FISH) that is the current clinical standard. We confirmed that TRIM63 mRNA was highly expressed in all classes of MiTF-RCC compared to other renal tumor categories, where it was mostly absent or low. While the TRIM63 RNA-ISH and TFE3/TFEB FISH results were largely concordant, importantly, TRIM63 RNA-ISH was strongly positive in TFE3 FISH false-negative cases with RBM10-TFE3 inversion. In conclusion, TRIM63 can serve as a diagnostic marker to distinguish MiTF-RCC from other renal tumor subtypes with overlapping morphology. We suggest a combination of TFE3/TFEB FISH and TRIM63 RNA-ISH assays to improve the accuracy and efficiency of MiTF-RCC diagnosis. Accurate diagnosis of MiTF-RCC and other RCC subtypes would enable effective targeted therapy and avoid poor therapeutic response due to tumor misclassification. (*Mod Pathol*. 2021 Aug;34(8):1596-1607).

Clinical Proteomic Tumor Analysis Consortium Studies

In collaboration with the NCI Clinical Proteomic Tumor Analysis Consortium, we were involved in two major published studies. Both of these studies yield valuable resources for the research community as well.

To understand the underlying molecular alterations that drive pancreatic ductal adenocarcinoma (PDAC) oncogenesis, comprehensive proteogenomic characterization of 140 pancreatic cancers, 67 normal adjacent tissues, and 9 normal pancreatic ductal tissues was carried out. In addition, whole-genome sequencing, whole-exome sequencing, methylation, RNA sequencing (RNA-seq), and microRNA sequencing (miRNA-seq) were performed on the same tissues to facilitate an integrated proteogenomic analysis and determine the impact of genomic alterations on protein expression, signaling pathways, and post-translational modifications. (*Cell*. 2021 Sep 16;184(19):5031-5052).

We also carried out a similar proteogenomic characterization of lung squamous cell carcinoma (LSCC) on 108 prospectively collected, treatment-naive, primary LSCC tumors and 99 paired normal adjacent tissues. We identified a subset of low-p63 tumors that were characterized by high levels of the known therapeutic target survivin. SOX2 is considered undruggable, but our analyses provide rationale for exploring LSD1 or other chromatin modifiers such as EZH2 to target SOX2 amplified / overexpressing tumors. Proteogenomic dissection of the downstream effects of CDKN2A mutations had clinical implications related both to the interpretation of trials utilizing CDK4/6 inhibitors in LSCC patients and to biomarker selection for future studies: though CDK4/6 inhibition

has shown limited efficacy in LSCC trials to date, our analysis suggested that a more nuanced assessment of RB1 protein expression and phosphorylation is required before declaring this approach unsuccessful. (*Cell*. 2021 Aug 5;184(16):4348-4371).

Characterization of SARS-CoV-2 and host entry factors distribution in a COVID-19 autopsy series

We previously reported that androgens regulate the expression of SARS-CoV-2 host entry factors ACE2 and TMPRSS2, and androgen receptor (AR) in lung epithelial cells. We also demonstrated that the transcriptional repression of the AR enhanceosome inhibited SARS-CoV-2 infection *in vitro*. Here, we characterized the tissue distribution and localization of SARS-CoV-2 virus, viral replication, and host entry factors in various anatomical sites sampled via autopsy. We applied RNA in-situ-hybridization (RNA-ISH), immunohistochemistry (IHC) and quantitative reverse transcription polymerase chain reaction (qRT-PCR) approaches. We also assessed histopathological changes in SARS-CoV-2 infected tissues. We detected SARS-CoV-2 virus and viral replication in pulmonary tissues by RNA-ISH and IHC and a variety of non-pulmonary tissues including kidney, heart, liver, spleen, thyroid, lymph node, prostate, uterus, and colon by qRT-PCR. We observed heterogeneity in viral load and viral cytopathic effects among various organ systems, between individuals and within the same patient. In a patient with a history of kidney transplant and under immunosuppressant therapy, we observed an unusually high viral load in lung tissue by RNA-ISH, IHC and qRT-PCR. SARS-CoV-2 virus was also detected in this patent's kidney, liver and uterus. We found ACE2, TMPRSS2 and AR expression to overlap with the infection sites. Overall, our findings show co-existence of SARS-CoV-2 infection and host entry factors in multiple pulmonary and non-pulmonary tissues, providing further insights into SARS-CoV-2 biology. (*Commun Med* (Lond). 2021 Aug 23;1:24.)

Morphological cell profiling of SARS-CoV-2 infection identifies drug repurposing candidates for COVID-19

We developed a quantitative high-throughput screen to identify efficacious agents against SARS-CoV-2. From a library of 1,425 US Food and Drug Administration (FDA)-approved compounds and clinical candidates, we identified 17 hits that inhibited SARS-CoV-2 infection and analyzed their antiviral activity across multiple cell lines, including lymph node carcinoma of the prostate (LNCaP) cells and a physiologically relevant model of alveolar epithelial type 2 cells (iAEC2s). Additionally, we found that inhibitors of the Ras/Raf/MEK/ERK signaling pathway exacerbate SARS-CoV-2 infection *in vitro*. Notably, we discovered that lactoferrin, a glycoprotein found in secretory fluids including mammalian milk, inhibits SARS-CoV-2 infection in the nanomolar range in all cell models with multiple modes of action, including blockage of virus attachment to cellular heparan sulfate and enhancement of interferon responses. Given its safety profile, lactoferrin is a readily translatable therapeutic option for the management of COVID-19. (*Proc Natl Acad Sci USA*. 2021 Sep 7;118(36):e2105815118)

Urinary MyProstateScore (MPS) to Rule out Clinically-Significant Cancer in Men with Equivocal (PI-RADS 3) Multiparametric MRI: Addressing an Unmet Clinical Need

We set out to evaluate the complementary value of urinary MyProstateScore (MPS) testing and multiparametric MRI (mpMRI) and assess outcomes in 540 patients with equivocal mpMRI. Patients underwent mpMRI followed by urine collection and prostate biopsy at the University of Michigan between 2015 -2019. MPS values were calculated from urine specimens using the validated model based on serum PSA, urinary PCA3, and urinary TMPRSS2:ERG. In the PI-RADS 3 population, the discriminative accuracy of PSA, PSAD, and MPS for GG≥2 cancer was quantified by the AUC curve. Decision curve analysis was used to assess net benefit of MPS relative to PSAD. Our data showed that in patients that underwent mpMRI and biopsy, MPS was significantly associated with GG≥2 cancer across all PI-RADS scores. In the PI-RADS 3 population, MPS significantly outperformed PSAD in ruling out GG≥2 cancer. These findings suggest a complementary role of MPS testing in patients that have undergone mpMRI. (*Urology*. 2022 Jun;164:184-190)

Clinical Activities

To exploit the rapid advances in high-throughput DNA sequencing technologies to realize the goals of "precision cancer medicine,"

we established the Michigan Oncology Sequencing Center (MI-ONCOSEQ) in 2011 (Roychowdhury et al, 2012). An "integrative sequencing approach" carried out in a CLIA-certified laboratory (#23D0366712) is utilized to provide a comprehensive landscape of the genetic alterations in individual tumor specimens for the purpose of identifying informative and/or actionable mutations. This approach enables the detection of point mutations, insertions/deletions, gene fusions and rearrangements, amplifications/deletions, and outlier expressed genes. Furthermore, we can identify certain germline alterations that may also be relevant. We continue to develop novel approaches for clinical sequencing and broadening the application of sequence data towards predicting response to immunotherapy and determination of epigenetic status. Thus far we have sequenced samples from over 5,500 adult and pediatric patients; a breakdown of the major cohorts for whom results are returned in the form of a molecular report is listed in the table below.

Cohort	Total Patients Enrolled	Patients Enrolled FY22
MO- (MiOncoseq)	1,732	52
TP- (Tumor Profiling)	972	53
PO- (Peds Oncoseq)	874	123
MMRF- MyDrug	180	29
VA - (PCF-VA)	205	61
BT - (Biliary Tract)	200	42
Total	**4,873**	**378**

Additionally, our sequencing facility supports several specialized programs and clinical studies. We have continued our contract with the Multiple Myeloma Research Foundation into the next phase, MyDrug, that selects patients for therapies/trials based on their sequencing results. We also serve as the sequencing center for the VA - PCF POPCAP program to comprehensively evaluate samples from veterans with metastatic prostate cancer in an effort to provide them access to better and less toxic therapy through targeted therapy.

Program	FY21 Revenue	FY22 Revenue	FY23 Projected Revenue
MMRF	$327,871	$136,389	$150,000
VA/PCF	$185,032	$254,00	$300,000

MI-ONCOSEQ has been supporting several ongoing clinical trials/studies, listed in table below (charges based on select cases chosen for sequencing). We have enrolled 799 total patients to date collectively through all studies. (*See list in Appendix,* ***pg. 80)***

The MCTP Histopathology team assists in the processing and evaluation of submitted specimens for MI-ONCOSEQ, MMRF as well as clinical studies in collaboration with various investigators such as Drs. Alumkal, Udager, Harms, Salami, Wahl, and Palapattu.

In association with MLabs, MCTP's Molecular Testing Lab (MTL) receives orders for and carries out PCA3, Mi-Prostate Score (MPS), and to a smaller extent, Cell Search Circulating Tumor Cell (CTC) assays. Since 2010, MTL has processed a total of 17,205 PCA3, 1,989 MPS and 1,757 CTC assays for clinical use. Additionally, 3,281 PCA3 and 3,281 MPS assays have been processed for research samples. In FY22, MTL processed 192 PCA3, 275 MPS and 88 CTC assays for clinical use; and 50 each of PCA3 and MPS for research.

MTL also procures biological samples such as urine, blood, and tissue for ongoing clinical and research projects. Since 2010, MTL has procured 1,790 tissue, 5,686 Urine, 5,444 serum, and 5,436 EDTA plasma samples.

MTL, working closely with the MI Prostate SPORE Biospecimen core, also supports the following clinical studies and research projects:

- **UMCC 2013.117:** A Randomized Phase II Study of Androgen Deprivation Therapy with or without PD 0332991 in RB-Positive Metastatic Hormone-Sensitive Prostate Cancer.
- **ENACT Study:** A Clinical trial assessing the efficacy of enzalutamide in men with prostate cancer on active surveillance.
- A Randomized Phase II trial of Abiraterone, Olaparib, or Abiraterone + Olaparib in Patients with Metastatic Castration-Resistant Prostate Cancer with DNA Repair Defects (c16-168).
- **UMCC 2016.106:** A Phase I Trial of Neoadjuvant Stereotactic Body Radiotherapy Prior to Radical Prostatectomy for High Risk Prostate Cancer.
- **UMCC 2021.046:** A phase II randomized trial of moderate versus

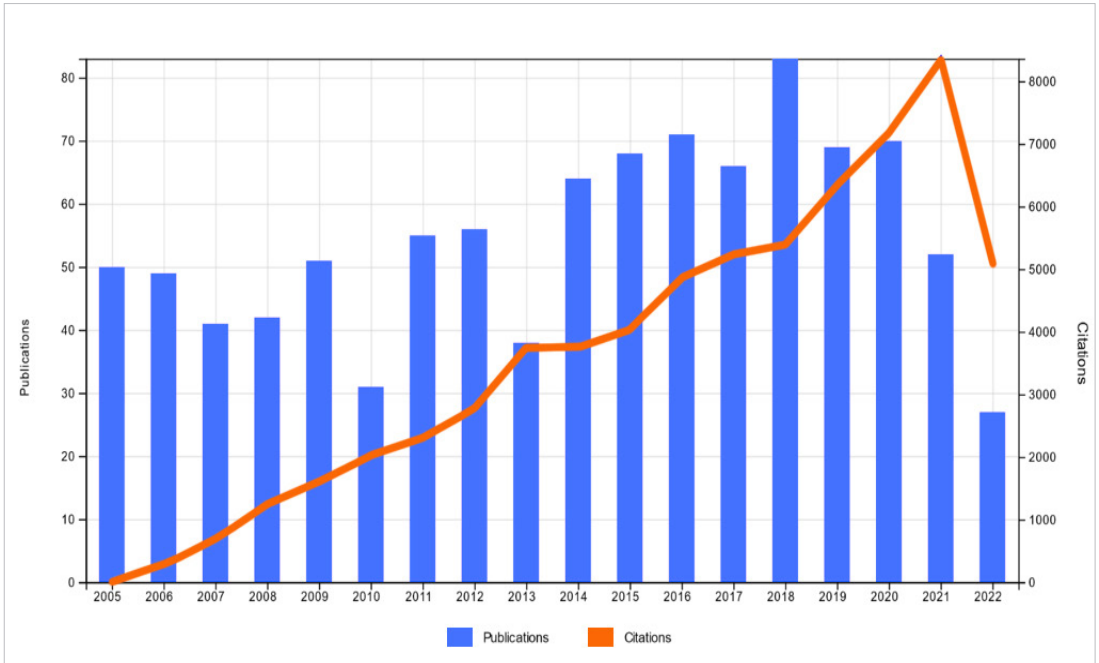
ultra-hypofractionated post-prostatectomy radiation therapy.

- **HUM00117711:** Targeted Early Detection Program in Men at High Genetic Risk for Prostate Cancer.
- **HUM00197931:** Prospective study to evaluate MiPS-NGS urine assay for predicting grade progression in men on active surveillance for prostate cancer. MI-ONCOSEQ (clinical sequencing program): The Tissue/Informatics Core has been critical for the success of this program. The Core supports this study by participating in biospecimen procurement from biopsies and preparing samples to undergo sequencing in a CLIA-certified facility.
- Collaborative project, "Validation of Mitochondrial Markers for Prostate Cancer" with Samantha Maragh (National Institute of Standards and Technology).
- Clinical trial EDRN Prostate MRI Biomarker Study and Reference set (NCI Early detection Research Net Work). (HUM00148970)
- Biomarkers and clinical parameters associated with Gleason score upgrading. (HUM00086525)
- Interstitial assessment of architectural heterogeneity in prostate cancer using a fine needle photoacoustic probe *ex vivo*. The ultimate goal of this research is to validate fine needle photoacoustic (PA) probe methods for the diagnosis of prostate cancer (PCa).
- Integrative molecular profiling of whole urine in African American men with aggressive prostate cancer. (PC200234)
- Collaborative project with Dr. Dev Karan (Medical College of Wisconsin) on how MIC-1 could be used as a clinical diagnostic biomarker for aggressive prostate cancer, specifically for African American men.
- **P20CA26735-01:** Reducing Cancer Health Disparities in Detroit.
- **20CHAL03: PC-REACTR:** A Multidimensional Tumor Atlas to Overcome Prostate Cancer Therapy Resistance.

The Core is also supporting researchers who are utilizing a novel targeted next-generation sequencing (NGS) method to profile urine-extracted RNA from men undergoing prostate biopsy, and we have recently validated a novel high-throughput method of extracting RNA from small amounts of post-DRE urine for various molecular analyses. Similarly, we have novel prostate cancer-focused targeted NGS assays available for profiling tissue-extracted DNA and RNA from prostate cancer tumor specimens, including formalin-fixed paraffin-embedded (FFPE) clinical biospecimens.

Academic Activities

- Total number of publications in FY22. Overall, Dr. Chinnaiyan authored 28 publications from July, 2021 – June, 2022, several in high-impact journals (*Cell; Nature; European Urology*). MCTP faculty collectively published over 115 papers in FY22 (All Core Faculty not including Chinnaiyan). Our publications are highly cited (see graph below) with an overall H-index of 140 for Dr. Chinnaiyan (Web of Science®).
- Total number of grants held and the total dollar value of the grants over the last 7 years can be seen in the chart below


Publications
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10
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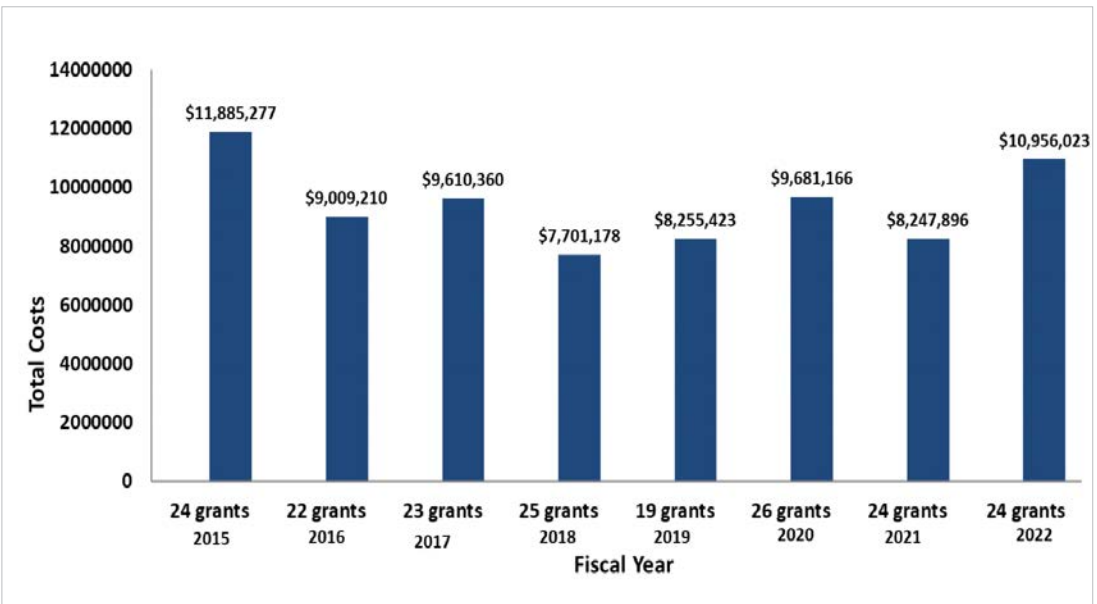
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4000000
6000000
8000000
10000000
12000000
14000000
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$9,009,210
$9,610,360
$7,701,178
$8,255,423
$9,681,166
$8,247,896
$10,956,023
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22 grants
2016
23 grants
2017
25 grants
2018
19 grants
2019
26 grants
2020
24 grants
2021
24 grants
2022
Fiscal Year

Jeffrey L. Myers, MD
Director, MLabs Reference Laboratory

Julia Dahl, MD
Associate Director, MLabs Reference Laboratory

Michigan Medicine Laboratories (MLabs)

MLabs is the Department of Pathology's full-service reference laboratory that leverages the combined strengths of our faculty, trainees, staff, and state-of-the-art laboratories. We value our vital role as the conduit that allows access for patients around the world to Michigan Medicine expertise. We strive to be a trusted partner to all, building strong relationships with pathologists, hospital laboratories, skilled nursing facilities, physician offices, and specialty physicians across Michigan and the nation. Our highly effective collaborations put the needs of the patient at the top of all we do, aligning strongly with the Michigan Medicine mission "To advance health to serve Michigan and the world."

As the COVID-19 pandemic continued a somewhat unpredictable but favorable trajectory toward something more closely approaching what we once knew as normal, COVID testing receded while other services continued to show strong growth in activity across nearly all sectors. For the first three quarters, our dedication to providing high quality laboratory services built on delivering expertise personally was balanced with continued investments in a collaboration with Michigan Medicine's Office of Strategic Planning and Business Development to explore breakthrough growth opportunities intended to position us to better serve the needs of patients, providers, outpatient and acute care facilities, integrated delivery networks, pathologists and pathology groups, nursing homes, and commercial clients. We expect the impact of that work, a continuation of the Michigan Medicine Laboratories Strategy for Transformation and Rebirth (MSTAR 2.0) highlighted in our FY21 report, to be more evident to those we serve.

Improving Service to Our Customers

Throughout the year our sales and marketing team, led by Karla Bialk and Kelly LaBarge, continued to refine the new territory management initiative intended to better serve our clients whether local, regional, or national. In the second quarter we launched regular interdivisional meetings to forecast shifts in MLabs work which was likely to impact our laboratories and other integrated activities while also learning about changes in laboratory staffing, test menu, and technology changes with the potential to impact our clients. Our account liaisons and Associate Medical Director hosted Michigan Medicine healthcare partners MyMichigan and UMH-West for tours of our facilities and engagement with our laboratory managers to align testing platforms and exchange information essential to collaboration in the care of our shared patients. In collaboration with Packard Health and our internal phlebotomy and informatics partners we opened a new patient service center at a new facility on Carpenter Road to better serve the needs of Washtenaw County residents. We used service gaps as learning opportunities within each of our market segments.

Local, Regional and National Visibility for Our Services and Faculty

With COVID restrictions being lifted at conferences, the MLabs Business Development team combined both in-person and web-based participation at conferences relevant to reference laboratory medicine and in support of our faculty. During FY22, MLabs exhibited at American Society for Clinical Pathology (November 2021); Florida Society of Pathologists (February 2022); United States and Canadian Academy of Pathology (March 2022), Executive War College (April 2022); Commission on Office Laboratory Accreditation (May 2022), and American Society of Clinical Oncology (June 2022).

