UCLA PATHOLOGY AND LABORATORY MEDICINE
2016 Annual Report
INTRODUCTION
Jonathan Braun, MD, PhD

CLINICAL SERVICES
1 Department Taking Important Strides to Fulfill Digitization’s Vast Promise
4 International Telepathology Partnership Continues to Flourish, Bringing Benefits to Both Sides
5 Move Toward Digital Pathology Helping to Streamline Molecular Diagnostics
6 Pathology a Key Player in Campus-Wide Precision Medicine Initiative
7 Superbug Outbreak Illustrates Value of Clinical Microbiology Lab
8 Successful Implementation of New Laboratory Information System a Team Effort

RESEARCH ENTERPRISE
10 Studies Contribute to Better Understanding of Lipid Metabolism
12 Stem Cell Studies Could Bring Major Benefits to Bone Marrow Transplant Patients
13 Novel Computational Methods Contribute to Better Understanding of Genetic Risk for Common Diseases
14 Discovery Could Lead to New Treatment for Cardiac Arrhythmia

EDUCATION
15 Peer Anatomy Tutoring Program Enhances Medical Students’ Knowledge of Key Concepts
17 Ensuring Point-Of-Care Testing Meets Highest Standards
18 New Hematologic Malignancy Sequencing Test Provides Important Training Experience
19 Resident “Superusers” Help Shape UCLA’s New Laboratory Information System

RESEARCH SERVICES
20 Core Facilities Play Critical Role for Campus Through Research Support and Education
22 Multiplex Immunofluorescence Offers UCLA Researchers Major Benefits Over Traditional Immunohistochemistry
23 UCLA Immunogenetics Center Applies New Technologies to Improve Outcomes for Transplant Patients
25 UIC Continues to Lead the Way in Standardizing Tests for Organ Transplantation

DEPARTMENT IN DEPTH
27 Metrics
Pathology and Laboratory Medicine in the Community
28 UCLA Health Path & Lab Med Volunteers Reach Out to the People Who Need Our Services the Most.
28 National Medical Lab Professionals Week
28 The Social Justice Learning Institute
29 Movember Health Fair
29 City of Angels Fun Ride Presented by Volkswagen
29 Greater Los Angeles County Heart Walk

INSIDE BACK COVER:
Opportunities for Giving

EDITORS: Justine Pomakian
WRITERS: Dan Gordon, Gordon Editorial, Inc.
CONTRIBUTING WRITERS: Khanh Andrews, Jonathan Braun, MD, PhD, Omai Garner, PhD, Linda Goss, Peter Heumann, Nathan Okawa.

PHOTOGRAPHY: Margaret Sison Photography
COVER ILLUSTRATION AND INTERIOR DETAILS: Andy Potts
DESIGN: Landesmann Design
AMONG THE NEW and unexpected in our department this year are all the dragons. As children, we each learn about dragons. In my parent’s family, dragons were violent flying dinosaurs who terrorized medieval villages until dispatched by fire-retardant knights. In my children’s family, they are messy under-bed companions who eat snacks and play with toys. And some of my friends enjoy dragons that play the game of thrones. But for so many more, dragons mean something entirely different—the symbol of a worthy life, and the power and good fortune that sometimes accompanies it.

In this annual report, you will read about what people do in our department. Innovating in digital pathology and telemedicine to create better ways to deliver clinical care for our patients across Los Angeles, California, and internationally. Deploying genomic medicine tools for diagnosis and treatment choice in cancer and chronic diseases, and to uncover and safely manage the historic “superbug” epidemic. Discoveries that open new paths in lipid diseases, stem cell therapy, cardiac arrhythmia; and tools to understand and address the genetic health disparities from common diseases to transplant management. And from Care Harbor the Social Justice Learning Institute, the commitment of so many in our department to serve the community around us.

There is a story about Zhang Sengyou, an artist from the Southern and Northern Dynasties (c. AD 500) famous for painting a wondrous dragon. But the image was without eyes, because with these final dots, the dragons would emerge and fly into the world. Like many in our department, in the year ahead take the chance and paint the eyes of your dragon.

画龙点睛

Jonathan Braun

Right: Zhang Sengyou, Five Planets and Twenty-Eight Constellations, Osaka City Museum of Fine Arts
The digitization of pathology slides has the potential to fundamentally transform the pathologist’s workstation and workflows, resulting in widespread and profound benefits, according to W. Dean Wallace, MD, associate professor and director of informatics for anatomic pathology in the UCLA Department of Pathology & Laboratory Medicine, which in recent years has launched a number of initiatives to capitalize on that promise.

Among the many advantages of digital slides is their ability to be readily accessed through any desktop computer or mobile device, Dr. Wallace notes. Within the department, integration of the whole slide image management system, eSlide Manager, with the laboratory information system, Beaker, allows for digitized scanned slides to be automatically filed and immediately accessible to anyone in the laboratory. This enables all laboratory personnel within the department to review and utilize the slides at any time and eliminates the need to physically transport the slides, as well as the possibility of slide misplacement.