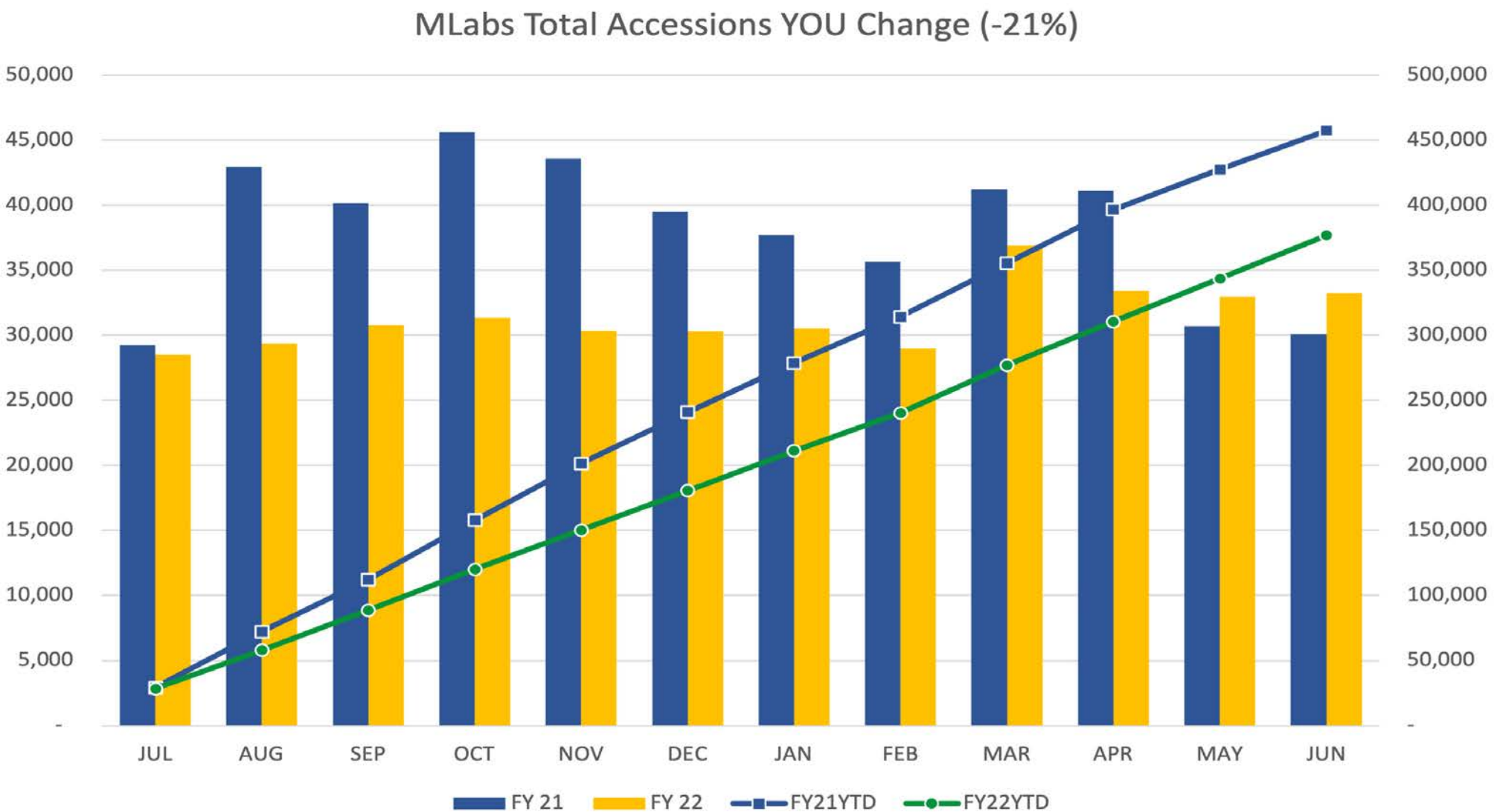


Figure 1. *FY2021 Total Accessions Showed 34% Year-Over-Year Increase*

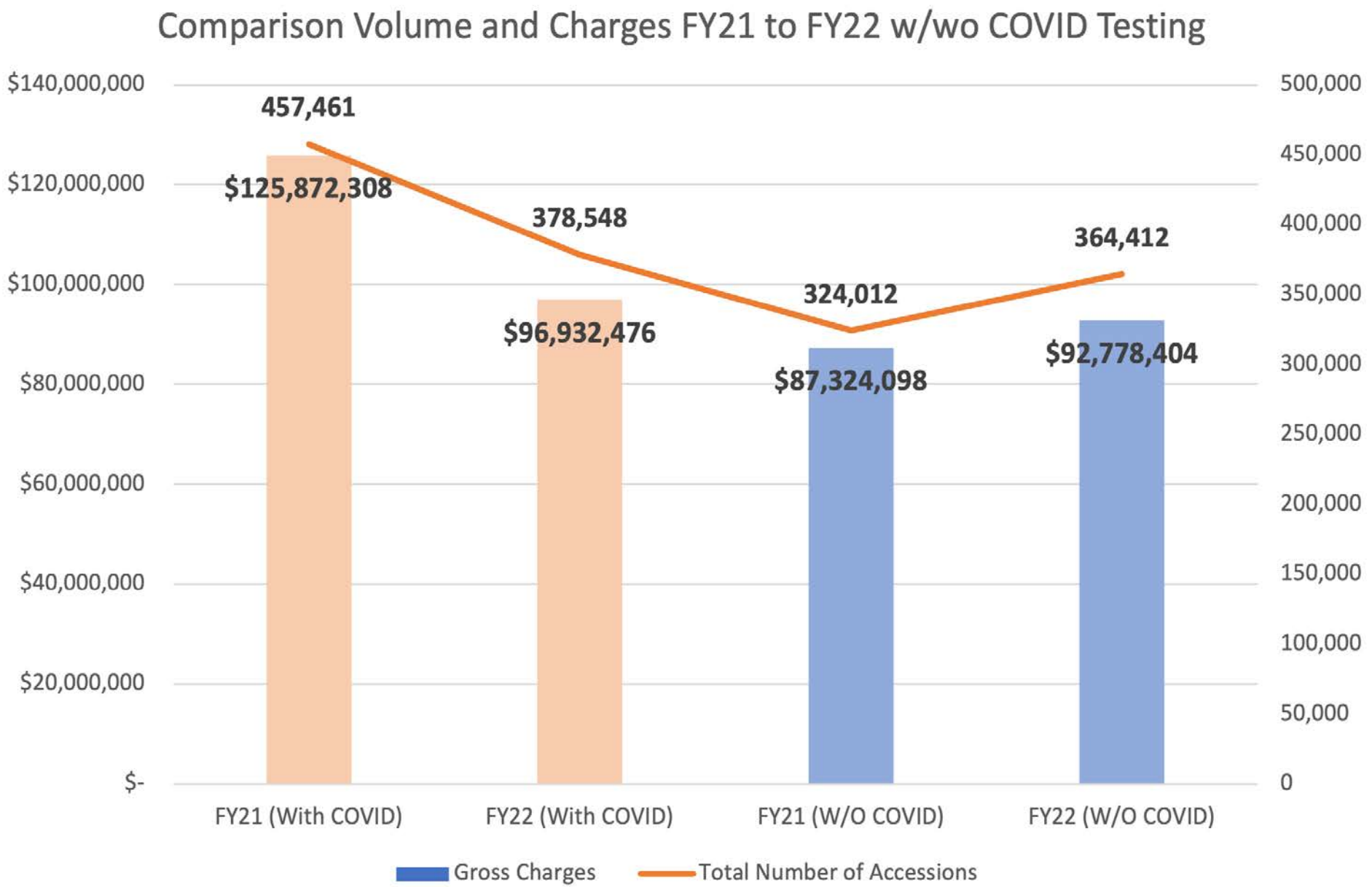


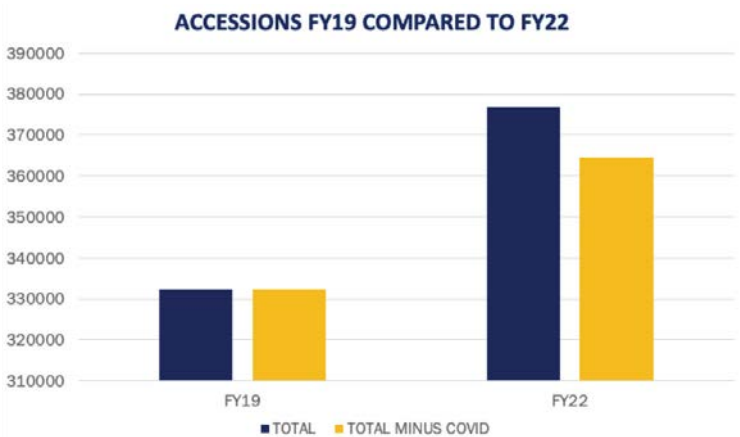
Figure 2. *Annual Gross Charges, FY16-FY21*

Volume of Referrals

MLabs saw a decline in COVID testing between FY21 and FY22; resulting in an overall decrease in total accessions compared to FY21.

To offset the decline in COVID testing, MLabs successfully grew referrals across all other tests. In FY21, the total number of accessions including COVID-related tests was 457,461; when COVID testing is excluded, the total number of accessions is reduced to 324,012. In FY22, though the total number of accessions including COVID-related tests declined by 18% from 457,461 to 378,548, when COVID testing is excluded, MLabs showed a 12% increase on volume of accessions across all other testing platforms (324,012 → 364,412) between FY21 and FY22.

MLabs showed growth of over 10% compared to pre-pandemic FY19 accessions:



Total Gross Charges with YOY Change

Financial benefits to the Department of Pathology of the work that comes to us through MLabs include direct revenue from testing performed for clinicians and patients outside of the Michigan Medicine Health System, reduced unit cost for all tests performed in our laboratories, more efficient utilization of equipment and personnel, and an expanded test menu that reduces not only the costs of sending tests out to other reference laboratories but also the downstream costs that accrue from prolonged turnaround times for the results. MLabs continues work with the Finance and Administration Division and members of the Office of Strategy and Business Development to replace gross charges, our current measure of financial performance, with more finely tuned, tangible, and meaningful performance measures such as net revenue and margin contribution. Until that data is available to us, gross charges are a reasonable measure of activity and an imperfect but frequently directionally correct predictor of net revenue. Gross charges decreased from $125.8M to $96.9M between FY21 and FY22; however, when COVID testing is excluded gross revenue from all other tests saw a 6% increase from $87.3M to $92.8M.

Total Gross Charges by Market Segment

MLabs continues to support a diverse portfolio of clients. Physician Office, Commercial Reference, Anatomic and Hematopathology Consultations to Hospital and other pathology groups and "Other" clients demonstrated significant growth, which offset the decreased volume and revenue seen in the Integrated Delivery Network (IDN)/Hospital Reference Laboratory and Skilled Nursing Facility market segments, which saw the largest decline in volume and revenue related to decline in COVID testing volumes. IDN/Hospital Reference Laboratory business continued to maintain the largest share of MLabs related charges (36%), followed by Physician Office (31%), AP and Hemepath Consultations (17%), Other (8%), Skilled Nursing Facilities (4%), and Commercial Reference Laboratories (4%).

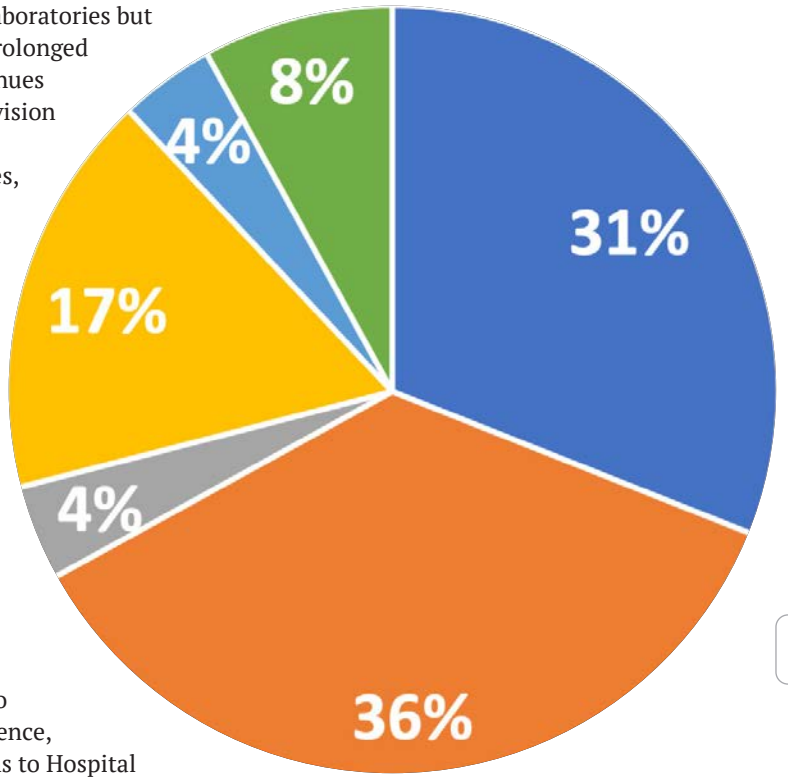


Figure 3. *FY22 Total Gross Charges by Market Segment.*

Darius Amjadi, MD, JD
Chief of Pathology and Laboratory Services, Veteran's Administration Hospital Laboratories, VA

Veterans Affairs Pathology & Lab Medicine

The Pathology and Laboratory Medicine Service of the Veterans Affairs Healthcare System, in Ann Arbor, Michigan, is staffed by pathologists with a joint appointment at the University of Michigan Medical School. The VA Ann Arbor is a designated cancer center providing regional full-service clinical laboratory testing. They support Anatomic Pathology services in Centers in Battle Creek, Saginaw, Detroit, and Northern Indiana. In addition, chemistry and hematology testing is offered at our Toledo, Ohio laboratory, and point-of-care testing is offered in Flint and Jackson, Michigan community outpatient clinics. Three new clinics opened in Canton, Adrian, and Howell in 2021. Data presented below is for the year that ended December 31, 2021.

Clinical Pathology workload in the Ann Arbor laboratory has a current average annual growth rate of 2% since 2009. Anatomic Pathology workload increased at an average rate of 6% annually in the prior decade, with the exception of an almost 30% decline in 2020 due to COVID-related reduction in cases. In 2021, AP experienced a 20% rebound increase.

The VHA establishes high standards of quality and timeliness. Laboratory faculty and staff work hard to meet these standards, meeting clinical pathology STAT specimen turnaround time goals in all sections more than 95% of the time. Our outpatient phlebotomy team serviced 75% of patients in less than 10 minutes due to short staffing, but satisfaction surveys indicated over 95% of patients were satisfied with their service.

In Anatomic Pathology, surgical pathology reporting exceeded targets in 2021. When compared to similar VA medical centers, the VA Ann Arbor workload was the highest among those facilities in 2020, more than double the average RVUs of other 1b facility laboratories and greater than all but four 1a facilities. Pathologist productivity is likewise among the highest with the lowest pathologist labor expense per billable test.

In 2021-2022, the laboratory entered a new phase as a regional reference lab for COVID testing, including starting a molecular testing section. Our cytology section began using remote robotic microscopy to allow pathologists to perform rapid aspiration evaluations (ROSE) from their offices. In 2023, the VA Ann Arbor is scheduled to convert to a Cerner-based information system.

Service	Accessions	Target	%Meeting
Surgical Pathology	12,343	95% reported <2d	97.68%
Non-Gyn Cytology	2,194	95% reported <2d	99.19%
Gyn Cytology	1,231	95% reported <14d	100%
Frozen Section	160	95% reported <20min	94.42%
Autopsy	11	100% completed <30d	100%

Highlights & Accomplishments in 2021

Asma Nusrat, MD
Director, Experimental Pathology

Research Mission

Experimental Pathology faculty have enjoyed a highly successful year. The faculty in this division span from junior faculty to senior investigators who occupy ~65,600 sq. ft. of research space in numerous buildings across the medical campus. The research focus is diverse and spans a wide spectrum of cancer biology, inflammation and immune response, genetics, and aging. Results emanating from the division are at the forefront of cutting-edge research which bridges new basic discoveries with the clinical practice of medicine. Discoveries have been in basic biology, disease pathogenesis, and therapeutics. Success of this division is further evidenced by outstanding grant funding, high impact publications, patents, and prestigious faculty awards.

EP division faculty received $29,106,535 in grant funding the past academic year. At the national level, we have the seventh highest number of R01 grants awarded to experimental pathology faculty. With inclusion of other federal grant dollar amounts, we rank eigth in the nation. These numbers clearly support the high productivity of EP faculty despite a very challenging national funding climate and the pandemic. A large fraction of the funds were awarded from federal sources (NIH, DoD) with additional funds from non-profit organizations and industry (Figure 1). Successful research awards include 32 NIH grants (R01 to R37 grants and subcontracts), 12 Department of Defense (DoD) grants, 2 Veterans Administration Grants and 25 foundation/industry grants (Figure 2). EP faculty also continue to be outstanding mentors, which is reflected in research fellowship and career development awards that were received by trainees in faculty laboratories. Members of our clinical divisions (AP/CP) participated in many of these extramural grant-funded initiatives supporting our collaborative clinical and research environment in the department.

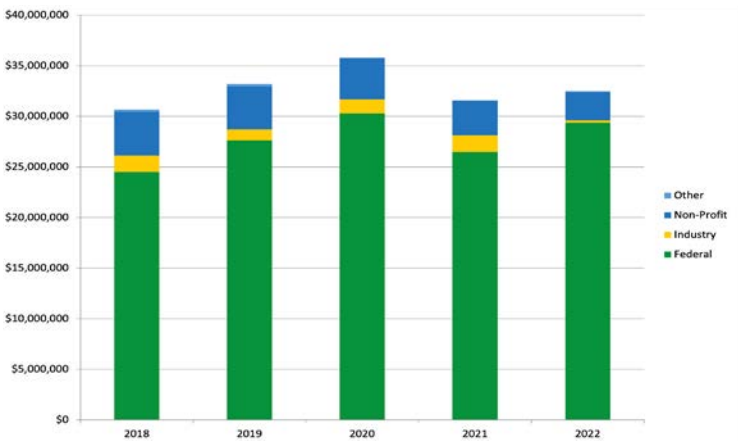


Figure 1: *Funds awarded from federal, non-profit, and industry.*

In addition to independent principal investigator grants, EP training awards have included career-development and fellowship grants from the NIH and private foundations. In keeping with these successful funding metrics, grant indirect costs excelled in the medical school and faculty continue to maintain high dollar density of research space thataverages more than $168/sq. ft.

Innovation and research success of EP faculty is further reflected in 46 patent applications and 54 issued patents,18 new invention reports and 13 new license/option agreements. A summary of these faculty achievements is shown in Figure 3 (pg. 44).

Experimental Pathology faculty continue to excel in all aspects of academics that include medical and graduate student education, participation and leadership positions in institutional, national/

National Institute of Health (NIH)

Type of Grant	Faculty Name
R01	*Lombard, David / Neamati, Nouri
R01	*Parkos, Charles / Collins, Kathleen
R01	*Nusrat, Asma / Parkos, Charles
R01	*Ferguson, David
R01	*Lieberman, Andrew
R03	*Cieslik, Marcin
R21	*Andjelkovic-Zochowska, Anuska
U24	*Nesvizhskii, Alexey / Chinnaiyan, Arul / Dhanasekaran, Saravana
R01	*Lieberman, Andrew
R01 - Subcontract	*Cho, Kathleen

Other Governmental Granting Agencies

Sponsor	Faculty Name
Critical Path Institute (FDA Prime)	*Johnson, Kent
Critical Path Institute (FDA Prime)	*Johnson, Kent
DoD	*Cieslik, Marcin
DoD	*DiFeo, Analisa
DoD	*Lombard, David
DoD	*Tien, Jean
DoD	*Udager, Aaron
DoD	*Xiao, Lanbo
DoD - Subcontract	*Yamada,Chisa

Industry & Nonprofits

Sponsor	Faculty Name
Alex's Lemonade Stand	*Venneti, Sriram
Alex's Lemonade Stand	*Venneti, Sriram
Andrew McDonough B+ Foundation	*Muntean, Andrew
ASIP	*Aslam, Muhammad
Bio-Rad Laboratories	*Bachman, Michael
BioVersys AG	*Nunez, Gabriel
ChadTough Foundation	*Venneti, Sriram
Francis Families Foundation	*Fonseca Aguilar, Wendy
MeMed	*Bachman, Michael
Michael Mosier Defeat DIPG Foundation	*Venneti, Sriram
Pfizer Incorporated	*Johnson, Kent
Prostate Cancer Foundation	*Chinnaiyan, Arul
PTM Therapeutics, Inc.	*Brazil, Jennifer / Parkos, Charles
University of Pennsylvania	*Schultz, Mark

Trainee and Career Development

Sponsor	Faculty Name
F31	*Chinnaiyan, Arul
F32	*Lukacs, Nicholas
T32	*Lieberman, Andrew / Nikolovska-Coleska, Zaneta
K01	*Matsumoto, Masanori
K99	*Bachman, Michael

Figure 2: *Research Funding*

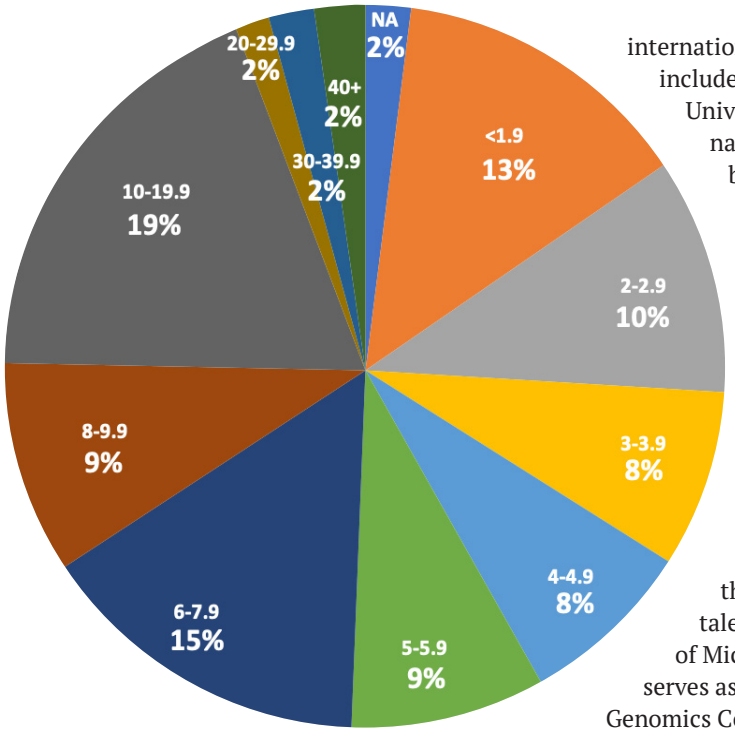


Chart: *Manuscripts published in FY22 by journal impact factor.*

international committees and seminars that include NIH T32 training grants, directorship of University of Michigan graduate programs, national grant review panels, editorial boards, scientific seminars, and meetings. Our chair, Dr. Charles Parkos, continues to serve as a board member representing the Federation of American Societies for Experimental Biology (FASEB) member societies. In this capacity, he has played an important role in advocating for the importance of scientific funding to members of congress in Washington, DC. Dr. Thomas Wilson and Gabriel Nuñez are members of the Biomedical Scholar Program committee that is instrumental in recruiting highly talented young scientists to the University of Michigan Medical School. Dr. Wilson also serves as the faculty director of the Advanced Genomics Core that has played an important role in providing cutting-edge genomics and single-cell sequencing facilities to medical school faculty. Dr. Kathleen Cho serves as a co-leader in the Cancer Genetics Program and Dr. Jolanta Grembecka is a co-leader of the Developmental Therapeutics program at the Rogel Cancer Center.

Numerous Experimental Pathology Faculty have important positions on scientific editorial boards. These include Dr. Gabriel Nuñez who is the Senior Associate Editor for the high-impact journal *Gastroenterology* while also serving as an Associate Editor for *Mucosal Immunology*. Dr. Andrew Lieberman is currently the Deputy Director for *Journal of Clinical Investigation Insight*. Dr. Thomas Wilson chairs the Genomics and Data Sciences Special Interest Group (SIG), Environmental Mutagenesis and Genomics Society (EMGS) and Dr. Zaneta Nikolovska-Coleska was elected as the president and member of the board of directors for the International Chemical Biology Society. Dr. Sriram Venneti and Dr. Andrew Lieberman have continued to excel in their neuroscience endeavors. Dr. Venneti was recently awarded the Alex Lemonade Stand New Innovator Award and he was appointed as the Scientific Director of the Chad Carr Pediatric Brain Tumor Center as well as the Director of Faculty Development and Recruiting in Experimental Pathology. Dr. Asma Nusrat is a member of the Crohn's and Colitis National Scientific Advisory Committee, and she chairs their Senior Research Awards Committee.

Pathology faculty, Drs. Nick Lukacs, Simon Hogan, Chang Kim, and Catherine Ptaschinski, are members of the Mary H. Weiser Food Allergy Center (MHWFAC) and Dr. Nick Lukacs serves as the scientific director for this center. This past year MHWFAC had a productive and impactful year moving out of the pandemic mindset and back to "normal". The Center has recruited two new assistant professors and a new endowed professor. Topping the list of accomplishments toward the Center goals was the 3rd Annual M-FARA Research Symposium that was held in-person in June at the BSRB Kahn Auditorium. The agenda included 12 outside participants in the program along with MHWFAC faculty. There were over 140 registrants and the 2-day event included 4 sessions and a poster session (~30 posters) along with social events. It was nothing less than a smashing success. For most of the participants, it was the first in-person event attended since the pandemic. This year, MHWFAC received the honor of becoming a World Allergy Organization (WAO) Center of Excellence that allows Centers from around world to interact and collaborate on research, clinical processes, and education. The MHWFAC faculty continue to provide outstanding science that has been published in top-tier journals with NIH and industry funding exceeding $9 million. Finally, the Center also had success in philanthropy with an additional $10 million in commitments, for a total of ~$50 million in total commitments since inception of the MHWFAC, which have been used for named professorships, research, and public policy efforts.

Dr. Steven Kunkel serves as the Chief Scientific Officer for Michigan Medicine. In his prominent leadership position, Dr. Kunkel has continued to play an important role in the development and implementation of robust strategic research plans that have facilitated novel directions for many research programs across Michigan Medicine.

Furthermore, high research productivity is supported by many new discoveries and high-impact publications. Pathology faculty published 393 manuscripts in high-impact journals that include, *Nature Communications*, *Nature Chemical Biology, Journal of Clinical Investigation, Cell Host and Microbes, Proceedings of the National Academy of Sciences*, among many others. 25% of manuscripts were published in journals with an impact factor of greater than 10 and an additional 24% were accepted in journals that have an impact factor of 6-10 (see pg 42). Among the many outstanding published manuscripts, a few highlights this year include the following:

- A recent study by **Drs. Grembecka and Cierpicki** describes development of the first-in-class small molecule inhibitors of the histone methyltransferase ASH1L. These compounds block enzymatic activity of ASH1L by directly targeting the catalytic SET domain. When applied in the MLL1-rearranged leukemia cells, the ASH1L inhibitors they developed block proliferation, induce apoptosis and differentiation, and downregulate key leukemia-relevant genes, demonstrating specific mechanism of action. In addition, the ASH1L inhibitors reported in this study strongly reduce leukemia burden *in vivo* in mouse models of leukemia. Overall, this study demonstrates for the first time that blocking catalytic activity of ASH1L can be therapeutically beneficial and provides a valuable molecular scaffold for future clinical translation.

  Reference: Rogawski DS, Deng J, Li H, Miao H, Borkin D, Purohit T, Song J, Chase J, Li S, Ndoj J, Klossowski S, Kim E, Mao F, Zhou B, Ropa J, Krotoska MZ, Jin Z, Ernst P, Feng X, Huang G, Nishioka K, Kelly S, He M, Wen B, Sun D, Muntean A, Dou Y, Maillard I, Cierpicki T, Grembecka J. (2021) Discovery of first-in-class inhibitors of ASH1L histone methyltransferase with anti-leukemic activity. *Nat Commun*. 12(1):2792.

- In an article published in *The Journal of Immunology*, **Dr. Nicholas Lukacs** investigated the ability of TSLP signaling pathways in driving systemic "trained" immunity in dendritic cells (DC) in early-life RSV-infected mice. Bone marrow-derived DCs (BMDC) from early-life RSV-infected mice at 4 weeks post-infection showed enhanced expression of costimulatory molecules and cytokines, including Tslp, that regulate immune cell function. The studies highlight the fact that the DCs were functionally different both *in vitro* and *in vivo*, and due to TSLP, promoted pathogenic responses. The underlying mechanism appears to be epigenetic alteration of chromatin that affects transcriptional control of Type I IFN genes that regulate immune efficacy toward viral infections. TSLP, through its primary transcription factor, IRF4, regulated the anti-viral pathway due to the RSV infection. These have long-term consequences on the developing immune response to both viral and non-viral associated disease pathogenesis.

  Reference: Malinczak CA, Parolia A, Fonseca W, Morris S, Rasky AJ, Bawa P, Zhang Y, Mire MM, Ziegler SF, Ptaschinski C, Chinnaiyan AM, Lukacs NW: TSLP-Driven Chromatin Remodeling and Trained Systemic Immunity after Neonatal Respiratory Viral Infection. *J Immunol* 206(6):1315-1328, 2021. PM33514510

- **Dr. Chang Kim**'s research team identified important roles of the gut microbial metabolites short-chain fatty acids (SCFAs) in supporting peripheral innate lymphoid cells (ILCs). The dietary fiber metabolites induce and activate SCFA-sensing GPCRs expressed by ILCs in the intestine. Activation of these GPCRs signals the expansion of ILC1, ILC2 and ILC3 in response to infection or alarmin cytokines. This SCFA-mediated expansion of ILCs is important for effective ILC activity in peripheral tissues, particularly the intestine and other mucosal and systemic tissues depending on host condition.

  Reference: Sepahi A, Liu Q, Friesen L, Kim CH. Dietary fiber metabolites regulate innate lymphoid cell responses. *Mucosal Immunol*. 2021 Mar;14(2):317-330. Epub 2020 Jun 15. PubMed PMID: 32541842

- Members of the **Parkos and Nusrat** labs investigated collective migration of epithelial cells and repair *in vivo* to highlight cross talk between a cell-cell junction protein and integrins in cell matrix adhesion to coordinate wound repair. They employed mice with inducible loss of a key intestinal epithelial tight junction-associated protein termed Junctional Adhesion Molecule A (JAM-A) to conclusively demonstrate its role in

All Issued Patents	
Patent Title	**Inventors**
Ash1L Inhibitors and Methods of Treatment Therewith	Dong Chen, Eungi Kim, Hao Li, Hongzhi Miao, Jing Deng, Jolanta Grembecka, Szymon Klossowski, Tomasz Cierpicki, Trupta Purohit
Dimethyl-Nonatetraenyl-Trimethyl-Cyclohexyl Compounds and Uses Thereof	Andrew White, Hollis Showalter, James Varani, Kent Johnson
Treatment of Staphylococcal Disorders	Gabriel Nunez, Jon Oscherwitz, Kemp Cease (Deceased), Yumi Nakamura
BET Bromodomain Protein Degraders With Cleavable Linkers	Donna McEachern, Ester Fernandez-Salas, Fuming Xu, Longchuan Bai, Shaomeng Wang, Weiguo Xiang
Using Phage Epitopes to Profile the Immune Response	Alexander Tsodikov, Arul Chinnaiyan, Xiaoju Wang
PRC1 Inhibitors and Methods of Treatment Therewith	Felicia Gray, Jolanta Grembecka, Qingjie Zhao, Tomasz Cierpicki, Weijiang Ying, Yiwu Yao
NSD Family Inhibitors and Methods of Treatment Therewith	Christina Howard, Eungi Kim, Huang Huang, Hyo Je Cho, Jolanta Grembecka, Mykhaylo Potopnyk, Sergei Zari, Sergii Dudkin, Tomasz Cierpicki, Wenbing Chen, Yassir Adam

Figure 3: *Patent Applications. Continued in Appendix on* pg. 82 *for Invention Reports.*

regulation of mucosal wound healing. Using two different *in vivo* models of mucosal injury and repair as well as primary cultures of JAM-A-deficient intestinal epithelial cells, this team demonstrated that JAM-A signals to promote closure of intestinal mucosal wounds by regulating focal adhesions through a pro-migratory protein signaling complex between the small GTPase Rap1A, Talin, and β1 integrin. These findings strongly support the existence of a JAM-A-dependent migratory protein complex that is essential for epithelial cell migration and wound repair.

Reference: Fan S, Boerner K, Muraleedharan CK, Nusrat A, Quiros M, Parkos CA. Epithelial JAM-A is fundamental for intestinal wound repair *in vivo*. *JCI Insight*. 2022 Sep 8;7(17):e158934. doi: 10.1172/jci.insight.158934. PMID: 35943805; PMCID: PMC9536273.

- **Dr. Gregory Dressler**'s lab designed a cell-based system to screen for small molecule inhibitors of the Pax family of developmental regulators that are highly expressed in renal cancer cells. Pax proteins recruit histone methyltransferases via the adaptor protein PTIP to imprint active epigenetic marks on chromatin. A family of small molecules was identified that blocked histone methylation at Pax binding sites on chromatin through inhibition of the Pax-PTIP interaction. Such compounds can provide a scaffold for further development of novel anti-cancer agents for Pax-expressing tumors.

  Reference: STJ Bradford, E Grimley, AM Laszczyk, PH Lee, SR Patel, GR Dressler (2022) Identification of Pax protein inhibitors that suppress target gene expression and cancer cell proliferation. *Cell Chem Biol* 29 (3), 412-422. e4

- **Dr. Jiaqi Shi**'s research on pancreatic ductal adenocarcinoma (PDAC), published in *Cellular and Molecular Gastroenterology and Hepatology*, found that PDAC is predicted to become the second leading cause of cancer death in the United States by 2030, with an overall 5-year survival rate of less than 11%. Approximately a quarter of the PDAC contain mutations in epigenetic and chromatin remodeling genes, and KDM6A is one of the most frequently mutated epigenetic genes in PDAC. However, the specific functions of KDM6A in PDAC development and metastasis, as well as the underlying mechanisms, have not been fully elucidated. In this study, the team unveiled a novel link between KDM6A and the noncanonical p38-dependent activin-A signaling as a major mechanism of cancer cell plasticity, tumorigenesis, and progression. These findings identified activin-A as a candidate therapeutic target for KDM6A-deficient PDACs.

  Reference: Yi Z, Wei S, Jin L, Jeyarajan S, Yang J, Gu Y, Kim HS, Schechter S, Lu S, Paulsen MT, Bedi K, Narayanan IV, Ljungman M, Crawford HC, Pasca di Magliano M, Ge K, Dou Y, Shi J. (2022) KDM6A regulates cell plasticity and pancreatic cancer progression by non-canonical activin pathway. *Cell Mol Gastroenterol Hepatol* 13 (2): 643-667. PMID: 34583087.

- Employing a mouse model of food allergy that mimics the disease course of food allergy diagnosis and treatment in humans, **Dr. Simon Hogan**'s lab identified biomarkers that predict reactivity during food challenge (FC) and responsiveness during oral immunotherapy (OIT) and how these outcomes are modified

by genetics. His research team showed that specific biomarkers (mast cell activation, severity of reaction and food-specific IgE) can predict food reactivity. Furthermore, they demonstrated that genetic factors such as gain-of-function mutation in IL-4Rα altered symptoms of food allergic reaction, food challenge outcome, and altered the frequency of adverse events and oral immunotherapy outcomes. These studies support deeper assessment of biomarkers during reactions in the community and exploring genetics in determining OFC and OIT outcomes and efficacy of OIT. Such work is likely to increase patient safety and improve current management of patients with food allergy.

Reference: Ganesan V, Sharma A, Tomar S, Schuler CF 4th, Hogan SP. IL-4 receptor alpha signaling alters oral food challenge and immunotherapy outcomes in mice. *J Allergy Clin Immunol*. 2022 Aug 4:S0091-6749(22)01021-1. doi: 10.1016/j.jaci.2022.07.011.

- In an article written in *Aging Cell*, **Dr. Richard Miller** reports that the NIA-funded Interventions Testing Program, the ITP, evaluated 5 to 7 drugs each year to see if they can extend healthy mouse lifespan. The group previously reported that 17a-estradiol, a non-feminizing isoform of estrogen (17b-estradiol), can extend lifespan in male mice if given from 9 months of age. This paper shows that the drug also extends lifespan if given starting in middle age, i.e. from 16 or 20 months, again working in males only. Other work from the Miller group has shown that late-start 17a-estradiol can preserve youthful levels of muscle strength, balance, and glucose control. Pathology faculty member Dr. Xinna Li has found that 17a-estradiol can modify the status of adipose tissue, macrophages, liver, muscle, and brain in ways similar to those seen in other kinds of slow-aging mice. The group is now searching for other estrogenic steroids that can perform these functions in both sexes.

  Reference: Harrison, D. E., R. Strong, P. Reifsnyder, N. Kumar, E. Fernandez, K. Flurkey, M. Javors, M. Lopez-Cruzan, F. Macchiarini, J. F. Nelson, A. Bitto, A. L. Sindler, G. Cortopassi, K. Kavanagh, L. Leng, R. Bucala, N. Rosenthal, A. Salmon, T. M.Stearns, M. Bogue, R. A. Miller. 2021. 17-a-estradiol late in life extends lifespan in aging UM-HET3 male mice; nicotinamide riboside and three other drugs do not affect lifespan in either sex. *Aging Cell*, Mar 31:e13328. PMID: 33788371.

- In an article published in *PLOS Pathogens*, **Dr. Michael Bachman** reports *Klebsiella pneumoniae* is a leading cause of healthcare-associated infections, which is often preceded by gut colonization. The Bachman lab previously found that the bacterial gene operon *ter* is associated with infection in colonized patients. This study demonstrates that the *ter* operon confers a fitness advantage during gut colonization in the presence of specific gut bacteria and in the presence of short-chain fatty acids. These results indicate that the ability of *K. pneumoniae* to compete with other bacteria in the gut is an important risk factor for subsequent infections, and that bacterial genes could be promising targets for screening tests to identify patients at risk of healthcare-associated infections.

  Reference: Vornhagen J, Bassis CM, Ramakrishnan S, Hein R, Mason S, Bergman Y, Sunshine N, Fan Y, Holmes CL, Timp W, Schatz MC, Young VB, Simner PJ, Bachman MA. A plasmid locus associated with *Klebsiella* clinical infections encodes a microbiome-dependent gut fitness factor. *PLoS Pathog*. 2021 Apr 30;17(4):e1009537. PMID: 33930099;

- In a recent study, **Dr. Zaneta Nikolovska-Coleska** demonstrates a novel approach to target epigenetic writer, histone methyltransferase DOT1L. *MLL1* (*KMT2a*) gene rearrangements underlie the pathogenesis of aggressive MLL-driven acute leukemia. AF9 (*MLLT3*), one of the most common MLL-fusion partners, recruits the histone H3K79 methyltransferase DOT1L to MLL target genes, constitutively activating transcription of pro-leukemic targets. The recent study (*Cancers* 2021) led by Dr. Nikolovska-Coleska, demonstrated and validated a potential novel therapeutic strategy for the treatment of patients bearing MLL translocations by blocking the protein-protein interactions (PPIs) and recruitment of DOT1L by MLL-AF9. Applying a genetic approach by establishing stable conditional knockout *Dot1l* murine lines that express both, MLL-AF9 oncofusion and wild type or mutant DOT1L proteins, based on the previous study from Nikolovska-Coleska's lab, they demonstrated complete disruption of DOT1L recruitment to critical target genes, *Hoxa9* and *Meis1*, in cells expressing DOT1L mutants with an

impaired AF9 binding site. This was followed by a significant decrease in H3K79me2 in the promoter regions of these genes, cell differentiation, and induction of apoptosis. To identify the potential therapeutic benefits of this novel targeting approach, the effect of DOT1L mutants with an impaired AF9 binding site or enzymatic activity was investigated on adult murine hematopoiesis. These *in vivo* studies, performed in collaboration with Drs. Andrew Muntean and Ivan Maillard, demonstrate that genetic interventions that result in loss of DOT1L enzymatic activity rapidly depletes hematopoietic stem and progenitor cells; however, hematopoiesis was preserved when the AF9-DOT1L interaction was disrupted. These studies provided an important proof of concept for the potential therapeutic advantage of inhibiting the AF9-DOT1L interaction and disrupting the integrity of the MLL-fusion complex. In addition, these results conclusively provide evidence that DOT1L recruitment can be abolished by a single point mutant (I867A), highlighting the crucial role of the hydrophobic interactions, and providing insights for further drug discovery. Nikolovska-Coleska's lab reported the first peptidomimetics targeting PPIs between MLL-AF9 and DOT1L (*ACS Med Chem* Lett 2018), providing proof of concept for the drugability assessment of this novel potential therapeutic approach. Currently, Dr. Nikolovska-Coleska, in collaboration with Circle Pharma, is working on developing drugs targeting the DOT1L/MLL-fusion protein complexes.