Dr. Wallace says this development could enable increases in departmental workload and individual productivity. Ultimately, improvements in workflows are likely to lead to faster turnaround times for rendering a diagnosis. “Digitizing the slides will greatly improve internal department workflows, since the ability for anyone to access slides immediately will markedly reduce conference preparation time and will allow for much easier review of older cases to compare with current cases,” Dr. Wallace explains.

Expanded digitization of the histology and immunohistochemistry labs will have far-reaching effects in pathology, touching on all service lines in the department, Dr. Wallace adds. He notes that the availability of scanning digital pathology platforms in histology and the frozen section suite will allow diagnostic support from specialist pathologists during
Intraoperative consultations, as well as after hours and on weekends, “The current workflow requires a pathologist to physically be on site in the frozen section suite to review the slides,” Dr. Wallace says. “By utilizing telepathology technology, we can project that image to anyone in the department at any location. This will enable improved diagnostic interpretations – and better care – for our surgical patients.”

In a similar innovative initiative, the UCLA departments of pathology and radiology have collaborated on an informatics project that takes advantage of image digitization through a novel and sophisticated system that extracts information and images from multiple pathology and radiology reports and combines them into a single reporting platform. RadPath, conceived of by Dr. Scott Binder, senior vice-chair of pathology, and Dr. Dieter Enzmann, chair of radiology, was designed by Dr. Wallace and Corey Arnold, PhD, assistant professor in the Department of Radiological Sciences. The RadPath report utilized lung cancer as the initial case but has since expanded to include prostate cancer, and will soon incorporate liver and breast disease. It has been proclaimed by many authorities in the field of pathology informatics as the most sophisticated biopsy report system in the world, leading to numerous speaking opportunities and increasing the exposure of the department’s informatics activities.

Digitizing pathology allows pathology slides and images to be seen by pathologists almost anywhere in the world, and enables UCLA pathology faculty to extend the department’s mission well beyond Westwood and ultimately increase the scope and size of the department.

UCLA’s international telepathology service began in 2011 with a relationship with Second Affiliated Hospital of Zhejiang University in Hangzhou, China; since that time, the department has provided more than 2,000 telepathology consultations. Through the work of Dr. Jianyu Rao and Dr. Serge Alexanian, the international telepathology service has continued to grow, with new clients in Beijing and Shanghai and more being developed. In addition, through funding provided by California Proposition 1D, the department has overseen the creation of the California telepathology network, which was established to enable expert pathology consultations to be available in underserved areas of the state.

Dr. Wallace notes that digitized slides are also amenable to image analysis algorithms that can assist the pathologist’s interpretation and add to the content of the pathology report. “By utilizing specialized image analysis algorithms, we will be able to provide much more information in a more objective fashion,” Dr. Wallace says. “This will increase the value of the pathology report to each patient’s healthcare record.”

Digitization will continue to play a larger role in the future. Dr. Wallace notes that with FDA approval for primary pathologic evaluation expected by 2017, the digitization of glass slides in the histology laboratory will facilitate a transformation from the microscope to the computer workstation as the primary clinical setting for the pathologist.

“By utilizing telepathology technology, we can project that image to anyone in the department at any location. This will enable improved diagnostic interpretations – and better care – for our surgical patients.” – W. Dean Wallace, MD
AN INTERNATIONAL telepathology partnership that started six years ago with a major academic medical institution in China has blossomed to the point that UCLA has become a premier international telepathology center in the United States.

Telepathology employs state-of-the-art digital scanners and telecommunications technology to transfer high-quality pathology images from around the world for the purposes of diagnosis, education and research. For the UCLA Department of Pathology & Laboratory Medicine, the international telepathology program began in 2010 as part of a broader collaboration between UCLA and Second Affiliated Hospital at Zhejiang University (SAHZU), China. Through that agreement, UCLA agreed to provide second-opinion pathology diagnosis for cases referred to SAHZU. More than 2,000 consultations have occurred in the six years since, one of the largest collaborations between a U.S. and Chinese academic medical institution.

But Jianyu Rao, MD, professor and director of international telepathology for the department, says the success of the partnership goes well beyond the number of cases. “Both institutions are benefiting in many ways,” Dr. Rao says. “We have helped to train Chinese pathologists and clinicians, and to bring in the concept of multidisciplinary care, especially in the area of cancer. And at UCLA we have gained a great deal by getting the opportunity to tackle unusual cases that we would otherwise see only in textbooks, as well as through academic collaborations with SAHZU – for example, in establishing a large database in thyroid cancer – that will stimulate important research.”

Serge Alexanian, MD, director of special operations, co-director of the pathology clinical observership program, and associate director of international telepathology for the department, notes that given the interest in the cases, regular teleconference tumor boards are held between the two sites during which education is provided by UCLA pathologists as the cases are being reviewed. “This is much more than a transactional business relationship,” Dr. Alexanian says. “We are providing an academic service that uplifts not only the level of patient care, but also the caliber of medical education throughout the region.”

While the SAHZU continues to flourish, UCLA has recently entered into several new partnerships in China, with telepathology again taking the lead. Among other things, Dr. Rao notes, this is helping to address the shortage of pathologists in China. In addition, the success of the initial collaboration has led to the Chinese National Health and Family Planning Commission designating SAHZU as one of the three centers of excellence in China.

“Many people feel that telepathology is the future in pathology – and that more diagnostics will increasingly be rendered this way, both internationally and domestically,” Dr. Alexanian says. “We are actively working with the largest and most innovative telepathology providers on the next generation of scanners and workflows so that we can continue to push this exciting field forward.”

MORE THAN 2,000 CONSULTATIONS HAVE OCCURRED IN THE SIX YEARS SINCE, ONE OF THE LARGEST COLLABORATIONS BETWEEN A U.S. AND CHINESE ACADEMIC MEDICAL INSTITUTION.
As part of the UCLA Department of Pathology & Laboratory Medicine’s continuing efforts to leverage the benefits offered by digital pathology, the department is beginning to use the technology to streamline molecular diagnostics.

In the Molecular Diagnostics Laboratory headed by Wayne Grody, MD, PhD, tissue-based oncology testing now involves digitally scanned, or whole-slide, images. “For pre-testing tissue review, the histology lab has always sent us an H&E-stained glass slide along with the unstained slides to serve as a reference so that we can be confident we have sufficient tissue and sufficient tumor before testing,” explains Rena Xian, MD, assistant professor in the department and a member of the lab’s faculty. “But for most cases, by having a digitally scanned image of the slide available, we can eliminate as much as two days from the turnaround time for molecular testing.”

Dr. Xian notes that the lab is also exploring a second area of digital pathology, laser capture micro-dissection, in which a laser attached to a microscope is used to isolate specific cells or groups of cells of interest, cut them out of the physical slide, and then deposit them into a DNA isolation tube. “This enables us to input a pure population of tumor cells, and allows us to test tissue that would have previously been deemed to have insufficient tumor since this method allows us to achieve higher recovery of tumor DNA,” Dr. Xian says.

Whether it’s using the whole-slide image to shorten turnaround time so that patients can get appropriate therapy sooner; allowing testing of tissues that previously would have been inadequate; or increasing the sensitivity of the test, Dr. Xian says, “there is great potential in digital molecular pathology being used to improve patient care.”

(L to R): Dr. Thomas Lee, Dr. Rena Xian, Cora Au
Pathology is central to this paradigm shift, Dr. Binder notes. It is where the tumors are stored; the diagnoses are made; and sequencing and other testing is conducted to characterize the patient’s disease, guiding treatment decisions as well as the research in pursuit of new, tailored drugs. “The point is to personalize the therapy, and pathology is how we open the door to precision medicine through these complex tests,” Dr. Binder says.

The UCLA Health system and David Geffen School of Medicine at UCLA have announced that a new institute for precision medicine will be developed to coordinate precision and genome medicine activities on the campus. Dr. Daniel Geschwind is leading the multidisciplinary effort as senior associate dean and associate vice chancellor of precision medicine, and in recognition of pathology’s key role in the success of the initiative, he has asked Dr. Binder to play a leadership role on patient-delivery issues and a second member of the pathology department’s faculty, Dr. Stanley Nelson, to play a leadership role for technology issues. “This will be a comprehensive and systematic approach involving a wide variety of experts and a dynamic interface between research and clinical work,” Dr. Binder says.
The ingenuity of two postdoctoral fellows who employed the sophisticated technologies of the UCLA Department of Pathology & Laboratory Medicine’s clinical microbiology lab was integral to the ability of the UCLA Health system to identify and take action against an outbreak of a “superbug” at Ronald Reagan UCLA Medical Center in late 2014 and early 2015.

The clinical microbiology lab headed by Romney Humphries, PhD, worked closely with the hospital epidemiology team to identify the culprit behind a cluster of carbapenem-resistant Enterobacteriaceae (CRE) bacterial infections that were resistant to all available antimicrobial drugs. Combining molecular microbiology studies with the hospital’s epidemiology findings made it apparent to the lab members that these bugs were being spread by two duodenoscopes used for an advanced endoscopic procedure.

The role of the clinical microbiology lab includes performing diagnostic testing for patients as well as supporting the activities of the hospital epidemiology team, through rapid recognition of clusters of unusual microbes among patients in the hospital and community.

Dr. Humphries is quick to credit two clinical microbiology fellows in her lab – Peera Hemarajata, MD, PhD, and Shangxin Yang, PhD – with discovering the outbreak. “They were instrumental in identifying this unusual organism and then developing a test that could rapidly identify it in clinical cultures,” Dr. Humphries says. “They were able to use sophisticated molecular technologies such as whole-genome sequencing, as well as developing a novel molecular technique, to track the outbreak. These are methods other clinical labs would not have been able to develop and use so quickly.”