Reference: Grigsby SM, Friedman A, Chase J, Waas B, Ropa J, Serio J, Shen C, Muntean AG, Maillard I, Nikolovska-Coleska Z. Elucidating the Importance of DOT1L Recruitment in MLL-AF9 Leukemia and Hematopoiesis. *Cancers* (Basel). 2021 Feb 5;13(4):642. PMID: 33562706

- In an article published in *Acta Neuropathologica*, **Dr. Andrew Lieberman** reports that human fetal cell transplantation has been tested in neurodegenerative disorders including Huntington's disease (HD) based on the notion that embryonic cells will slow or reverse clinical decline. While efficacy has been reported in a primate model, results in HD patients have been underwhelming. He described a case of HD >20 years post-transplantation which showed both intraventricular and cortical glioneuronal nodules containing donor-derived cells, as established by DNA microsatellite analysis. These iatrogenic nodules showed no evidence of integration into surrounding brain parenchyma, consistent with a lack of clinical benefit from transplantation. Notably, striking differences in neuronal differentiation were observed in cortical vs intraventricular nodules. This case thereby provides a tantalizing suggestion that the adult human brain retains microenvironment signaling cues sufficient to drive progenitor cells towards site-specific differentiation.

  Reference: Donor-containing cortical and intraventricular glioneuronal nodules in Huntington's disease brain decades after fetal cell transplantation. Pinarbasi ES, Liu EA, Yu Z, Kopyov O, Brown NA, Dayalu P, Lieberman AP. *Acta Neuropathol*. 2021 Jun;141(6):979-981.

- In a recent study, Dr. Alexey Nesvizhskii reports that mass spectrometry-based proteomics methods depend on database search engines, such as the Nesvizhskii lab's MSFragger, to convert raw mass spectrometry data into useful information about the peptides and proteins present in a sample. These search engines in turn require "preprocessing" of the raw mass spectrometer output into a list of peaks representing the fragment ions of peptides. In an article published in *Journal of Proteome Research*, the Nesvizhskii lab discussed an ultrafast method for identifying and removing peaks corresponding to naturally occurring heavy isotopes and incorporated it into MSFragger. This deisotoping method allowed MSFragger to annotate up to 30% more peptide spectra and to do so up to 50% faster than previously, allowing more peptides and proteins to be identified from the same raw data. Deisotoping was most helpful in analyzing larger peptides, such as those found in glycoproteomics and immunopeptidomics analyses.

  Reference: Teo GC, Polasky DA, Yu F, Nesvizhskii AI: Fast Deisotoping Algorithm and Its Implementation in the MSFragger Search Engine. *J Proteome Res* 20(1): 498-505, 2021. PM33332123


Verschließzange

Kathleen Cho, MD
Interim Director, Division of Education Programs

Education Mission

In FY22, The University of Michigan Pathology Residency Program graduated seven AP/CP trainees, five of whom stayed at Michigan Medicine to continue their training in a pathology subspecialty fellowship program. These fellowship programs include forensic pathology, gastrointestinal pathology, hematopathology, and thoracic pathology. The remaining two graduates embarked on pathology subspecialty training in pediatric pathology at the University of Colorado and hematopathology at Stanford University. Key achievements of our graduating residents include:

- All graduating residents earned certificates in Lab Management University
- All graduating residents participated in at least one cycle of the QI curriculum
- All graduating residents participated in a CAP inspection or mock inspection
- Six of the seven graduating residents were successfully certified by the American Board of Pathology, with one scheduled to take the exam this Fall.
- Our 5-year certification rate is 97% for first-time takers.

Our residency curriculum consists of daily didactic, gross, or slide presentations, 14 AP and 8 CP core subspecialty rotations, quality improvement course, Path 862 Translational Pathology course (combined with PhD students), and ASCP Lab Management University with certification. A vibrant and varied morning Pathology Educational Series takes place most mornings at 8 am, from September through mid-June. In FY22, there were 155 educational conferences, most offering CME credit. Following state and CDC guidelines, the majority were offered as a hybrid or modified in-person and virtual format.

Our residents continued their strong academic productivity in FY22. Twenty-one peer-reviewed articles were published in 14 different scientific journals as well as by Cold Spring Harbor Press and PathologyOutlines.com. The mean impact factor for journals in which our residents published in FY22 was 5.80, with the highest impact factor being 31.74. Fourteen individual residents were first authors. Furthermore, nine abstracts were presented at regional, national, and international meetings, including four platform presentations or other similar talks.

Our residents are highly engaged members of medical, pathology, and scientific communities with many serving in local, regional, and national organizations. They contributed to efforts to improve patient safety, quality standards and practices, health equity, DEI, wellness, education, leadership training, and the promotion of pathology as a career. As part of their service, three residents also took advantage of additional training via the Community of Medical Educators in Training Program or the Healthcare Equity and Quality Scholars Program at Michigan Medicine.

Service

Department of Pathology

- Social Media Committee
- Resident Trainee Diversity, Equity and Inclusion Committee
- Resident Wellness Committee
- Histology Committee

Sean Li, MD, PhD
Director, Residency Training Program


UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
Department of Pathology
Mark Rudolf, MD, PhD
Department of Pathology
Lauran J. Miller, MD, MJ
JANG WON CHO MD

Michigan Medicine

- Advisory Committee for the Advancement of LGBTQIA+ Health
- Culture Education Advisory Group - Education Advisory Subcommittee
- Patient Safety Committee
- House Officer Quality and Safety Council
- Residency Leadership Training Program Task Force
- Residents and Fellows for Global Health Equity
- COMPASS

National/International

- CAP Residents Forum
- CAP Quality Practices Committee
- ASCP Career Ambassador
- CAP Engaged Leaders Network
- ASCP Pathology Ambassador
- CAP Foundation

For our incoming resident cohort, we received 567 applications to fill 7 open slots. The number of applications increased from 494 in the previous year. We interviewed 97 total candidates, including 18 specifically for the Physician-Scientist Training Program. We had an exceptionally talented pool of applicants with diverse backgrounds, and our new residents came mostly from the Midwest and Eastern region. Meet our class of 2026:

- **Eric Chang, MD** / Wayne State University Medical School
- **Jang Cho, MD** / Georgetown University
- **Timothy Dinh, MD, PhD** / University of North Carolina at Chapel Hill
- **Isabella Dishong, DO** / Lake Erie College of Osteopathic Medicine
- **Sarah Farran, MD, MPH** / American University of Beirut
- **Lauren Miller, MD, MJ** / Medical College of Wisconsin
- **Mark Rudolf, MD, PhD** / University of Virginia School of Medicine

Pathology Fellowship Programs

In 2021, the Department of Pathology had 10 ACGME accredited fellowship programs with 18 approved positions plus an additional 8 clinical fellowship programs with 12 potential positions. On July 1, 2021, we welcomed:

- Bone and Soft Tissue Fellow Douglas Rottman, MD
- Breast Pathology Fellow Sundis Mahmood, MD
- Cytopathology Fellows Xiaobing Jin, MD, PhD and Mohammed Saad, MBBS
- Dermatopathology Fellows Michael Huang, MD and Behzad Salari, MD
- Forensic Pathology Fellow Eleftherios Vouyoukas, MD
- Gastrointestinal Pathology Fellow Chelsea Styles, MD
- Genitourinary Pathology Fellow Alexander Taylor, MD
- Gynecologic & Breast Pathology Fellow Lucy Ma, MD
- Hematopathology Fellows Kathryn Gibbons, MD and Ania Owczarczyk, MD, PhD
- Laboratory Genetics & Genomics Fellow Benjamin Kang, PhD (Year 2)
- Molecular Genetic Pathology Fellow Erica Vormittag-Nocito, MD
- Neuropathology Fellow Emile Pinarbasi, MD, PhD (Year 2)
- Surgical Pathology Fellows Preeti Behl, MD, Ashley Bradt, MD, Fernanda Carolina Cordeiro-Rudnisky, MD, Cisley Hines, MD
- Thoracic Pathology Fellow Chaehwa Kim, MD

William Perry, MD
Chief Resident

Batoul Aoun, DO
Assistant Chief Resident

Margaret Fang, MD
HO IV

Efrain Gutierrez-Lanz, MD
HO IV

Justin Kelley, MD, MPH
HO IV

Lauren Kroll-Wheeler, MD
HO IV

Tim Miller, MD
HO IV

Catherine Perez, MD
HO IV

Geoffrey Halling, MD
HO III

Ryan Landvater, MD
HO III

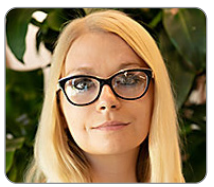
David Nai, MD
HO III

Emile Pinarbasi, MD, PhD
HO III

Jaclyn Plotzke, MD
HO III

Julianne Szczepanski, MD
HO III

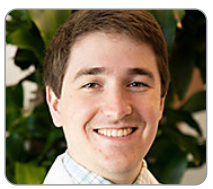
Katelyn Zebrowski, MD
HO III



Haley Amoth, MD
HO II

Thomas Herb, MD
HO II

Vincent Laufer, MD, PhD
HO II



Nathan McCammon, MD
HO II

Corey Post, MD
HO II

Fysal Shennib, MD
HO II

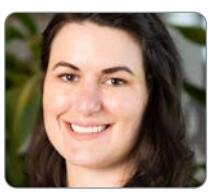
Nicole Tomm, MD
HO II

Maxwell Wang, MD
HO II

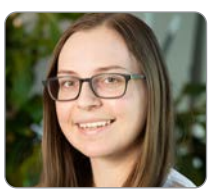
Ashley Brent, MD
HO I

Ryan Cecchi, MD
HO I

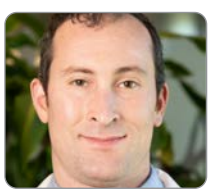
Elaina Daniels, MD
HO I



Elizabeth Higginson, MD
HO I

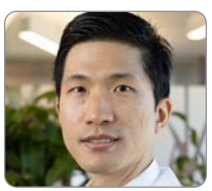


Amber Holtz, MD
HO I



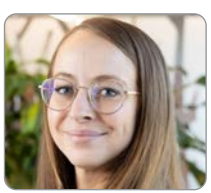
Michael Olp, MD
HO I

Eric Chang MD
Incoming HO I

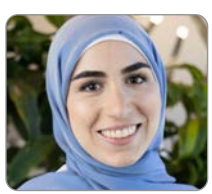


Jang Cho, MD
Incoming HO I

Timothy Dinh, MD, PhD
Incoming HO I

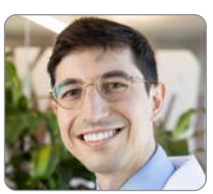


Isabella Dishong, DO
Incoming HO I



Sarah Farran, MD, MPH
Incoming HO I

Lauren Miller, MD, MJ
Incoming HO I



Mark Rudolf, MD, PhD
Incoming HO I

2021-2022 Pathology Residents

Madelyn Lew, MD
Director, Medical School Pathology Education Curriculum

Medical Student Teaching

The Department of Pathology has a long history of playing an integral role in pre-clinical medical student education. In Foundations of Medicine 2, one of the first sequences encountered by medical students in the Scientific Trunk, we introduce the foundational principles of Pathology – Cell Injury & Death, Inflammation, and Neoplasia. This lays the groundwork upon which students build in subsequent organ-based blocks. Lectures and laboratories are conducted by many pathology faculty members including Drs. Madelyn Lew, Scott Owens, Evan Farkash, Scott Bresler, Alexandra Hristov, Allecia Wilson, Tao Huang, Paul Killen, Aaron Udager, Karen Choi, Jiaqi Shi, Angela Wu, Tom Giordano, Sara Abbott, David Chapel, Caroline (Libby) Simon, May Chan, Charles Ross, Laura Cooling, Sandra Camelo-Piragua, Andrew Lieberman, Stephanie Skala, and Paul Harms. Under the direction of Dr. Madelyn Lew, Director of Medical Student Education for the Department of Pathology, our faculty members are working to continue integrating pathology content with other clinical and basic science elements in blocks and to incorporate new interactive methods of delivering education material.

In the Surgery & Applied Sciences Clerkship, students partake in a week-long pathology rotation that exposes them to various facets of pathology. In January 2021, a revamped curriculum was launched which incorporated educational grossing and microscopic sessions directed specifically to medical students. Using these sessions along with case-based small group sessions and supplemental electronic resources, students will consolidate foundational principles learned in the Scientific Trunk, enhance their understanding of clinicopathologic correlations, and increase lab stewardship.

In their third and fourth years of the medical school curriculum, students enroll in the Branches curricula. In the Branches, pathology faculty participate as mentors and career advisors for the Diagnostics & Therapeutics Branch as well as Science Consultants for Branch students preparing their Patient Based Scientific Inquiry (PBSI). Branch students can also participate in a variety of integrated electives that include multiple disciplines to enhance their understanding of disease process, presentation, and management within the pathology department.

Zaneta Nikolovska-Coleska, PhD
Director of Molecular and Cellular Pathology Graduate Program

Pathology Elective Rotation

The Pathology Elective experience, under the direction of Dr. Madelyn Lew, allows students to take a closer look at the daily practice of academic pathologists across multiple subspecialties. In 2022, we redesigned the elective with a “Pathology Passport” in which students self-develop an experience tailored to their interests and complete a combination of required and optional rotation-specific activities for designated point values (based on difficulty and effort) that accumulate to Pass, High Pass, or Honor grades. These activities include observation and participation in macroscopic evaluation of specimens, independent previewing of active clinical cases, and leading group discussion about case-related ancillary studies and clinicopathologic correlations. While many of the students rotating in our elective may choose other fields of practice, a distinct subset take part in our elective to evaluate pathology as a possible career choice. For these students, individualized mentoring is provided by faculty in the department.

Molecular & Cellular Pathology Graduate Program

The Molecular and Cellular Pathology Graduate Program (MCP) is one of the Program in Biomedical Sciences (PIBS) graduate programs and is supported through the Department of Pathology. The MCP Graduate Program, under the direction of Dr. Zaneta Nikolovska-Coleska, has 38 Pathology research mentors/labs from which to choose and 25 students performing their PhD thesis research in Pathology Department laboratories during FY22.

The 2021-2022 academic year continued to be a challenging year. Due to the pandemic we had to modify many of the events that normally take place in person. Most of our events were conducted virtually including courses, preliminary exams, weekly seminar series, annual research symposium as well as the T32 TPTR workshops and retreat. We also started holding regular office hours through Zoom, providing a platform for our students to interact with the MCP leadership, ask questions, get information or just enjoy some conversation. To address the social needs of the MCP students, we organize multiple events throughout the year including

Preeti Behl, MD
Surgical Pathology

Ashley Bradt, DO
Surgical Pathology

F. Cordeiro-Rudnisky, MD
Surgical Pathology

Kathryn Gibbons, MD
Hematopathology

Cisley Hines, MD
Surgical Pathology

Michael Huang, MD
Dermatopathology

Xiaobing Jin, MD, PhD
Cytopathology

Benjamin Kang, PhD
Lab Genetics & Genomics

Chaehwa Kim, MD
Thoracic Pathology

Lucy Ma, MD
Gynecologic Pathology

Sundis Mahmood, DO
Breast Pathology

Ania Owczarczyk, MD, PhD
Hematpathology

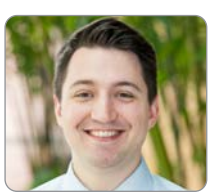
Emile Pinarbasi, MD, PhD
Neuropathology

Douglas Rottman, MD
Bone & Soft Tissue

Mohammed Saad, MBBS
Cytopathology

Behzad Salari, MD
Dermatopathology

Chelsea Styles, MD
GI Pathology



Alex Taylor, MD
GU Pathology

Erica Vormittag-Nocito, MD
Molecular Genetic Pathology

Terry Vouyoukas, MD
Forensic Pathology

2021-2022 Graduating Fellows

Fellow	New Position	Institution
Preeti Behl, MD	Pathologist	Yosemite Pathology Medical Group, Visalia, CA
Ashley Bradt, DO	Cytopathology Fellowship	Michigan Medicine
F. Cordeiro-Rudnisky, MD	GU Pathology Fellowship	Michigan Medicine
Kathryn Gibbons, MD	Surgical Pathology Fellowship	Michigan Medicine
Cisley Hines, MD	Head & Neck Pathology Fellowship	Michigan Medicine
Michael Huang, MD	Pathologist / Dermatopathologist	Cleveland Skin Pathology / Metrohealth Medical Center, OH
Xiaobing Jin, MD, PhD	Surgical Pathology Fellowship	Michigan Medicine
Benjamin Kang, PhD	Lab Genetics & Genomics Fellowship	Michigan Medicine
Chaehwa Kim, MD	Bone & Soft Tissue Fellowship	Michigan Medicine
Lucy Ma, MD	Assistant Professor	Jefferson University Hospitals
Sundis Mahmood, DO	Surgical Pathology Fellowship	Michigan Medicine
Ania Owczarczyk, MD, PhD	Pathology Associate Staff	Cleveland Clinic
Emile Pinarbasi, MD, PhD	Neuropathology Fellowship	Michigan Medicine
Douglas Rottman, MD	Assistant Professor	Michigan Medicine
Mohammed Saad, MBBS	GI Pathology Fellowship	Indiana University
Behzad Salari, MD	Dermatopathologist	Twin Cities Dermatopathology, Plymouth, MN
Chelsea Styles, MD	Pathologist	Spectrum Health Grand Rapids, MI
Alex Taylor, MD	Gynecological Pathology Fellowship	Michigan Medicine
Erica Vormittag-Nocito, MD	Director, Diagnostic Molecular Biology Lab	Northwestern University Medical Group, Chicago, IL
Terry Vouyoukas, MD	Assistant Chief Medical Examiner	Office of the Chief Medical Examiner of Alberta, Canada

happy hours, picnics, and ice cream socials. These activities give the students and faculty an opportunity to interact and strengthen their sense of community. This year, because of the pandemic and restrictions on gathering, we were not able to organize these regular events. Fortunately, following the CDC recommendations and social distancing guidelines, we were able to organize an ice cream social event where the students walked to a nearby park to spend time with their peers. After several months of being at home, the attendees enjoyed coming together again for some social interaction.

Because of the pandemic, our admissions and recruiting events were held online again, but this year PIBS organized in-person visits for the students who received an offer. This was an excellent opportunity for us to show prospective students what the Molecular & Cellular Pathology program has to offer. We organized lab tours in the medical campus and NCRC, and had several meetings with faculty and students presenting the research programs and discussing living in Ann Arbor. Despite the challenges, we succeeded in recruiting eight excellent students for our program, which is a reflection of our successful recruiting efforts and outstanding training environment. In August 2022, our new MCP and PIBS students participated in a half-day event to discuss the program and to learn about available research rotation projects.

Each year, the Director of the MCP meets individually with each student to discuss their progress. In addition, students are invited to an annual MCP Student Council meeting to provide their feedback, opinions, and suggestions. These activities are organized to ensure students remain on track and their needs are being adequately addressed during their graduate studies.

Students are also engaged with outreach and professional development activities to build their leadership and mentoring skills with younger students and undergraduates. In FY22, the students participated in many events led by a variety of organizations, including:

- Science Olympiad tutor
- Annual Biomedical Research Conference for Minoritized Scientists recruiting
- miLEAD consulting
- University of Michigan Young Science Innovators (U-MYScI)
- UM- SMART Undergrad Summer Program mentor
- Michigan DNA Day ambassador
- Rogel Cancer Center's One Day Closer event
- Organized a team to participate in a 5K run for Ovarian Cancer research
- Letter to a Pre-Scientist – Letters to a Pre-Scientist connects students to STEM professionals through snail mail to broaden students' awareness of what STEM professionals look like and do at work and inspire all students to explore a future in STEM.
- Project SHORT – A student-led organization committed to working to shrink the socioeconomic gap in medical and graduate school.
- Wolverine Pathways Career Day presenter
- Science Education and Engagement for Kids (SEEK)

Every year MCP students organize the Department Research Symposium. This year it was held virtually on November 5, 2021. The invited keynote speaker was Dr. Jeffrey Rathmell from Vanderbilt University, presenting Metabolic Checkpoints to Immunity in Cancer & Inflammatory Diseases.

During this fiscal year, four students joined the MCP graduate program. They and their mentors were encouraged to attend mentoring sessions offered by Rackham's Office of Student Success and prepare their mentoring plan. Three students successfully completed their preliminary exams in December 2021, and passed to candidacy status allowing them to focus on their research thesis work. By the end of the winter semester 2022, students had their first thesis committee meetings and presented their thesis research proposals. This year, two students graduated with their PhD degrees.