Drs. Hemarajata and Yang worked tirelessly with the cutting-edge techniques – even giving up their Thanksgiving holiday – to identify the problem. “One of the strengths of UCLA’s clinical microbiology lab is that we really care about what we do, and we are vigilant in using the protocols we have in place to detect abnormalities in the trends of the organisms we see,” says Dr. Hemarajata.

The team’s identification of the duodenoscopes as contributing to the spread of CRE led to recalls by the U.S. Food and Drug Administration as well as Congressional discussions aiming to prevent future outbreaks. “This issue of antibiotic-resistant superbugs is a major public health problem,” says Dr. Yang. “Our ability to discover this outbreak shows the value of the research infrastructure that Dr. Humphries has been building.”

EXPLORE Clinical Microbiology at http://pathology.ucla.edu/clinical-microbiology
SUCCESSFUL IMPLEMENTATION OF NEW LABORATORY INFORMATION SYSTEM A TEAM EFFORT

As a trained clinical lab scientist who has spent years working at the bench, C.K. Or is well versed in the complexities of the laboratory. But C.K. also took time away from the lab, spending more than 20 years as an IT specialist with a focus on laboratory information systems before returning to his roots. In his current position as program manager, clinical labs in the UCLA Department of Pathology & Laboratory Medicine, C.K. serves as the liaison between the lab and the hospital IT team, helping to coordinate implementation of Beaker – the new laboratory information system designed to integrate seamlessly with CareConnect, UCLA’s electronic medical record system.

To me, C.K. is a hero for his work with Beaker," says Thomas Drake, MD, professor and vice-chair for informatics in the department, who helped to oversee implementation of the clinical pathology aspects of Beaker. “Most people on the laboratory side know what they have to do to get their job done, but have limited understanding of the intricacies of the information systems. And conversely, most people on the IT side don’t have the clinical laboratory background. CK was essential to Beaker implementation because he could be accepted as a bona fide colleague by both sides, and so he was able to serve as a bridge in communicating the needs, challenges, and concerns from the laboratory to the Beaker team, and vice versa.”

For many years, the department’s anatomic and clinical components have functioned with various laboratory information systems. But Beaker is different – fully integrated and in sync with UCLA’s electronic medical record system for all laboratory functions, including placing orders, collecting and tracking specimens, testing, and reporting results.

“Beaker installation was an enormous project that involved reconfiguring almost every aspect of the department,” says W. Dean Wallace, MD, associate professor and director of informatics for anatomic pathology. “It took many months, thousands of hours and hundreds of people, some of whom went well beyond the call of duty to make it work.” In addition to C.K., Dr. Wallace points to the indispensable contributions of his counterpart on the anatomic pathology side of the department, Greg Hohman. “At the risk of overlooking many, many people who contributed many, many hours, I would also like to acknowledge Greg Hohman for his tireless efforts and near omnipresence,” Dr. Wallace says. “His expertise with both IT and AP operations really helped cover gaps and prevent problems before they arose.”

Dr. Steven Hart, chief of pathology and medical director of clinical laboratories at UCLA Medical Center, Santa Monica, who played a major role in helping to oversee implementa-
tion of Beaker, adds that “because Beaker is so integrated with CareConnect and ordering of AP tests has shifted from paper to electronic ordering by clinicians, we have had to work very closely with colleagues outside of our department, including physician and nursing informaticists, to develop ordering workflows that work for both clinicians and pathology. The work is ongoing and we will probably always be improving the process as time goes on.”

An integrated computer system brings significant operational and technical efficiencies, Dr. Drake notes. Besides the convenience of having all data easily retrievable in a central location, information can be shared between anatomical and clinical pathology, supporting a broader trend toward closer collaboration.

The effort involved in implementing the new system also yielded social benefits. “People in different parts of the laboratory tend to work within their own sphere, but this process brought everyone together,” Dr. Drake says. “And maybe even more important, it brought those of us in the laboratory together with the clinical physician services, the nursing services, and others in a way I have never seen. We are going to work hard to make sure that continues beyond the Beaker implementation, because the more communication you have across the services, the better.”

C.K. spent more than two years immersed in working with the hospital team and department colleagues on the implementation of Beaker, which went live last March. It wasn’t easy, but he has no regrets. “The reason I went from IT back to the lab is I see IT as a tool with the potential to make a huge impact on the laboratory operation, and I wanted to be involved in helping to fulfill that potential,” C.K. says. “It is gratifying to see that we are headed in the right direction to accomplish that.”

Opposite page: Dr. Thomas Drake
Below (L to R): C.K. Or, Gregory Hohman, Dr. Steven Hart, Dr. W. Dean Wallace

EXPLORE the UCLA Department of Pathology at http://pathology.ucla.edu/default.cfm
Leading causes of death and disability such as atherosclerosis, diabetes, and obesity share a common biological trait. “These and other major human diseases are, fundamentally, disorders of lipid metabolism,” says Peter Tontonoz, MD, PhD, professor in the UCLA Department of Pathology & Laboratory Medicine.