Graduate	Current Position
Xiofang Shi	Immunogenicity Scientist, Amgen, Inc.
Hanjia "Angela" Guo	Scientist, Epigenetics Applications Group, Cell Signaling Technology

Our graduate students continue to be successful in obtaining prestigious research awards and extramural grants during their graduate studies. The following awards were received this year:

Student Name	Award
Derek Dang	NIH F31 Fellowship
Jessica McAnulty	NIH F31 Fellowship
Kristen Lozada Soto	NIH F30 Fellowship
Alexander Monovich	Proteogenomics of Cancer Training Program

The MCP students regularly published their research work in high-impact peer-reviewed journals. Ten manuscripts were published by the following students as co-authors: Derek Dang et al, *Science Translational Medicine*, 2021 and *Acta Neuropathologica*, 2021; Brian Basinski et al, *Stem Cell Reports*, 2021; Alexander Monovich et al, *Autophagy*, 2022; Sahiti Marella et al, *Cellular and Molecular Gastroenterology and Hepatology*, 2021, *Clinical & Experimental Allergy*, 2022; and *Toxicology and Applied Pharmacology*, 2022; Michael Pitter et al, *Oncoimmunology*, 2022; Siva Kumar Natarajan et al. *Science Translational Medicine*, 2021; and Sanjana Eyunni et al, *Nature*, 2022.

The NIH NIGMS T32 Training Program in Translational Research (TPTR), which started on July 1, 2016, and is directed by Drs. Andrew Lieberman and Zaneta Nikolovska-Coleska, supported 6 pre-doctoral trainees for year 1 of the program's second 5-year cycle.

Trainee	Academic Program	Mentor	Year
Nicole Cady	Microbiology & Immunology	Dr. Thomas Schmidt	1st
Noah Puleo	Molecular & Cellular Pathology	Dr. Analisa DiFeo	1st
Miranda Walker	Neuroscience	Dr. Jack Parent	1st
Brian Basinski	Molecular & Cellular Pathology	Dr. Rajesh Rao	2nd
Alec Chu	Molecular & Cellular Pathology	Drs. Marcin Cieslik & Arul Chinnaiyan	2nd
Anthony Garcia	Pharmacology	Dr. Yoichi Osawa	2nd

Collectively, sixteen students have been funded by the T32 TPTR program and eight graduated. Importantly, all graduated trainees successfully continued their careers in the biomedical research workforce focusing on translational research: Lucas Huffman (Mentor: Dr. Roman Giger) is a Research Operations, Management & Strategy Fellow at the University of Michigan Medical School; Shawn Whitefield (Mentor: Dr. Evan Snitkin), is a Product Lead in Infectious Disease at Invitae; Andi Cani (Mentor: Dr. Scott Tomlins), recipient of the UM Precision Health Scholars Award in 2018, is a postdoctoral fellow at University of Michigan; Karson Kump (Mentor: Dr. Zaneta Nikolovska-Coleska), recipient of the American Association for Cancer Research Scholar in-Training Award 2020, is the Associate Director of Corporate Development & Market Insights at C4 Therapeutics; Samantha Kemp (Mentor: Dr. Marina Pasca di Magliano) is a postdoctoral fellow at University of Pennsylvania; Hanjia Angela Guo (Mentor: Dr. David Lombard) is a Scientist in the Epigenetics Applications Group at Cell Signaling Technology; Filipe Cerqueira (Mentor: Nicole Koropatkin) is a Clinical and Public Health Microbiology Fellow at the University of Texas Medical Branch and Anna Michmerhuizen (Mentor: Corey Speers) earned her PhD degree in August 2022 and is currently interviewing for positions.

In FY22, the second 5-years of the T32 TPTR started off with six funded slots, proving that our program is achieving and exceeding its goals to improve the training of future scientists in the translational research field.

Conferences and Symposia

20th Annual Pathology Research Symposium / Nov. 5, 2021
This symposium is planned and led by graduate students. The symposium featured a keynote speaker, Dr. Jeffrey Rathmell, Cornelius Vanderbilt Professor of Immunobiology, Professor of Pathology, Microbiology and Immunology and Cancer Biology, and Director of the Vanderbilt Center for Immunobiology, along with talks and posters by our students and faculty, as well as a career panel with experts from different career paths. To highlight the scientific accomplishments of the MCP graduate students, we presented several awards at this Symposium. The awardees of 2021 were: Siva Kumar Natarajan (Venneti lab) received the Outstanding Research Award; Sahiti Marella (Hogan lab) earned the Best Oral

Presentation; Rita Agazalho Avelar (DiFeo lab) and Sanjanna Eyunni (Chinnaiyan lab) were selected for the Best Poster Awards.

5th Annual T32 TPTR Retreat / May 11, 2022
At this event the trainees presented their translational research projects. The keynote speaker was Arul Chinnaiyan, MD, PhD, S.P. Hicks Endowed Professor of Pathology & Professor of Urology, and Director of the Michigan Center for Translational Pathology at Michigan Medicine.

The research seminar series is held weekly and highlights research from our own faculty and trainees as well as research conducted by invited guest lecturers. This year we invited the following speakers: Soman Abraham, PhD (Duke University), David Adams, PhD, FMedSci, FRCPath (Sanger Institute), Chenghua Gu, PhD (Harvard Medical School), Birgit Knoechel, MD, PhD (Harvard Medical School), and Min Gyu Lee, PhD (MD Anderson Cancer Center).

The T32 TPTR holds monthly workshops covering topics of relevance to translational research and showcases the work being done by our trainees. This year we had presentations from Drs. Christine Ye and Carl Koschmann from University of Michigan and Dr. Tim Somervaille from Cancer Research UK Manchester Institute, Manchester, England. We also had presentations by trainees Brian Basinski (Rao lab), Anthony Garcia (Osawa lab), Miranda Walker (Parent lab), Nicole Cady (Schmidt lab), Alec Chu (Cieslik lab) and Noah Puleo (DiFeo lab).

Ulysses Balis, MD
Director, Pathology Informatics

Pathology Informatics

The Division of Pathology Informatics (PI), one of the functional units of the overall Pathology Department, serves the tripartite missions of the department, including clinical operations support, original research, and education. As an informatics division, it is somewhat unique among contemporary academic pathology departments, in that it maintains both its own embedded teams of technical staff IT specialists and associated IT infrastructure, while still maintaining active dialog and alignment with the health enterprise's central IT group. This unique governance model allows the division to maintain its critically needed self-autonomy with respect to project oversight and prioritization, while at the same time leveraging consistent best-practice IT standards and methodologies, as determined by the health system at large. It affords the division both the ability to conduct internal prioritization of the department's many projects, as well as the ability to independently carry out original IT development efforts.

In addition, the division hosts its own active thrusts in fundamental areas of information technology, machine vision, and deep learning research, including computational imaging of Whole Slide Imaging (WSI) subject matter, asset tracking solutions, computational pathology, natural language processing, and medical information interoperability. Fundamentally, PI operates as a service unit within the greater department, covering a wide range of operational, strategic, and educational functions, with these various missions tied together by a centrally governed team of superbly trained information technology specialists who, at the same time, possess substantial familiarity with the clinical lab and its associated workflows.

The division is comprised of two full-time faculty, two adjunct faculty (with primary appointments in Anatomic and Clinical Pathology, respectively), one informatics fellow, and forty-three full- or part-time staff. Our former Informatics fellow Dr. Mustafa Yousif, rejoined the department from Vanderbilt University as a breast-service pathologist on faculty and as a pathology informaticist, allowing him to fully leverage his informatics fellowship training towards major clinically centered projects. In this capacity, he has accepted the role of faculty sponsor for the ongoing Digital Pathology Primary Diagnosis initiative, working closely with both Dr. Pantanowitz and the Informatics Division at large.

Similarly, Dr. Lee Schroeder continues in his role as an adjunct faculty member of the Informatics Division, assisting with instrumentation implementation efforts and IT policy issues that have overlapping jurisdiction between the clinical labs and IT governance.

The critical mass of the division's full-time and adjunct informatics faculty has allowed for the continued assignment of effort towards both intramural and extramural academic endeavors. U-M's PI division remains one of the largest academic informatics units in the US, where all faculty hold Clinical Informatics board certification or are board eligible.

The 2021–2022 fiscal year witnessed a significant expansion of the division's utilization of web-accessible dashboard technology and associated underlying data analytics/machine learning technology. These efforts extended far beyond the initial efforts of simply representing daily COVID testing performance metrics to now include extensive real-time workflow and case volume logistics for various departmental laboratory sections.

This past fiscal year also benefitted from the division aggressively reactivating its global LIS upgrade effort, which was paused due to redirected operational efforts during the pandemic. The Informatics Division also continued supporting the ongoing PRR project (phase

2.x) with multiple concurrent IT and AV planning efforts, which allowed corrective specification actions to be taken during the final schematic design phase, and prior to the purchase or installation of incorrect equipment.

Also, the Informatics Division completed many operational projects in partnership with the enterprise-at-large. Some of the major projects include moving to Office 365 from an exchange-server email system and from Box to Dropbox, replacing P7-based servers with P8-based servers, multiple software upgrades, and several application development projects.

Additionally, the Pathology Informatics team supported our laboratories with software upgrades, installation of new equipment, development of new interfaces to integrate with new sites and software products, and general support. Process improvement projects to streamline faculty annual reviews, provide disaster recovery protection for our website, and enhance our HR Tools program, among others, were also successfully completed.

The Informatics Division has a long list of ongoing projects to continue to support our clinical, research, and education missions. One of the primary new areas of work is centered around launching and enhancing our digital pathology workflows. From reviewing and selecting a Digital Pathology Case Management Solution through implementation of multiple aspects of workflow, the Informatics Team is providing expert support to our Anatomic Pathology colleagues. Preparations are also underway for our Laboratory Information System upgrade and enhancement of our MLabs client development software suite. The division is also completing a new ServiceNow portal which will enable even better service within the Department. Finally, in a never-ending process, new interfaces are being developed to provide bidirectional data flow between clients and within our own health system.

During this past year, the division activated its new educational curriculum for residents, offering both a series of didactic morning lectures and a two-week rotation in Pathology Informatics Fundamentals, which will be offered biannually, thus ensuring that all residency program trainees will be exposed to core content from this increasingly important aspect of the contemporary practice of Pathology. The first instance of this rotation was offered with uniformly positive feedback from residents indicating that this content was addressing a previously unmet need. The division plans to continue to update and expand the curriculum for both the lecture series and rotation, allowing for timely coverage of current and developing topics such as: digital pathology workflow, LIS design and operation, AI & machine learning techniques, data sciences stewardship, lean concepts, and workflow error-proofing, just to name a few.

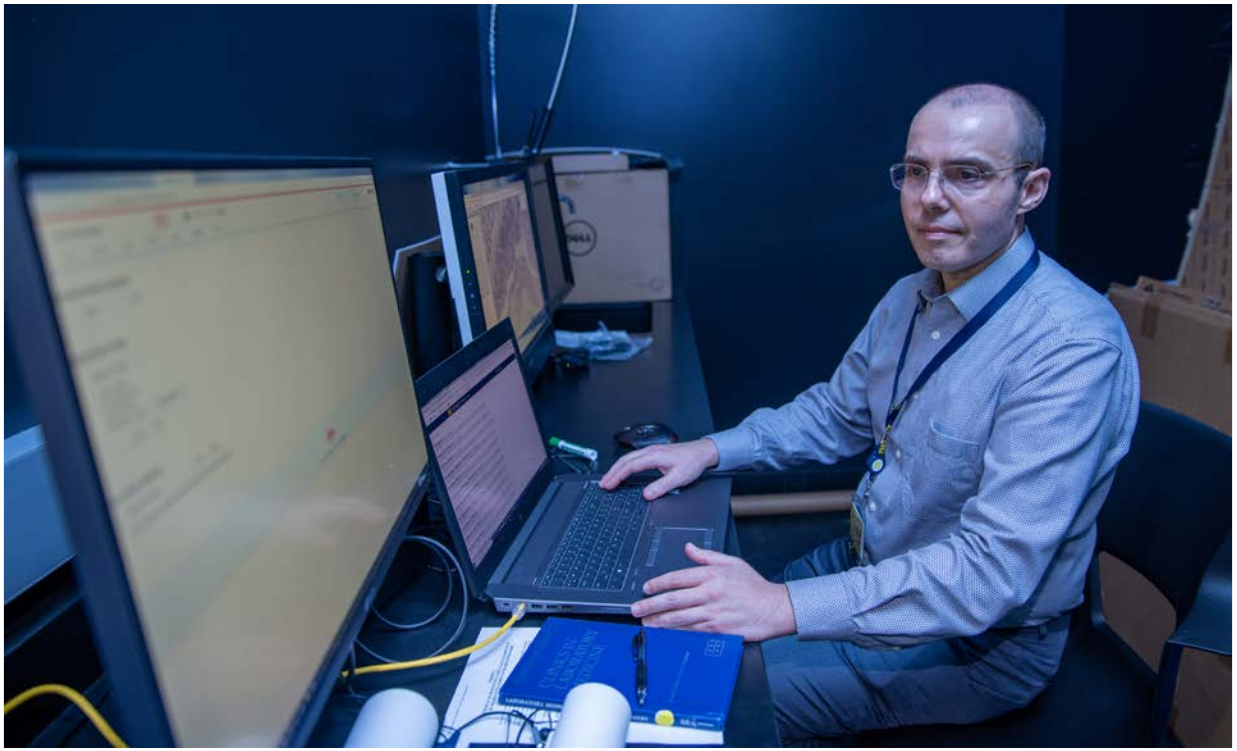


Photo Above: *Peter Ouillette, Operations Manager in Digital Pathology.*

At the national & international levels, the division continued in its educational tradition of serving as the co-secretariat for the long-standing Pathology Informatics Summit Meeting series. As a salient development, the organizing committee decided to bring the meeting to the Ann Arbor area starting May 2024, with the meeting now scheduled to take place at the nearby Eagle Crest Resort in

Ypsilanti. This will afford opportunities for meeting attendees to visit the department and observe active Pathology Informatics-associated projects, including the anticipated primary diagnosis digital pathology workflow, which will be live and extensively deployed by that time.

In terms of academic efforts, the Informatics Division witnessed another productive year with major support renewed for the ongoing NIDDK Kidney Precision Medicine Project, with the division serving as one of the anchoring labs in support of IT logistics for curation and analysis of whole slide images from study participants. Efforts in support of computational pathology similarly continued, with the division procuring the first of several high-performance computational resources targeting the growing machine learning and AI needs of the department for discovery and clinical data analytics purposes. One of the major deliverables from this longstanding participation and collaboration has been the development and refinement of a high-performance image segmentation tool, VIPR Studio, which is now in its fourth version of release. This tool allows for pixel-level segmentation of entire whole slide images or even libraries of whole slide images, thus greatly accelerating the ground truth generation process intrinsic to the creation of training data sets for image-based machine learning investigations in histopathological datasets.

On the global front, the division remains active in investigational initiatives in Kenya, Ghana, and Sri Lanka, with efforts primarily focused upon deployment of productivity tools that are useable in low- and middle-income country settings to increase effective laboratory utilization (Ghana) and to increase the availability of machine learning tools supporting the interpretation of diagnostic results in primary care settings (Kenya & Sri Lanka).

Finally, over the past year, the division has provided ongoing technical and strategic mentoring to one of our residents, Dr. Ryan Landvater, allowing him to expedite the completion of a promising whole slide image viewing technology, which provides improved user response performance as compared to any of the contemporary commercially available viewing platforms. Currently, he is pursuing patent protection.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Scott Owens, MD
Director, Division of Quality and Health Improvement

Division of Quality & Health Improvement

The Division of Quality and Health Improvement (DQHI) in the Department of Pathology at Michigan Medicine made significant progress on several fronts during FY22. Once more fully staffed after pressures from the COVID pandemic eased, DQHI personnel were able to contribute to many different projects in the areas of laboratory process improvement, operational support, laboratory stewardship/test utilization, and patient care improvement in partnership with laboratory staff and leadership, as well as clinical partners throughout the enterprise. Important guiding principles for DQHI leadership and personnel in choosing and proposing projects include an emphasis on efficiency and high-reliability principles, an expectation that changes and results will be solidly focused on adding value and as generalizable as possible throughout the department and institution, a commitment to scoping projects for achievable results, and a focus on obtaining a mixture of subjective and objective measurements that allow for both assessment of impact and sharing of results in an academic format. A number of these efforts are detailed herein.

Education

As detailed in last year's report, DQHI leadership engaged the new leadership team from the Division of Educational Programs to discuss the role of DQHI in resident quality and patient safety education. Because of a shift in resident attitudes surrounding the pathology quality curriculum, which had served as a significant portion of the basis for the institutional quality curriculum for house staff to meet ACGME requirements, it was decided to pause DQHI's direct involvement in the process for the time being. In part, this was an effort to allow the Education Division's leadership to revitalize their co-sponsorship of the curriculum, which had diminished over the preceding two years (in no small measure due to changes forced by the pandemic). Both parties agreed that it is critical for leadership from the Education Division to be directly involved in the curriculum, given its crucial role in fulfilling ACGME requirements for house officer training.

Operational Support

Several important DQHI projects focus on operational support for the clinical laboratories. These projects stem from DQHI's belief that our division is in an ideal position to both cross boundaries between clinical labs and other clinical divisions – allowing for the creation and support of cross-functional teams sustained by our project managers, process improvement specialist, and data scientist – and to provide the appropriate staff bandwidth and expertise to shoulder this type of effort, allowing laboratory leadership and personnel to concentrate on their clinical work. To this end, our staff have organized, supported, and participated in a department-wide complete equipment inventory in support of departmental administration and supply management. This effort has focused on the creation and population, in partnership with Pathology Informatics, of an electronic log into which all clinical equipment is being entered, with DQHI personnel and volunteers from throughout the laboratories canvassing the department to document and record the stock (Figure 1).

A second example of operational support activities is the development, in collaboration with leadership and staff from the microbiology laboratory, of an updated and streamlined supply management system for that lab. This effort updated a paper-based process with a visual and digital management system that has made improvements in both reducing the number of supplies ordered and kept in long-term reserve and in reducing the time to locate supplies for laboratory personnel, among other benefits. In addition, the laboratory has moved from devoting essentially an entire FTE

to supply management activities, to having a streamlined system in which several laboratory personnel can participate in supply logistics as part of their regular workflow. Efforts are underway to quantify the savings in time and other resources as part of the P-D-C-A cycle.

DQHI personnel also worked on projects in collaboration with clinical personnel outside the Department to improve broader patient care activities. These include working with Hospital Information Technology and Services (HITS) personnel and clinical leadership on streamlining laboratory orders management (including changes to reduce unnecessary standing laboratory orders), as well as work with Hematology laboratory leadership/personnel and Hematology/Oncology personnel to improve the process of scheduling bone marrow biopsies, with a goal of optimizing the timing and organization of these procedures to best benefit patients and providers.

Finally, a large project was undertaken to standardize and streamline the process of developing and onboarding new laboratory tests throughout the Department. Growing directly out of the MSTAR initiative, this project took disparate and laboratory-localized approaches to the process of new test development and using input from across the clinical labs, created a standardized approach to this work (Figure 2). Now fully deployed, this system will allow the labs to address market demands more nimbly for new tests from both Michigan Medicine clinical customers and outside clients via Michigan Medicine Laboratories/MLabs (MML).

Process improvement

Several projects involving DQHI personnel have focused on process improvement throughout the Department. Some of these have been undertaken in the wake of challenges that were identified in the course of normal operations in the areas of specimen tracking from outside clients and frozen section diagnosis in the University Hospital operating room suite. Using both project management and quality improvement expertise from DQHI, we have partnered with stakeholders in Anatomic Pathology (AP), MML, and institutional clinical operations to improve the tracking of dermatology specimens from outside clients. This work stems from a handful of episodes in which specimens from outside Michigan Medicine failed to reach their destination within the Department for surgical pathology analysis and has resulted in a (currently) paper-based manifest system that better identifies what specimens we should expect to receive, and where to begin investigation should a specimen go missing. This has been piloted with both low- and high-volume dermatology clients with opportunities for feedback and P-D-C-A. The process should be generalizable to other clients and, although currently paper-based, has been designed with a future state of an electronic solution involving digital interfaces between clients and MML in mind.

In response to an episode in which specimens from the operating suite were misidentified as routine/permanent section tissue rather than as tissue intended for intraoperative frozen section analysis, DQHI personnel partnered with stakeholders in AP and clinical operations to improve the process of frozen section specimen identification. This has resulted in separate work streams aimed at creating a better visual identification system for the specimens themselves, as well as changes aimed at more effective communication of frozen section results to surgeons and other personnel in the operating rooms. These changes should allow for both a more definitive and obvious designation of which specimens from a patient require intraoperative analysis before and after arrival in the frozen section laboratory, and for a "back-end" check by personnel in the operating rooms that the expected specimens were in fact analyzed by frozen section.

Finally, a project is underway to improve the utilization of the information gleaned from patient safety incident reports entered by and about the clinical laboratories in the institutional patient safety reporting system. Historically, the information contained in this system has been a mixture of useful material that could potentially be utilized for process analysis and improvement, and less fruitful data that provides relatively little beyond documentation of specific events, making the "signal-to-noise" ratio quite low. To better utilize the beneficial portion of this data, DQHI personnel have instituted a project aimed at leveraging data analytics to parse out actionable reports that may be best leveraged to become process improvement and/or operational support projects. Work is ongoing.

Laboratory stewardship

As an area of interest for DQHI, laboratory stewardship and clinical

decision support has a long history, with work aimed at optimizing clinical test utilization among the first large projects undertaken by our team. DQHI personnel have a record of supporting and leading efforts in this area in collaboration with like-minded faculty and staff within the Department and broadly around the institution, particularly in the various divisions of the Department of Internal Medicine. Much of this work has occurred in the context of the Laboratory Stewardship Subcommittee of the Department's Laboratory Formulary Committee, although the challenges of the COVID pandemic slowed the subcommittee's work to a substantial degree. Currently, this subcommittee's formal meetings are on hold, but work in this area has continued unabated, partially under the aegis of the MSTAR initiative.

One key project for FY22 grew out of a collaboration with colleagues in the Cardiology division of Internal Medicine, after DQHI was approached by Cardiology leaders to help them understand how their practitioners are using laboratory testing in the context of analytic and treatment protocols for patients with clinically significant heart failure. In a collaborative quality initiative-like project, DQHI personnel have provided project management, data science, data visualization, and clinical expertise that has thus far resulted in the development of a provider dashboard that is in early use to monitor provider behavior and ordering patterns in comparison to published and local care guidelines. The aim for this part of the project is to provide Cardiology leadership with the tools needed to provide direct feedback to practitioners and encourage standard practice. This platform is generalizable across clinical practices and could easily serve a similar purpose throughout the institution. The second phase of the project has centered on the use of laboratory testing and data science to provide practitioners with ongoing information about the optimal titration of medications to treat heart failure. Providing a "medication optimization score" (MOS) to clinical caregivers, this will give up-to-date therapeutic and patient health data that will allow more focused medication adjustments and, it is anticipated, better patient outcomes as measured by readmission rates, heart failure severity scores, and others. Demonstrating this type of direct connection between optimal laboratory studies and patient outcomes has been a goal of DQHI since its inception.

Other laboratory stewardship projects have been a continuation and expansion of efforts described in previous versions of this report. To estimate opportunities for reducing low-value laboratory testing, DQHI and other departmental leaders partnered with the Michigan Program on Value Enhancement (MPrOVE) in a systematic and data-driven approach to identify areas where decision support and other interventions could be pursued using the electronic order entry system (MiChart/EPIC) to promote appropriate laboratory utilization (Figures 3 A/B). Among others, opportunities were identified in thyroid disease testing (37% of T4 tests were ordered without a prior abnormal TSH within 60 days), celiac disease screening (97% not using an available reflex testing algorithm), and thrombophilia panel testing (up to 27% of assays were ordered inappropriately, e.g., for inpatients who are often anticoagulated).

These findings and others led to the implementation of specific MiChart/EPIC interventions, including the development of reflex testing algorithms and decision support tools for thyroid and celiac disease, and the removal of ordering options for thrombophilia testing of anticoagulated inpatients. Preliminary data indicate that these interventions have reduced low-value testing at Michigan Medicine, with a post-intervention increase in appropriate thyroid testing patterns (Figures 4 A/B) and an effective elimination of thrombophilia testing for anticoagulated inpatients. Demonstrating added value, the use of our celiac algorithm appears to have had a normalizing effect on biopsy ordering practices across medical providers (Figures 5 A/B). This work resulted in the collaboration between DQHI and the Laboratory Stewardship Subcommittee being recognized by the American Society for Clinical Pathology (ASCP) with a "Choosing Wisely Champion" award in 2022.

Summary

DQHI continues to work on projects involving operational quality improvement and value creation, aiming to transform the experience of patients at Michigan Medicine and beyond by using the expertise inherent in laboratory medicine to impact patients' lives from a laboratory medicine and pathology platform. Efforts in quality education, operational support, process improvement, and laboratory stewardship, detailed above, provide evidence of continued commitment to and impact in these areas.

Thyroid Function Testing

Recommended for initial thyroid dysfunction screening in primary care

TSH with reflex algorithm including FT4 and FT3: includes Thyroid Stimulating Hormone (TSH). If the TSH screen result is between 0.30 - 5.00 mU/L, no further testing is performed. If the TSH screen result is <0.3 mU/L, Free T4 (Thyroxine) (FT4) will be performed at an additional charge. If the FT4 is <1.76 ng/dL, Free T3 (Triiodothyronine) (FT3) will be performed at an additional charge. If TSH screen is >5.0 mU/L, FT4 will be performed at an additional charge.

For testing patients on thyroid hormone replacement therapy (levothyroxine, liothyronine, desiccated thyroid extract)

* In case of primary hypothyroidism (e.g., status post thyroidectomy, 1 or 2 months after radio-iodine ablation for hyperthyroidism, or Hashimoto's thyroiditis)
  - TSH only recommended
* In case of secondary hypothyroidism (e.g., pituitary insufficiency)
  - FT4 only recommended

For testing patients receiving treatment for hyperthyroidism (methimazole, propylthiouracil, radioiodine ablation)

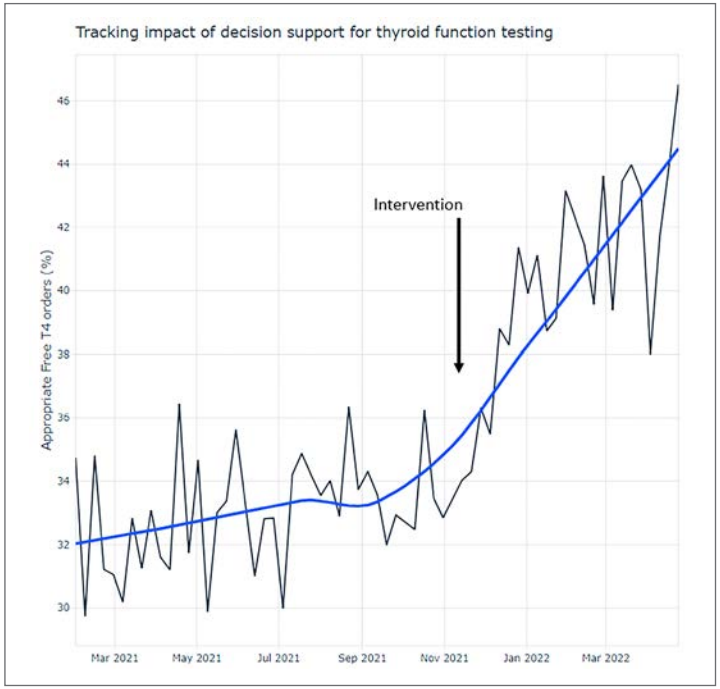
* If early in medical treatment or soon after ablation (e.g., first 2 months):
  - FT3 and FT4 recommended
* If later in treatment (e.g., after 2 months):
  - Thyroid Dysfunction Algorithm recommended

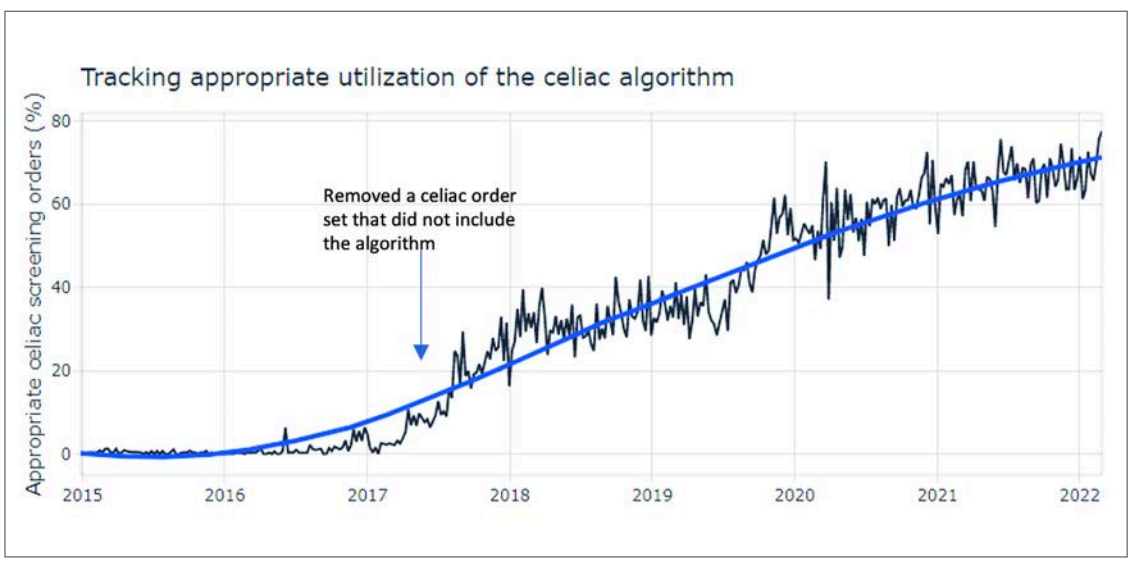
Individual tests (if patient does not fit above descriptions)

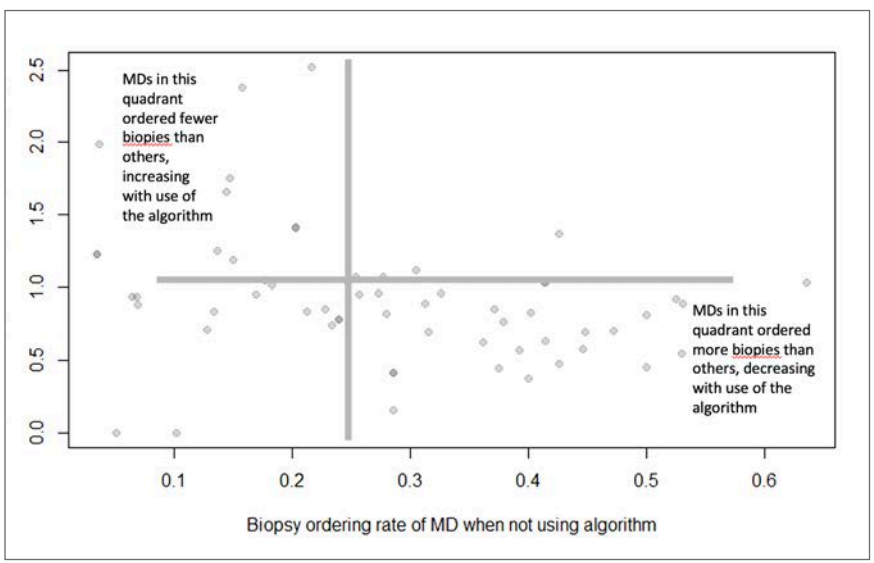
- TSH
- FT4
- FT3 or Total T3

May have utility in a limited set of patients only

- Total T4 (when thyroxine-binding globulin or albumin are well outside reference range, an unexpected FT4 may be due to interference; in this setting Total T4 may be useful)
- T3 uptake (needed to appropriately interpret Total T4 results)







Charts: *(Top Left to Right) Figures 4A/B; (Bottom Left to Right) Figures 5 A/B.*

David Golden
Interim Director, Finance and Administration

Finance & Administration

The Division of Finance and Administration, which is under the auspices of the Office of the Chair, is responsible for the business, operational, and fiscal affairs of the Department of Pathology, as mandated by the policies of the Chair, Michigan Medicine, and the University. In this section, key achievements of the Finance and Administration team are highlighted as well as the supporting services provided by this division. Mr. David Golden accepted the role of interim Chief Department Administrator in September 2021 after the unexpected passing of Mr. Martin Lawlor. David has stepped into and provided administrative leadership to the Department while continuing his role as Director of Finance. David administratively oversees annual expense budgets of $260 Million and over $1.1 Billion in gross revenue.

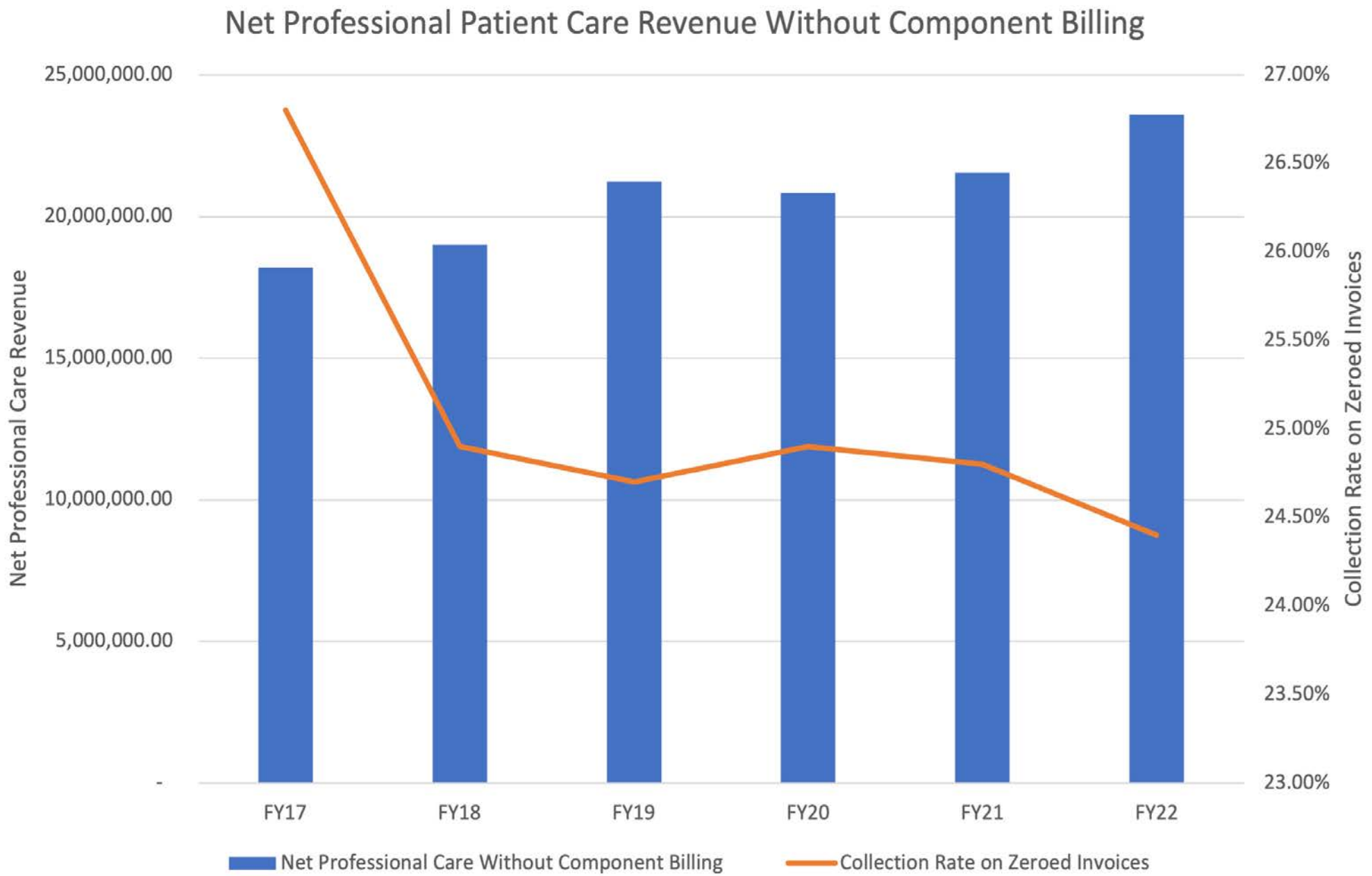
Some key divisional highlights for this academic year include:

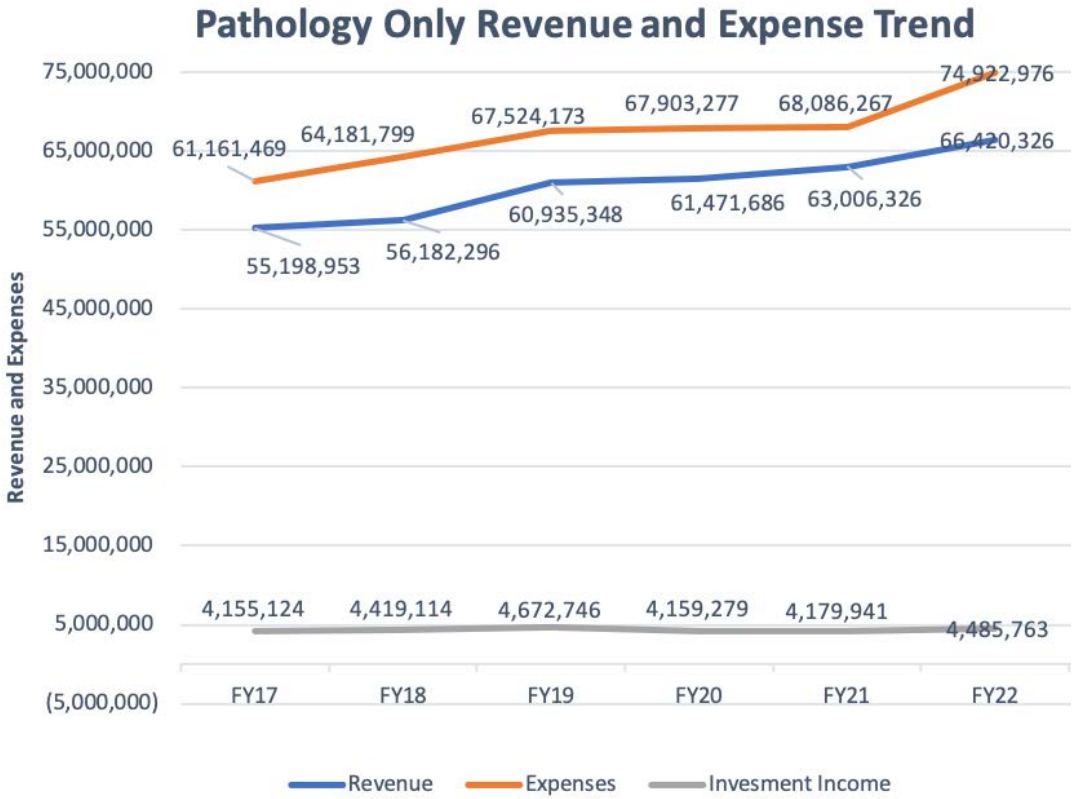
- Successfully renegotiated a new Part A agreement with Michigan Medicine.
- Pathology has over 1,000 staff and David reviews and approves all new and replacement positions in collaboration with the Medical Directors of the various divisions. We addressed staffing shortages in our clinical laboratories and pathology informatics. Reviewed all staffing requests and developed a good track record of getting them approved by senior leadership in UMHS.
- Deployed labor market adjustments in January 2022 for select clinical staff and continue to work on further labor market adjustments to address compression issues.
- Created and funded a new professorship in Pathology Informatics
- Worked closely with Dr. Parkos on several key faculty and staff recruitments and retentions.
- Analyzed and implemented salary changes in our tenure track faculty.
- Completed our three-year forecast of faculty workforce plans.
- Developed a proposal to implement Digital Pathology in the Department in FY23.

The Division of Finance and Administration is divided into support services for the pathology laboratories; academic and business affairs; and human resources, faculty affairs, and education.

Pathology Laboratories

The administrative support center for pathology laboratories is responsible for the preparation and monitoring of all hospital laboratories' revenue, expense, and capital budgets, and personnel and payroll systems. During this period, total laboratory operating expenditures were $181 million. Staffing levels in the laboratories remained largely flat at 831 FTES. In part, this is a result of the nation-wide trend in technical staffing shortages. We developed several incentives to attract new hires as well as retain existing staff during the year. We are also looking at ways to develop staffing pipelines by partnering with local schools. Pathology is responsible for 9.0% of total hospital gross revenue and 3.7% of total expense. Gross Revenue and expenses were impacted by the COVID-19 pandemic. Gross revenue was down 3.1% when compared to FY21 as COVID testing for our patients, students, faculty, staff, and community declined significantly as the pandemic waned. The gross revenue decline was partially offset by increased testing as we returned to more normal operations in anatomic and clinical pathology. Billed tests in FY22 were 7.2 million vs. 7.4 million in FY21 (primarily the result of Covid testing).