Dr. Tontonoz’s laboratory is engaged in research aiming to unravel the complex biological processes involved in lipid metabolism. Specifically, he and his colleagues are investigating the molecular pathways that regulate lipid metabolism in animals. “We hope that by understanding the normal pathways by which the body metabolizes and stores lipids, we can better understand how some of these pathways go wrong in the setting of disease,” Dr. Tontonoz explains. “Ultimately, that could lead to new targets for drugs that could better treat these diseases.”

The most recent important contribution made by Dr. Tontonoz’s lab to the understanding of lipid metabolism appeared in the journal *Nature* earlier this year. Scientists have increasingly recognized the existence of non-coding RNAs – functioning RNA molecules that are transcribed by DNA but do not produce proteins. Researchers in Dr. Tontonoz’s lab identified one such non-coding RNA, which it named LeXis, that appears to regulate genes involved in cholesterol metabolism – reducing cholesterol levels in the blood of mice. The paper’s lead author was Tamer Sallam, MD, PhD, who at the time was a cardiology fellow doing his PhD training in Dr. Tontonoz’s laboratory. Dr. Sallam is now a clinical instructor in the Division of Cardiology at the David Geffen School of Medicine at UCLA.

Currently, approximately 10 postdoctoral fellows and three students work in Dr. Tontonoz’s lab.
RESEARCHERS IN DR. TONTONOZ’S LAB IDENTIFIED ONE SUCH NON-CODING RNA, WHICH IT NAMED LEXIS, THAT APPEARS TO REGULATE GENES INVOLVED IN CHOLESTEROL METABOLISM – REDUCING CHOLESTEROL LEVELS IN THE BLOOD OF MICE.

lab, and many will go on to careers as researchers. The group is currently following up on the Nature findings with an effort to identify the human counterpart to LeXis. More fundamentally, Dr. Tontonoz’s group is homing in on the activities of this non-coding RNA in regulating what may be a key pathway in cholesterol metabolism.

EXPLOREx Molecular Metabolism at http://pathology.ucla.edu/molecular-metabolism

Above: Cholesterol-loaded macrophages (foam cells) in spleen of mice lacking the transcription factors LXRα and LXRβ.

Left: Dr. Peter Tontonoz
STEM CELL STUDIES COULD BRING MAJOR BENEFITS TO BONE MARROW TRANSPLANT PATIENTS

Leading a team of approximately a dozen students, research assistants and postdoctoral fellows in her UCLA Department of Pathology & Laboratory Medicine lab, Dr. Gay M. Crooks is investigating questions that could make a difference in the outcomes of the patients she sees as a pediatric bone marrow transplant physician in the Division of Pediatric Hematology-Oncology at Mattel Children's Hospital UCLA.

Dr. Crooks’ lab focuses on better understanding the stem cells that are used in bone marrow transplants. These blood-forming, or hematopoietic, stem cells are mostly found in the bone marrow, although they can also be detected in blood or extracted from the umbilical cord. “These are the cells from which everything starts,” says Dr. Crooks, the Rebecca Smith Professor in the pathology department. “They provide a lifelong supply of blood cells and remake the blood and immune system after transplantation. Our lab’s interest is in how that occurs and how the process is regulated.”

Dr. Crooks and her colleagues are pursuing these questions through a variety of approaches, ranging from studies of the genes that regulate the process to studies of the cells themselves – including how to identify them and manipulate their growth through various strategies.

Much of the lab’s current work is being driven by the recent findings of two scientists in the lab: Amelie Montel-Hagen, PhD, a project scientist; and Christopher Seet, M.D, who is pursuing PhD training in the UCLA Specialty Training and Advanced Research (STAR) Program. Together they have discovered an efficient way to make the immune cells known as T cells from these hematopoietic stem cells. The finding could have major implications for one of the most exciting recent developments in cancer research – turning the immune system against tumors.

“Starting with a human hematopoietic stem cell in a culture dish, we can now make functioning, mature T cells,” says Dr. Crooks. “This not only gives us a system to study the process, but we can now also potentially engineer the stem cells into T cells that could be primed to target a specific tumor. We hope this new system that Amelie and Chris have developed may be useful as a new source of immune cell therapy for patients with cancer.”

Dr. Gay Crooks, Dr. Christopher Seet, and Dr. Amelie Montel-Hagen

“THESE ARE THE CELLS FROM WHICH EVERYTHING STARTS ... THEY PROVIDE A LIFELONG SUPPLY OF BLOOD CELLS AND REMAKE THE BLOOD AND IMMUNE SYSTEM AFTER TRANSPLANTATION. OUR LAB’S INTEREST IS IN HOW THAT OCCURS AND HOW THE PROCESS IS REGULATED.”