Net Professional Patient Care Revenue Without Component Billing
25,000,000.00
20,000,000.00
15,000,000.00
10,000,000.00
5,000,000.00
-
Net Professional Care Revenue
27.00%
26.50%
26.00%
25.50%
25.00%
24.50%
24.00%
23.50%
23.00%
Collection Rate on Zeroed Invoices
FY17
FY18
FY19
FY20
FY21
FY22
Net Professional Care Without Component Billing
Collection Rate on Zeroed Invoices



The administrative support center team worked diligently in FY22 as we continued the remodeling of the University Hospital clinical laboratories. The renovation of these spaces was paused during the early months of the pandemic but began again in earnest in the Summer of 2021. Led by the PRR team with the support of the Pathology Informatics team, the renovations proceeded on a modified schedule and without excess disruption. Throughout FY22, our facilities managers and the PRR team diligently addressed issues as they arose, especially with unanticipated issues surrounding logistics of maintaining clinical laboratory operations during the renovations.

Members of the administrative support center team served as departmental liaisons with nursing, the office of clinical affairs, office of clinical safety, biomedical engineering, and hospital finance. They served on the quality month committee, pathology diversity, equity and inclusion committee, pathology patient and family advisory council, pathology social media committee, and others. The team addressed patient safety issues and cooperated on process improvement initiatives with partners such as the Rogel Cancer Center, UH operating rooms, and various medical procedure units.

FY22 Pathology Income Statement

REVENUE	FY22	FY21
Patient Care Revenues	$23,922,185	$21,491,758
UMHS Service Payments	$8,149,368	$9,774,171
Net Total Research (Directs & Indirects)	$24,760,445	$22,278,142
Gifts and Other Income (Wayne/Washtenaw ME, etc.)	$9,588,329	$9,462,255
Total Revenue	$66,420,327	$63,006,326
EXPENSES		
Total Salaries	$55,374,180	$50,520,050
Total Non-Payroll Expense	$19,548,796	$17,566,217
Total Operating Expenses	$74,922,976	$68,086,267
Operating Margin (Loss)	($8,502,649)	($5,079,941)
Non-Operating Income and Expense (Includes Investment Income, UMHS Margin Sharing, Departmental Commitments, etc.)	$9,478,084	$9,909,751
Total Margin	$975,435	$4,829,810

Office of Academic and Business Affairs – Medical School

The office of academic and business affairs – medical school, is responsible for all administrative and academic operations associated with the Department, including management of department finances (budgets, contracts, research grants, forecasts, and analyses), as well as clinical billing (professional and technical front-end operations). In collaboration with the Chair, Mr. David Golden implements and directs strategic goals for Medical School operations including development of policy and business plans, management of faculty compensation and departmental funds, and use of departmental facilities, including modifications, renovations, and reassignment of

department space.

The office also manages the Michigan Medicine and All Funds expenditures and forecast processes. Key departmental metrics include:

- Total Medical School All Funds expenditures including the MCTP for FY22 were $85 million and Hospital expenditures were $181 million.
- Hospital technical gross revenue for FY22 was $985 million, compared to $1.02 billion in FY21, a decrease of 3.1%.
- Professional fee gross charges were $91.1 million in FY22 compared to $88.0 million in FY21, an increase of 3.5%.
- Overall gross charges for Pathology's group practice were up 3.4% ($3 million).
- In FY22, our faculty received 51 awards from the NIH and ranked 8th in the nation in funding by the NIH, an improvement of our 9th place in FY21, and 6th in the nation when considering number of awards received. Total grants submitted in FY22 was $31.7 million, an increase of 37% over FY21. Our total sponsored research spending in FY22 was $36.4 million, up from $33.2 million in FY21, a 9.6% increase.

Business Affairs

Business Affairs is responsible for oversight of all accounting and financial transactions for the Department as well as ensuring appropriate hospital and medical school funds flows. Our billing office handles all send-out, component, and MLabs billing, and any interdepartmental, MLabs, or Hospital patient billing error corrections. The grants management office handles the day-to-day management of research funds to ensure compliance with funder requirements, and to ensure the funds are distributed appropriately both within Pathology as well as across internal and external research groups.

Business Affairs is also responsible for Hospital and Medical School financial reporting and budget preparation for the Department and in administering numerous contracts, including those for the Washtenaw and Wayne County Medical Examiner's Office contracts. As part of the budgeting process, they also develop and maintain the capital equipment process, prepare financial analyses, produce numerous *ad hoc* reports. They also oversee the Pathology Renovation and Relocation project to ensure contract terms are met, budgets are managed, and capital investments are approved according to Michigan Medicine and Pathology procedures, and facilities are prepared for the renovation of University Hospital spaces that occurred in FY22. In addition, all faculty and staff effort and funding changes are processed through this unit.

Finance

The Department of Pathology is in a strong financial position and continues to thrive under the leadership of Dr. Charles Parkos and Mr. David Golden, with endowments and FFAE to support our clinical, research, and educational missions, exceeding $135.9 million. In FY22, we experienced a larger gap between our revenues and expenses, with Revenues at $71.6 million, up 5.3% over FY21 and expenses at $84.9 million, up 10.5% over FY21, mostly due to increases in payroll and supplies as we returned to more normal operations as the pandemic wanes. This resulted in an operating loss of $13.3 million. The loss was offset by non-operating income (investments, dean's contributions, and other institutional support payments). Including our non-operating income, FY22 ended with a net loss of $3.4 million. In contrast, in FY21 we experienced a margin of $1.17 million.

Michigan Medicine has long-range expansion and upgrades budgeted, including Pathology's Renovation and Relocation Project, that requires greater-than-average net budget increases as compared to those seen over the past decade. As a result, there is significant pressure on Departments to reduce expenses and increase revenues. While our revenues continue to grow, the collection rate is at its lowest point in the past 15 years, at just 24.4% of charges. Pathology faculty and staff paid FTEs have remained relatively flat at 1,210.67 in FY22 versus 1,196.7 in FY21. The combination of the pandemic and the economic recovery plan has forced us to do more with less staffing. Increased workloads and decreased collection rates pose challenges for meeting Michigan Medicine targets for the Department. As a result, filling vacant staff positions has become more difficult. We are grateful to our staff, who have stepped up

Thomas Morrow
Administrative Manager, Clinical Operations

Kristina Martin
Manager, Clinical Operations

Christine Rigney
Assistant Administrator, Operations, Division of Anatomic Pathology

Christine Shaneyfelt
Financial Analyst Senior,
Hospital

Mike McVicker
Financial Analyst Senior,
Medical School

John Harris
Manager, Research Administration

to the plate to take on additional duties to ensure the missions of Pathology continue to meet and exceed expectations.

We have outstanding faculty and staff who continue to support exceptional scholarship and clinical care. Our clinical services continue to grow and maintain the highest quality. New educational opportunities continue to attract top trainees and our future looks bright as we move forward into our new facilities, designed for the future. Overall, FY22 has been a tremendous year for our department.

Human Resources, Faculty Affairs and Education

Our Staff Human Resources Team provides support for Pathology's hospital laboratories (approximately 831.11 FTEs) and Medical School support staff, including our research programs (approximately 232.42 FTEs). This includes processing all new hires, promotions, merit increases, orientation, as well as transfers when staff move to other departments, or terminations for those who leave our institution. They also help to coordinate employee recognition events and awards.

Faculty Affairs is responsible to coordinate appointments, reappointments, and promotions for our 164 active faculty and the 23 supplemental appointments in the Department. In FY22, nine new faculty joined the Department of Pathology while we bid farewell to seven faculty members. Twelve of our faculty successfully completed the promotion process (Table on right).

Our faculty received numerous awards in recognition of their achievements in academics, research, and clinical service. (See Appendix on pg. 78)

The Education Office includes the Residency and Fellowship Training Programs (26 residents and 18 fellows in 10 ACGME and 8 non-ACGME programs), the Medical Student Education Teaching Programs for the M1 and M2 laboratories, and the M4 Clerkship Program, as well as the Molecular and Cellular Pathology PhD program with 25 students actively pursuing their doctoral degrees. Management responsibilities are focused around curriculum management (including the Research Seminar Series), academic records, budget planning and financial operations, recruitment, and program activities, such as the annual departmental research symposium. The department also holds two NIH training grants

Faculty Promoted in FY22

Name	New Rank	Division
Sandra Camelo-Piragua	Professor	AP
Richard Cantley	Associate Professor	AP
Roberta Caruso	Assistant Professor	EP
Jerome Cheng	Associate Professor	PI
Tomasz Cierpicki	Professor	EP
Jolanta Grembecka	Professor	EP
Alexandra Hristov	Professor	AP
Shih-Hon (Sean) Li	Associate Professor	CP
Miguel Quiros Quesada	Assistant Professor	EP
Dan Robinson	Associate Professor	EP
Douglas Rottmann	Assistant Professor	AP
Mark Schultz	Assistant Professor	--

(PIs Nicholas Lukacs, PhD; Andrew Lieberman, MD, PhD, Zaneta Nikolovska-Coleska, PhD) which support four pre- and six post-doctoral trainees. The education office performs the human resource functions for the department's graduate students (31 including 6 non-MCP students with Pathology mentors and four training grant trainees).

Office of the Chair

The staff in the Office of the Chair coordinates the Advances in Forensic Medicine and Pathology conference, which was held in the Spring 2022. They also reconcile departmental purchasing cards, renew medical licenses, process CME requests for faculty, coordinate and develop departmental communications including the *Inside Pathology* magazine and the annual report, and prepare numerous reports and presentations for various meetings. In addition, they provide support to the Chair and Department Administrator, including scheduling, travel arrangements, data collection, event planning, correspondence, committee support, and faculty recruitment.

Community Service

In support of our mission as a non-profit healthcare provider, our

faculty and staff engage in numerous service activities throughout the year. Some of the activities our faculty and staff engaged in this year included:

Local Activities (UM, Ann Arbor or Michigan)

- Relay for Life Teams to raise funds for cancer treatment
- Assisted MetroHealth in validating the Verify-Now assay for aspirin and Plavix-specific platelet aggregation
- Gift of Life Michigan board and committee memberships
- Patient and Families Advocacy Committee (PFAC)
- Numerous Medical School and Health System committee leadership/membership, see our list of new leadership positions.
- High school genetics, ethics, Doctors of the Future, and other programs as well as volunteering to coach or direct athletic programs
- High School Ethics Bowl judge
- Service on multiple non-profit boards of directors

National

- Assisted in multiple inspections for College of American Pathologists (CAP), American Association of Blood Banks (AABB), American Society for Histocompatibility and Immunogenetics (ASHI)
- Serving on multiple national and international professional organization boards and committees, see our list of new leadership positions added in FY22 (pg. 78)

International

- Exploring transport solutions for patient samples in remote African villages to laboratory testing facilities
- Developing Essential Diagnostic Test List for low resource settings
- Implementing comprehensive 8-marker flow cytometry to accurately diagnose acute pediatric and adult leukemia patients in low-middle income countries, implementing it in Addis Ababa, Ethiopia
- Cervical cancer screening initiative in India

Employee Recognition

The Department of Pathology recognizes the valuable contributions made by our faculty and staff alike. In FY22, we recognized the years of service for faculty and staff who have served for 10, 20, 30, and even 40 years, as well as those who received Above and Beyond Awards, as nominated by their peers. (Appendix pg. 82) The number of employees who have been in the department for over 20 years speaks to the dedication of the employees as well as to the collegial atmosphere of our Pathology Department. This year we also honored our retirees. (Appendix pg. 83)

Sarah Dudley-Short
Manager, Faculty Affairs

Christine Baker
Project Manager, PRR

Pathology Relocation & Renovation Project

The Pathology Relocation and Renovation (PRR) Project is a multi-year, multi-phase project embracing the opportunities to relocate a large sector of the department into an off-site facility at the North Campus Research Complex (NCRC) and to renovate and right-size critical functions within University Hospital. Christine Baker has been with the Department of Pathology for more than eight years and is the leader for this effort. She facilitates and manages the tasks needed to design and activate the new spaces and serves as the liaison to colleagues within Michigan Medicine Facilities and Operations as well as the construction teams led by the Architecture, Engineering, and Construction group.

Construction for Phase 1 of the PRR, which was over 140,000 square feet of newly renovated space at NCRC, finished in FY18. The activation of the new space started during the summer months and completed in November 2018. This included several major clinical laboratories as well as key administrative divisions.

The design of Phase 2, the renovation of the laboratory and support spaces at UH, formally finished in 2017, but further revisions and re-phasing continued through early 2019. Phase 2 of PRR is a very complicated and unique challenge—all current labs and the Apheresis Patient Care Unit (APU) at University Hospital must remain fully operational while the new laboratory space is constructed and then activated. The first design effort included a complicated, 19-phase plan, which was revised and edited to reduce the duration of the entire project.

Phase 2 now has five unique and distinct construction phases, with each construction phase followed by a period of activation. FY21 saw the completion and activation of both the second and third phases of construction in Phase 2.

The first major milestone of FY21 was the completion of the second phase of construction in July 2021. This milestone included new automation functions for Hematology and Chemistry, as well as new Specimen Processing space, new Anatomic Pathology space, and new space for the Microbiology stat-functions. The installation and activation of the automation lines took many months and significant coordination from medical leadership, laboratory leadership, laboratory staff, facilities teams, informatics professionals and our vendor support team. This cohesive team worked together week after week to ensure a seamless activation and integration of multiple components of automation.

The result from this significant work effort includes the following:

- Hematology Automation integrated into overall automation; this line runs over 2500 specimens daily and increased throughput by one-third.
- Coagulation Automation came online in Fall 2021 and automated 70% of the Coagulation Lab as well as allowing auto-verification of results.
- Chemistry Automation was a whole-scale upgrade of technology and automation; this increased capacity from 14 million tests annually to 52 million tests annually (6000/hour).

The second major milestone of FY22 was the completion of the third phase of construction in April 2022 and the subsequent activation of the Blood Bank Laboratory as well as the Supply Storage space and office spaces to support the Core Lab. This phase marked the beginning of work on the Transfusion Medicine neighborhood, and the completion of construction on the Core Lab neighborhood. The relocation of the Blood Bank Laboratory was a significant

achievement, and one that recognizes the value of teamwork, patience and cooperation.

During the past year, the faculty and staff within the Clinical Laboratories at University Hospital worked through numerous obstacles and challenges. Specimen Processing survived being separated into two sections and were reunited in their new space within the Clinical Core lab. Chemistry saw the building, validation, and integration of the new Chemistry Automation line, and then the removal of the old automation line and upgrade and completion of their lab space. The APU continued to thrive in their new location in Med Inn, allowing the new Blood Bank space to finish construction and activate the new lab. The entire UH team saw hallways closed, endured power outages, and lived in close proximity to the sounds, interruptions, and dust that major construction projects bring.

Later phases include the new Cell Therapy Laboratory, the new Phlebotomy space, as well as spaces for the Education Program, administration functions and other support spaces. The entire project is scheduled to complete in Fall 2023.

Anatomic Pathology Case Volumes

Cardiovascular Case Volumes	FY18	FY19	FY20	FY21	FY22	1-YR	5-YR
Cardiovascular 1	--	--	--	--	120	--	--
Cardiovascular 2	--	--	--	--	226	--	--
David Gordon	5	166	217	445	209	-53.03%	4,080.00%
Total	**5**	**166**	**217**	**445**	**555**	**24.72%**	**11,000.00%**
Cytopathology Case Volumes							
FNA by Pathologist w/ ROSE[1]	164	183	142	134	114	-14.93%	-30.49%
FNA, No ROSE[1]	687	842	767	871	837	-3.90%	21.83%
FNA, w/ ROSE[1]	2,101	2,102	1,788	2,048	2,243	9.52%	6.76%
Gyn Case[1]	23,003	23,580	18,608	24,384	24,630	1.01%	7.07%
Non-Gyn Case	7,392	8,128	7,432	7,868	8,118	3.18%	9.82%
Total	**33,347**	**34,835**	**28,737**	**35,305**	**35,942**	**1.80%**	**7.78%**
Dermatopathology Case Volumes							
Derm In-House	16,327	15,979	13,470	15,733	15,038	-4.42%	-7.89%
Derm Outside	7,170	7,400	6,518	6,382	6,756	5.86%	-5.77%
MLabs Derm	10,398	9,748	7,549	7,979	8,644	8.33%	-16.87%
Total	**33,895**	**33,127**	**27,537**	**30,094**	**30,438**	**1.14%**	**-10.20%**
Hematopathology Case Volumes							
Hemepath In-House	1,939	2,301	2,657	3,669	3,598	-1.94%	85.56%
Hemepath Outside	2,604	2,707	2,347	2,400	2,712	13.00%	4.15%
Total	**4,543**	**5,008**	**5,004**	**6,069**	**6,310**	**3.97%**	**38.90%**
Neuropathology Case Volumes							
Muscle In-House	139	86	78	98	102	4.08%	-26.62%
Muscle Outside	203	266	218	189	196	3.70%	-3.45%
Neuro In-House	773	834	741	786	761	-3.18%	-1.55%
Neuro Outside	496	522	597	879	1,146	30.38%	131.05%
Total	**1,611**	**1,708**	**1,634**	**1,952**	**2,205**	**12.96%**	**36.87%**
Ophthalmic Case Volumes							
Ophthalmic In-House	1,311	1,455	1,367	1,397	1,462	4.65%	11.52%
Ophthalmic Outside	56	52	73	75	83	10.67%	48.21%
Total	**1,367**	**1,507**	**1,440**	**1,472**	**1,545**	**4.96%**	**13.02%**
Pediatric and Perinatal Pathology Case Volumes							
Fetal Exams	215	230	215	256	257	0.39%	19.53%

(continued)

Peds Autopsy	37	27	24	24	27	12.50%	-27.03%
Peds In-House	3,564	3,747	3,307	3,677	3,615	-1.69%	1.43%
Peds Outside	432	477	407	408	456	11.76%	5.56%
Placentas	2,071	2,148	1,894	1,825	2,149	17.75%	3.77%
Total	**6,319**	**6,629**	**5,847**	**6,190**	**6,504**	**5.07%**	**2.93%**
Renal Case Volumes							
Renal In-House	1,294	1,413	943	811	859	5.92%	-33.62%
Renal Outside	56	59	43	34	52	52.94%	-7.14%
Total	**1,350**	**1,472**	**986**	**845**	**911**	**7.81%**	**-32.52%**
Technical Only Case Volumes							
Technical Only	2,062	2,005	1,673	1,722	1,930	12.08%	-6.40%
Technical w/ Interpretation		160	460	399	285	-28.57%	
Total	**2,062**	**2,165**	**2,133**	**2,121**	**2,215**	**4.43%**	**7.42%**
Outside Case Volume							
Breast	1,765	1,737	1,541	1,509	1,767	17.10%	0.11%
Cardiac	13	20	21	24	15	-37.50%	15.38%
Cytology	1,372	1,196	1,192	1,076	1,223	13.66%	-10.86%
Dermatopathology	7,170	7,400	6,518	6,382	6,756	5.86%	-5.77%
Endocrinology	598	613	551	539	510	24.09%	25.31%
Gastrointestinal	5,088	5,220	5,043	5,107	5,548	8.61%	9.04%
Genitourinary	2,038	2,148	1,959	1,845	2,252	22.06%	10.50%
Gynecologic	1,480	1,696	1,571	1,520	1,734	14.08%	17.16%
Head & Neck	1,300	1,366	1,255	1,303	1,403	7.67%	7.92%
Hematopathology	2,604	2,707	2,347	2,400	2,712	13.00%	4.15%
InterDepartmental Consult	370	635	356	608	296	-51.32%	-20.00%
Misc. Outside Case	31	22	9	6	1	-83.33%	-96.77%
Muscle	14	33	29	22	34	54.55%	142.86%
Neuropathology	496	522	597	879	1,146	30.38%	131.05%
Ophthalmic	56	52	73	75	83	10.67%	48.21%
Pediatric	432	477	407	408	456	11.76%	5.56%
Pulmonary	2,971	3,184	2,712	2,564	2,962	15.52%	-0.30%
Renal	56	59	43	34	52	52.94%	-7.14%
Soft Tissue	1,507	1,630	1,481	1,696	1,830	7.90%	21.43%
Total	**29,361**	**30,717**	**27,705**	**27,997**	**30,925**	**10.45%**	**5.33%**

Table 1 : *Anatomic Pathology Case Volumes 2018-2022 (From pg. 8)*

Clinical Pathology Billed Test Volumes

	FY17	FY18	FY19	FY20	FY21	FY22	1-Yr	5-Yr
Clinical Chemistry and Toxicology								
Chemical Pathology	2,861,047	2,990,055	3,165,847	2,985,204	3,277,102	3,177,933	-3.0%	11.1%
Special Chemistry	642,556	650,105	714,738	649,436	771,761	816,337	5.8%	27.0%
Clinical Chemistry and Toxicology	3,503,603	3,640,160	3,880,585	3,634,640	4,048,863	3,994,270	-1.3%	14.0%
Transfusion Medicine								
Blood Bank Bone Marrow	1,155	1,118	1,034	1,490	1,353	1,426	5.4%	23.5%
MM Pathology Blood Bank	307,395	315,601	327,245	326,459	335,100	323,820	-3.4%	5.3%
Blood Procurement	61,994	64,254	66,414	59,056	66,279	60,800	-8.3%	-1.9%
Transfusion/Apheresis	1,804	1,965	2,008	2,132	1,238	2,015	62.8%	11.7%
Total	**372,348**	**382,938**	**396,701**	**389,137**	**403,970**	**388,061**	**-3.9%**	**4.2%**
Other Clinical Laboratories								
Path Hemo/Coag Unit UH	1,220,890	1,236,698	1,268,568	1,227,916	1,293,850	1,319,143	2.0%	8.0%
Flow Cytometry Lab	78,390	87,062	105,598	99,902	101,981	101,563	-0.4%	29.6%
Cytogenetics Lab	8,399	9,296	12,313	11,709	14,249	16,315	14.5%	94.2%
Histocompatibility	21,085	23,801	23,480	19,157	22,209	25,917	16.7%	22.9%
Microbiology & Virology	520,905	549,418	571,808	566,888	963,936	752,331	-22.0%	44.4%
Molecular Diagnostics	15,899	17,026	20,106	17,860	19,169	19,098	-0.4%	20.1%
Path Reference Tests	129,294	126,650	151,392	141,665	145,234	164,397	13.2%	27.1%
MCTP	2,487	1,355	393	248	283	549	94.0%	-77.9%
Total	**2,518,254**	**2,600,724**	**2,725,466**	**2,652,233**	**3,524,847**	**2,399,313**	**-31.9%**	**-4.7%**

Table 2 : *Clinical Pathology Billed Test Volumes (From pg. 18)*

Table 3 ***(Right):*** *Transfusion Medicine Number. (From pg. 22)*

Transfusion Medicine

Blood Bank Main Laboratory	FY17	FY18	FY19	FY20	FY21	FY22	Change
Red Blood Cells	30,905	32,004	33,065	31,040	34,340	31,838	-14%
Random/Pooled Platelets	6,009	6,080	5,880	51	--	--	--
Apheresis Platelets	10,120	10,648	11,000	13,640	16,193	15,992	-2%
Plasma	6,997	7,267	7,073	6,676	8,144	5,974	-31%
Cryoprecipitate	6,437	7,404	7,840	6,676	7,504	7,090	-6%
Total Components Transfused	**60,462**	**63,403**	**64,858**	**58,475**	**66,181**	**60,894**	**-8%**
Immunohematology Reference Lab							
Antibody Identifications	1,376	1,240	1,153	1,516	1,685	1,613	-4%
ABO Resolution	111	187	233	312	258	262	2%
BMT	203	320	319	284	298	246	-19%
Eulates	227	215	255	265	326	226	-36%
Adsorptions	464	319	402	547	318	388	20%
Titers	324	295	477	484	616	568	-5%
Special Antigen Typing	6,314	5,896	6,137	6,384	7,097	6,948	-2%
Total Activity*	**9,861**	**9,097**	**10,624**	**11,402**	**12,619**	**11920**	**-6%**
**Includes procedures not listed above*							
Cellular Therapies Laboratory							
Collections Processed	452	427	452	454	485	414	-16%
Bags Frozen	718	619	608	703	809	637	-24%
Transplants, Autologous	122	136	130	113	130	119	-9%
Transplants, Allogeneic	36	32	54	43	51	47	-8%
Transplants, Unrelated	44	67	75	64	58	57	-2%
CAR-T Products	4	12	54	24	26	19	-31%
Total Transplants	**202**	**235**	**259**	**220**	**239**	**223**	**-7%**
Apheresis Service							
Therapeutic Plasmapheresis	1,207	1,220	1,310	1,416	1,334	1,302	-3%
HPC Collections	370	345	308	346	347	331	-5%
Donor Pre-Evaluations	219	255	308	236	202	253	22%
LDL Apheresis	89	106	94	95	62	76	20%
RBC Exchange	103	112	170	175	199	244	20%
CART-T Collections	4	12	33	20	40	44	10%
Total Procedures	**2,024**	**2,074**	**2,206**	**2,288**	**2,184**	**2,250**	**3%**

Faculty Awards 2021-2022

Faculty	Award Name	Organization
Arul Chinnaiyan, MD, PhD	• Sjöberg Prize • Science of Oncology Award • Lifetime Achievement Award • Catchment Area Cancers Award	• Royal Swedish Academy of Sciences • American Society of Clinical Oncology • American Society of Indian Cancer Science Researcher • Rogel Cancer Center
Kathleen Cho, MD	2021 Rosalind Franklin Excellence in Ovarian Cancer Research Prize	Ovarian Cancer Research Alliance
Tomasz Cierpicki, PhD	2022 Rogel Scholar	Rogel Cancer Center
Jolanta Grembecka, PhD	Richard and Susan Rogel Professor in Cancer Therapeutics	University of Michigan
Celina Kleer, MD	2022 Rogel Scholar	Rogel Cancer Center
Rohit Mehra, MD	GUPS Award for Excellence in Uropathology Research	Genitourinary Pathology Society
Abhijit Parolia, MD	• Junior Faculty Award • 2022 Harold M. Weintraub Graduate Student Award • 2021 Young Investigator Award	• American Society of Indian Cancer Science Researcher • Michigan Medicine • Prostate Cancer Foundation
Rajesh Rao, MD	Career Advancement Award	Research to Prevent Blindness
Lanbo Xiao, PhD	• Career Advancement Award • 2022 Young Investigator Award	• Michigan Prostate SPORE • Prostate Cancer Foundation

Table 5-8 *(Above)*: *List of Faculty Awards received 2021-2022. (From pg. 70) Followed by New National Leadership Positions and Leadership Appointment from pg. 70.*

Table 9 *(Right)*: *Full list of Departmental and Institutional Committee Service.*

New National Leadership Positions - 2022

Faculty	Role	Organization
Kristina Davis, MD	Co-Chair, Transplant Diagnostics Community of Practice	American Society of Transplantation
L. Priya Kunju, MD	Board of Directors	United States and Canadian Academy of Pathology
Zaneta Nikolovska-Coleska, PhD	• President • Member	• Interational Chemical Biology Society • Therapeutics Pipeline Advisory Committee, Ontario Institute for Cancer Research
Liron Pantanowitz, MD, PhD, MPH	Vice President	American Society of Cytopathology
Charles Parkos, MD, PhD	Board of Directors	Federation of American Societies for Experimental Biology
Lina Shao, PhD	Chair	American College of Molecular Genomics Lab QA Committee and Cytogenetics Subcommittee
Jiaqi Shi, MD, PhD	Associate Editor	Frontiers in Oncology

New Department Leadership Appointments

Faculty	Role	Area/Specialty
Sara Abbott, MD	Assistant Residency Director	Anatomic Pathology
Darius Amjadi, MD, JD, FCAP	Lead	Diagnostics Integrated Clinical Community for AAVAHS
Ul Balis, MD	Chief Medical Advisor	Massachusetts Clear Bill of Health/ COVID Reporting
Kathleen Cho, MD	Interim Director	Pathology Education Programs
David Gordon, MD	Director of Faculty Programs	Office of Health Equity and Inclusion, University of Michigan Medical School
Sean Li, MD, PhD	Residency Program Director	UM Pathology
David Manthei, MD, PhD	• Assistant Residency Director • Section Director	• Clinical Pathology • Clinical Immunology and Special Chemistry Laboratory
Rohit Mehra, MD	Member	Genitourinary Pathology Society Education Committee
Aaron Udager, MD, PhD	Associate Director	Pathology PSTP Training Program
Riccardo Valdez, MD	Ambulatory Care Clinical Chief for Pathology	Pathology PSTP Training Program

Departmental and Institutional Committee Service

ACGME Self-Study Committee	Cytopathology Director Faculty Search Committee	Pathology Relocation and Renovation (PRR) Project Resident Representative
Advisory Committee on Promotions and Tenure	Histocompatibility Director Search Committee	(PRR) Executive Steering Committee
Advisory Council for Patient and Family Centered Pathology Care	Histology Committee	(PRR) Project Committee
Blood Transfusion Committee	House Officer Quality and Safety Council	Pathology Social Media Team Member
Clinical Pathology Director Search Committee	Laboratory Communications Committee	Phlebotomy Working Group
Clinical Pathology Operations Director Search Committee	Laboratory Formulary Committee	Program Evaluation Committee
Clinical Pathology Operations Committee	MLabs Executive Committee	Search Committee for Anatomic Pathology Director
Clinical Pathology Quality Assurance Committee	Pathology Diversity, Equity, and Inclusion Committee	Search Committee for HLA and Blood Bank Associate Director
Clinical Pathology Symposium Planning Committee	Pathology Document Control Vendor Selection Committee	Search Committee for Toxicology/Chemistry Faculty
Cytogenetics Faculty Search Committee	Pathology Executive Committee	

Professional Society Membership and Engagement

A. James French Society of Pathologists	American Society of Dermatopathology	International Society of Urological Pathology
Academy of Clinical Laboratory Physicians and Scientists	American Society for Histocompatibility and Immunogenetics	Michigan Association of Medical Examiners
American Academy of Family Physicians	American Society of Hematology	Michigan Society of Pathologists
American Association for Clinical Chemistry	American Society for Microbiology	Michigan State Medical Society
American Association of Blood Banks	Association for Molecular Pathology	National Association of Medical Examiners
American Association for Cancer Research	College of American Pathologists and Residents' Forum	Pan American Society for Clinical Virology
American Association for the Advancement of Science	Hans Popper Hematopathology Society	Rodger C. Haggitt Gastrointestinal Pathology Society
American Board of Pathology	Infectious Diseases Society of America	Society for Hematopathology
American Medical Association, and Resident & Fellow Section Delegates	International Association of Therapeutic Drug Monitoring and Clinical Toxicology	South Central Association for Clinical Microbiology
American Society for Bioethics and Humanities (ASBH)	International Society of Bone and Soft Tissue Pathology	United States and Canadian Academy of Pathologists, and Resident Advisory Subcommittee and Ambassadors
American Society for Clinical Oncology	International Society of Gynecological Pathologists	Washtenaw County Medical Society
American Society for Clinical Pathology, and Resident Representatives, Resident Council and Chair of the Resident Council	International Society for Heart and Lung Transplantation	
American Society for Clinical Oncology	International Society of Laboratory Hematology	

Invention Reports

Title	Inventors
Transepidermal Water Loss as an Anaphylaxis Monitoring Tool	Bridgette Kaul, Charles Schuler IV, Cristyn Zettel, James Baker Jr., Nicholas Lukacs
Epithelial-Mesenchymal Transition-based Gene Expression Signature for Kidney Cancer	Aaron Udager, Randy Vince Jr, Simpa Salami, Srinivas Nallandhighal
Kidney Cancer Gene Expression Signature	Marcin Cieslik, Rohit Mehra, Simpa Salami, Srinivas Nallandhighal, Todd Morgan
Diagnostic Biomarkers of Food Allergy and Anaphylaxis	Ankit Sharma, Simon Hogan, Sunil Tomar
Small Molecule Inhibitors of Pax2/5/8 Transcription Activation	Gregory Dressler, Shayna Bradford
Using AI Tools to Evaluate Genitourinary Tumors	Liron Pantanowitz, Rohit Mehra
Development of Primary Endometrial and Ovarian Cancer Cell Lines and Patient-Derived Xenografts	Analisa DiFeo, Michele Cusato
Discovery of a Highly Potent and Selective Dual PROTAC Degrader of CDK12 and CDK13	Arul Chinnaiyan, Xiaoju Wang, Yu Chang
Maresin 2 Encapsulated in Nanoparticles for use in Promoting Wound Repair	Aaron Morris, Asma Nusrat, Lonnie Shea, Miguel Quiros Quesada, Ryan Pearson
MSFragger-Core	Aleksey Nesvizhskiy, Andy Kong, Fengchao Yu
MSFragger-Glyco	Aleksey Nesvizhskiy, Andy Kong, Daniel Polasky, Fengchao Yu
IonQuant	Aleksey Nesvizhskiy, Fengchao Yu
MSFragger-LOS	Aleksey Nesvizhskiy, Andy Kong, Fengchao Yu
MSFragger-DIA	Aleksey Nesvizhskiy, Andy Kong, Fengchao Yu
Identification of DL78 as Targeted Anti-Mitotic Agent that Regulates Myc and can be used as a Therapeutic Target for Ovarian Cancer	Analisa DiFeo, Andrew White, Jessica McAnulty, Pil Lee
2-Hydroxybenzoic Acid Derivatives as Inhibitors and Degraders of Sirtuins	David Lombard, Nouri Neamati, Surinder Kumar, Yanghan Liu
Human I1061T NPC1 mice	Andrew Lieberman, Mark Schultz
Discovery of a highly potent and selective dual PROTAC degrader of CDK12 and CDK13 and their derivatives	Arul Chinnaiyan, Jean Tien, Xiaoju Wang, Yu Chang

Ongoing Clinical Trials/Studies Supported by MI-ONCOSEQ / 2022

NCT ID	Clinical Trial	PI	Patients	Sites
NCT05038332	UMCC 2021.046	Alva	-	University of Michigan
NCT04140162	UMCC 2018.056	Heath	11	University of Michigan, Karmanos, University of Rochester, University of Texas Southwestern
NCT00261456	UMCC 2018.050	Alva	56	University of Michigan, Memorial Sloan Kettering, Johns Hopkins, Washington University St Louis, UCSF
NCT03456804	UMCC 2019.031	Gadgeel	10	Karmanos
NCT03287050	UMCC 2017.069	Chinnaiyan	6	University of Michigan
NCT03242915	UMCC 2017.057	Alva	33	University of Michigan, Karmanos, Montefiore Medical Center, Rush University, Henry Ford, Cleveland Clinic
SU2C/PCF	VA Multisite	Sahai	254	University of Washington, University of Michigan, Karmanos, Royal Marsden Hospital
POPCAP-VA/PCF	Multisite	Jackson	217	Ann Arbor VA, Bay Pines VA, Jesse Brown VA, James Haley VA
NCT03639935	UMCC 2018.044	Reichert	30	University of Michigan, Vanderbilt University
NCT04194554	UMCC 2019.117	Alva	60	University of Michigan
NCT04748042	UMCC 2020.080	Sahai	9	University of Michigan
NCT03300505	UMCC 2017.055	Sahai	9	University of Michigan
NCT04497038	UMCC 2020.007	Sahai	2	University of Michigan
NCT03785873	UMCC 2018.101	Sahai	34	University of Michigan Rogel Cancer Center, Cancer and Hematology Centers of Western Michigan, University of Utah, Virginia Mason, University of Wisconsin
NCT04203160	UMCC 2019.116	Sahai	68	University of Arizona Cancer Center, Northwestern University, Lurie Comprehensive Cancer Center, University of Michigan Rogel Cancer Center, Atlantic Health System, University Hospitals - Seidman Cancer Center, Vanderbilt-Ingram Cancer Center, UT Southwestern -- Simmons Comprehensive Cancer Center, Fred Hutch/University of Washington Cancer Consortium, University of Wisconsin - Carbone Cancer Center

Table 10-11 *(Above)*: *Inventions Report continued from pg. 44. Then the Ongoing Clinical Trails/Studies Supported by MI-ONCOSEQ from pg. 31.*

Graduate Student Thesis Defense and Current Positions

Name	Defense Date	Thesis Title	Mentor(s)	Current position	Current Company
Xiaofang Shi	*February 23, 2022*	*Regulation of mTOR Complexes in Long-Lived Growth Hormone Receptor Knockout and Snell Dwarf Mice*	Richard Miller	Immunogenicity Scientist	Amgen

Table 12 (right): *Graduate Thesis Defenses 2021-2022 mentioned on pg. 54.*

Years of Service Recognition - 2022

10 Years		
Turquessa Brown-Krajewski	Sharon Kerr	Misty Sayar
Kelly Columbus	Christopher Lenton	Elsie Sedayao
Michele Cusato	Annette Leonard	Debra Sexton
Amy Drouillard	Emily Manion	William Sherman
Nancy Fritzemeier	Shannon McClintock	Gregory Simmons
Matthew Heilbronn	Susan Papa	Andrea Skiff
Shirley Hoffman	Krupa Patel	Irina Snell
Amanda Howard	Erica Rabban	Andrew Szczembara
Michele Hunter-Clark	Andrew Rasky	Cynthia Wang

20 Years		
Jennifer D'Agostino	Yelena Kleyman	Jason Schwartzenberger
Kevin Forbing	Jianhong Liu	Teresa Thomas
Maria Gonzalez-Martinez	Kimberly Meekins	Christopher White
Chia-Mei Huang	Melissa Provost	Wei Zhao
Theotis Jones	Peggy Rost	

30 Years		40 Years
Brian Englehart	Laura Gable	Peggy Otto
Michelle Herrst		

Above and Beyond Award Recipients

Anatomic Pathology		
Muntajib Alhaq	Danielle Hood	Threase Nickerson
Kelli Farhat	Kathryn Kearns	Sally Smith
Nancy Fritzemeier	Eric LaPres	Alexis Snyder
Casey Hollier	Cassandra Lee	Cortney Sullivan
Team Awards		
Histology	Cytology Labs	IPOX
Clinical Pathology		
Tierra Banks	Zachary Harmon	Alpa Patel
Jacquelyn Bates	Matthew Heilbronn	Yusuf Peaks
Ryan Boughton	Emily Hilliker	Hannah Riggs
Brenda Church	Christopher Lenton	Jodi Smiley
Larry Clayton	Sheridan Mattson	Rita Spiegelberg
Kayci Drake	Michele McGee	Renee Stoklosa
Marche Ellis	Santana McIntyre	Todd Teifer
Bradley Exell	Michelle Merkel	Juan Torres
Christine Falkiewicz	Laverne Miner	Katherine Turner
Michelle Garrasi	Brandon Newell	Eric Vasbinder
Khaleel Geheim	Tifani Nicole	Dawn Wright
Tina Gray	Kelly O'Brien	Hong Xiao
Joanne Guan	Andrea Parkinson	
Team Awards		
Specimen Processing Team: Entire Afternoon/Midnight Shifts	Cancer Center Blood Draw Team	

Table 13-14 ***(Above):*** *Years of Recognition and Above and Beyond Award Recipients (From pg. 71).*
Table 15 ***(Right)*****:** *Retired Faculty and Staff 2021-2022 (From pg. 71).*

(Continued)

Pathology Informatics		
Christine Gaunt	William Hubbard	Sravan Kilaru
Andrea Hawk	Joshua Jacques	Brent Temple
Ivan Holland	Jeremy Kendzorski	
Finance & Administration		
Yvonne Beadle	Regina Ferguson	Angela Suliman
Ashley Boguslaski	Jennifer Mattison	Michal Warner
Stephanie Edwards	Catherine Niemiec	
Division of Quality & Health Improvement		
Keisha Beck	Christine Gaunt	Eleanor Mills
Michelle Garrasi	Tina Gray	Eric Vasbinder
Team Awards		
Launch of New Tests Development Process		
Michigan Medicine Laboratories		
Melina Adler	Jacquelyn Goodman	

Retired 2021-2022

Name	Job Title	Date	Years
Laura Jean Smith	Medical Technologist, Hemo/Coag Unit UH	*July 2021*	31
Kathleen A. Williams	Laboratory Technician, Necropsy Pathology	*July 2021*	27
Dawn M. Lossos	Laboratory Technician, Chemical Pathology	*July 2021*	33
Denise M. Ziemba	Medical Technologist Spec, Hemo/Coag Unit, UH	*August 2021*	20
Evelyn Wright	Phlebotomist Specialist, Satellite Support	*August 2021*	18
Annette T. Rush	Phlebotomist Specialist, Out-Patient Phlebotomy	*October 2021*	43
Charlene F. Reppuhn	Phlebotomist, Out-Patient Phlebotomy	*October 2021*	16
Robin G. Kunkel	Research Lab Specialist Lead	*October 2021*	41
Cynthia L. Schuholz	Phlebotomist Specialist, Satellite Support	*December 2021*	23
Joyce A. Seleska	Patient Care Tech Associate, Histocompatibility	*December 2021*	21
Mary M. Bahrou	Allied Health Associate Supr, In-Patient Phlebotomy	*January 2022*	17
Alan J. Machcinski	Business Systems Analyst Inter, Pathology Informatics	*January 2022*	47
Alain J. Dudus	Medical Technologist, Microbiology	*February 2022*	32
Nancy Parker	Admin Manager Assoc Healthcare, Clinical Lab Administration	*March 2022*	16
Susette R. Miller	Business Systems Analyst Inter, Pathology Informatics	*May 2022*	18

Annual Report compiled by Pathology Communications: Lynn McCain, Editor; Anastazia Hartman, Editor; Alma Hearin. Editor; Brent Temple, Design and Layout; and Camren Clouthier, Photography. A special thanks to the many contributors who provided the content for this report.

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