- Gay M. Crooks, MD

EXPLORE Hematopoietics at: http://pathology.ucla.edu/hematopoietics
NOVEL COMPUTATIONAL METHODS CONTRIBUTE TO BETTER UNDERSTANDING OF GENETIC RISK FOR COMMON DISEASES

By developing new computational and statistical methods, the research group of Dr. Bogdan Pasaniuc in the UCLA Department of Pathology & Laboratory Medicine and Department of Human Genetics is contributing to a better understanding of genetic risk factors for common human diseases.

“Our focus is on integrating multiple sources of data as well as utilizing massive public data repositories to pinpoint the genetic risk for a disease,” says Dr. Nick Mancuso, a postdoctoral fellow in the lab.

Dr. Mancuso is one of two postdocs in Dr. Pasaniuc’s group, which also currently includes four PhD students, two undergraduates and several rotating students at any one time. The computational frameworks developed by members of the lab have enabled large-scale explorations. “In the past year there have been multiple methods that look at fine mapping of risk for disease – whether it’s trying to pinpoint causal variances or estimating the total variation in risk,” Dr. Mancuso says. “This fine-tuned exploration of risk is something that really sets our lab apart.”

The Pasaniuc lab is particularly interested in methods that take advantage of the genetic diversity across and within populations to conduct large-scale studies. “In the future we will be integrating additional sources of information,” Dr. Mancuso says. For example, the lab plans to make greater use of epigenetics, an area of growing scientific interest that looks at non-DNA-related changes in gene expression. “As more publicly available resources are developed with these epigenetic markers as well as additional molecular phenotypes,” Dr. Mancuso says, “we can incorporate them to better understand the causes of diseases.”

Above Left to Right: Robert Brown (PhD student), Malika Kumar (PhD student), Nick Mancuso (Post-doctoral researcher), Kathy Burch (PhD student).
Above: Dr. Bogdan Pasaniuc

EXPLORE the Bogdan Lab at: http://bogdan.bioinformatics.ucla.edu/
Cardiac arrhythmias – irregular heart rhythms – affect more than 14 million people in the United States, and are the leading cause of sudden cardiac death. Standard treatments, including medications, medical procedures and surgery, often fall short. In the laboratory of Haodong Xu, MD, PhD, a professor in the UCLA Department of Pathology & Laboratory Medicine, researchers have homed in on molecular mechanisms that play a key role in cardiac arrhythmias in ischemic heart disease (hardening of the arteries) – a discovery that could pave the way for new and better treatments.

Dr. Xu’s lab recently found that DNA-binding proteins known as transcription factors, FoxO1 and a complex of b-catenin/TCF4, are activated in ischemic heart disease and negatively regulate cardiac sodium channel activity by decreasing expression of the sodium channel NaV1.5 protein through the inhibition of the SCN5a gene. Further studies by Dr. Xu and colleagues showed that mice with cardiac activation of b-catenin as a result of deleting the exon3 of b-catenin gene were susceptible to ventricular tachycardia (a life-threatening arrhythmia) being induced by the antiarrhythmic drug flecainide – a consequence of the decrease in their cardiac sodium channel activity. “Our findings indicate that FoxO1 and b-catenin-NaV1.5 signaling pathways play very important roles in the regulation of sodium channel activity, which make them potential targets for the development of agents to treat myocardial infarction-induced ventricular tachycardia or ventricular fibrillation,” Dr. Xu explains.

Dr. Xu is currently assisted by two postdoctoral fellows, Dr. Rong Huo and Dr. Chaowei Hu, and an assistant project scientist, Dr. Yan Lu. A third postdoctoral fellow, Dr. Ning Wang, the lead author on the most recent paper, has since returned to the Department of Pharmacology at Harbin Medical University in China, where she has established a robust cardiac research program. Dr. Xu’s group plans to follow up on these findings in studies looking at the molecular alterations in myocardial infarction. “Cardiac arrhythmias affect many people, including as a cause of sudden cardiac death,” Dr. Xu says. “The medications we have for them come with significant side effects. We hope our work can lead to therapeutic agents that will target these specific pathways and lead to better treatments for these patients.”

“OUR FINDINGS INDICATE THAT FOXO1 AND B-CATENIN-NAV1.5 SIGNALING PATHWAYS PLAY VERY IMPORTANT ROLES IN THE REGULATION OF SODIUM CHANNEL ACTIVITY, WHICH MAKE THEM POTENTIAL TARGETS FOR THE DEVELOPMENT OF AGENTS TO TREAT MYOCARDIAL INFARCTION-INDUCED VENTRICULAR TACHYCARDIA OR VENTRICULAR FIBRILLATION.” — Haodong Xu, MD, PhD

W EXPLORE Haodong Xu’s Lab at: http://pathology.ucla.edu/xu-lab

Yan Lu, Dr. Haodong Xu, Rong Huo and Chaowei Hu

14 PATHOLOGY & LABORATORY MEDICINE AT UCLA
An innovative peer-based anatomy tutoring program overseen by the UCLA Department of Pathology & Laboratory Medicine continues to bring benefits to both first-year David Geffen School of Medicine at UCLA (DGSOM) medical students, who gain more supervised time in the anatomy lab, and the second-year DGSOM students who tutor them.

DGSOM teaches gross anatomy in parallel with other basic sciences during the first year of medical school. “Anatomy is a foundational block of medical knowledge,” says Elena Stark, MD, PhD, professor and vice chair for medical and dental education in the Department of Pathology & Laboratory Medicine and director of the Anatomy Division for DGSOM. “Learning the material presented in that first year is critical to the students’ overall success.”

Dr. Stark explains that the first-year DGSOM students are required to visit the anatomy lab several times on their own to master the material presented by faculty. “I believe our students are aware of the foundational importance of anatomy on their overall medical education and on the understanding of clinical aspects of medicine, so they are enthusiastic about the opportunity to participate in additional anatomy lab study sessions,” Dr. Stark says.

While many medical schools offer tutoring programs for anatomy and other subjects, the program started by Dr. Stark in 2011 is innovative in that it employs second-year students to teach their peers the material they learned the previous year, in a small-group format, using a variety of quizzing techniques. The tutors are recruited, trained and supervised by Dr. Stark, who is in regular communication with them to ensure that their instruction is consistent with what is being taught by the faculty in the curriculum.

“ANATOMY IS A FOUNDATIONAL BLOCK OF MEDICAL KNOWLEDGE ... LEARNING THE MATERIAL PRESENTED IN THAT FIRST YEAR IS CRITICAL TO THE STUDENTS’ OVERALL SUCCESS.” – Elena Stark, MD, PhD

Dr. Elena Stark with a group of Anatomy teaching assistants for academic year 2016-2017, David Geffen School of Medicine students, class of 2019.

AN INNOVATIVE peer-based anatomy tutoring program overseen by the UCLA Department of Pathology & Laboratory Medicine continues to bring benefits to both first-year David Geffen School of Medicine at UCLA (DGSOM) medical students, who gain more supervised time in the anatomy lab, and the second-year DGSOM students who tutor them.

PEER ANATOMY TUTORING PROGRAM ENHANCES MEDICAL STUDENTS’ KNOWLEDGE OF KEY CONCEPTS

Dr. Elena Stark with a group of Anatomy teaching assistants for academic year 2016-2017, David Geffen School of Medicine students, class of 2019.

AN INNOVATIVE peer-based anatomy tutoring program overseen by the UCLA Department of Pathology & Laboratory Medicine continues to bring benefits to both first-year David Geffen School of Medicine at UCLA (DGSOM) medical students, who gain more supervised time in the anatomy lab, and the second-year DGSOM students who tutor them.

DGSOM teaches gross anatomy in parallel with other basic sciences during the first year of medical school. “Anatomy is a foundational block of medical knowledge,” says Elena Stark, MD, PhD, professor and vice chair for medical and dental education in the Department of Pathology & Laboratory Medicine and director of the Anatomy Division for DGSOM. “Learning the material presented in that first year is critical to the students’ overall success.”

Dr. Stark explains that the first-year DGSOM students are required to visit the anatomy lab several times on their own to master the material presented by faculty. “I believe our students are aware of the foundational importance of anatomy on their overall medical education and on the understanding of clinical aspects of medicine, so they are enthusiastic about the opportunity to participate in additional anatomy lab study sessions,” Dr. Stark says.

While many medical schools offer tutoring programs for anatomy and other subjects, the program started by Dr. Stark in 2011 is innovative in that it employs second-year students to teach their peers the material they learned the previous year, in a small-group format, using a variety of quizzing techniques. The tutors are recruited, trained and supervised by Dr. Stark, who is in regular communication with them to ensure that their instruction is consistent with what is being taught by the faculty in the curriculum.

“ANATOMY IS A FOUNDATIONAL BLOCK OF MEDICAL KNOWLEDGE ... LEARNING THE MATERIAL PRESENTED IN THAT FIRST YEAR IS CRITICAL TO THE STUDENTS’ OVERALL SUCCESS.” – Elena Stark, MD, PhD

Dr. Elena Stark with a group of Anatomy teaching assistants for academic year 2016-2017, David Geffen School of Medicine students, class of 2019.

AN INNOVATIVE peer-based anatomy tutoring program overseen by the UCLA Department of Pathology & Laboratory Medicine continues to bring benefits to both first-year David Geffen School of Medicine at UCLA (DGSOM) medical students, who gain more supervised time in the anatomy lab, and the second-year DGSOM students who tutor them.

DGSOM teaches gross anatomy in parallel with other basic sciences during the first year of medical school. “Anatomy is a foundational block of medical knowledge,” says Elena Stark, MD, PhD, professor and vice chair for medical and dental education in the Department of Pathology & Laboratory Medicine and director of the Anatomy Division for DGSOM. “Learning the material presented in that first year is critical to the students’ overall success.”

Dr. Stark explains that the first-year DGSOM students are required to visit the anatomy lab several times on their own to master the material presented by faculty. “I believe our students are aware of the foundational importance of anatomy on their overall medical education and on the understanding of clinical aspects of medicine, so they are enthusiastic about the opportunity to participate in additional anatomy lab study sessions,” Dr. Stark says.

While many medical schools offer tutoring programs for anatomy and other subjects, the program started by Dr. Stark in 2011 is innovative in that it employs second-year students to teach their peers the material they learned the previous year, in a small-group format, using a variety of quizzing techniques. The tutors are recruited, trained and supervised by Dr. Stark, who is in regular communication with them to ensure that their instruction is consistent with what is being taught by the faculty in the curriculum.

“ANATOMY IS A FOUNDATIONAL BLOCK OF MEDICAL KNOWLEDGE ... LEARNING THE MATERIAL PRESENTED IN THAT FIRST YEAR IS CRITICAL TO THE STUDENTS’ OVERALL SUCCESS.” – Elena Stark, MD, PhD

Dr. Elena Stark with a group of Anatomy teaching assistants for academic year 2016-2017, David Geffen School of Medicine students, class of 2019.

AN INNOVATIVE peer-based anatomy tutoring program overseen by the UCLA Department of Pathology & Laboratory Medicine continues to bring benefits to both first-year David Geffen School of Medicine at UCLA (DGSOM) medical students, who gain more supervised time in the anatomy lab, and the second-year DGSOM students who tutor them.

DGSOM teaches gross anatomy in parallel with other basic sciences during the first year of medical school. “Anatomy is a foundational block of medical knowledge,” says Elena Stark, MD, PhD, professor and vice chair for medical and dental education in the Department of Pathology & Laboratory Medicine and director of the Anatomy Division for DGSOM. “Learning the material presented in that first year is critical to the students’ overall success.”

Dr. Stark explains that the first-year DGSOM students are required to visit the anatomy lab several times on their own to master the material presented by faculty. “I believe our students are aware of the foundational importance of anatomy on their overall medical education and on the understanding of clinical aspects of medicine, so they are enthusiastic about the opportunity to participate in additional anatomy lab study sessions,” Dr. Stark says.

While many medical schools offer tutoring programs for anatomy and other subjects, the program started by Dr. Stark in 2011 is innovative in that it employs second-year students to teach their peers the material they learned the previous year, in a small-group format, using a variety of quizzing techniques. The tutors are recruited, trained and supervised by Dr. Stark, who is in regular communication with them to ensure that their instruction is consistent with what is being taught by the faculty in the curriculum.

“ANATOMY IS A FOUNDATIONAL BLOCK OF MEDICAL KNOWLEDGE ... LEARNING THE MATERIAL PRESENTED IN THAT FIRST YEAR IS CRITICAL TO THE STUDENTS’ OVERALL SUCCESS.” – Elena Stark, MD, PhD

Dr. Elena Stark with a group of Anatomy teaching assistants for academic year 2016-2017, David Geffen School of Medicine students, class of 2019.

AN INNOVATIVE peer-based anatomy tutoring program overseen by the UCLA Department of Pathology & Laboratory Medicine continues to bring benefits to both first-year David Geffen School of Medicine at UCLA (DGSOM) medical students, who gain more supervised time in the anatomy lab, and the second-year DGSOM students who tutor them.

DGSOM teaches gross anatomy in parallel with other basic sciences during the first year of medical school. “Anatomy is a foundational block of medical knowledge,” says Elena Stark, MD, PhD, professor and vice chair for medical and dental education in the Department of Pathology & Laboratory Medicine and director of the Anatomy Division for DGSOM. “Learning the material presented in that first year is critical to the students’ overall success.”

Dr. Stark explains that the first-year DGSOM students are required to visit the anatomy lab several times on their own to master the material presented by faculty. “I believe our students are aware of the foundational importance of anatomy on their overall medical education and on the understanding of clinical aspects of medicine, so they are enthusiastic about the opportunity to participate in additional anatomy lab study sessions,” Dr. Stark says.

While many medical schools offer tutoring programs for anatomy and other subjects, the program started by Dr. Stark in 2011 is innovative in that it employs second-year students to teach their peers the material they learned the previous year, in a small-group format, using a variety of quizzing techniques. The tutors are recruited, trained and supervised by Dr. Stark, who is in regular communication with them to ensure that their instruction is consistent with what is being taught by the faculty in the curriculum.

“ANATOMY IS A FOUNDATIONAL BLOCK OF MEDICAL KNOWLEDGE ... LEARNING THE MATERIAL PRESENTED IN THAT FIRST YEAR IS CRITICAL TO THE STUDENTS’ OVERALL SUCCESS.” – Elena Stark, MD, PhD

Dr. Elena Stark with a group of Anatomy teaching assistants for academic year 2016-2017, David Geffen School of Medicine students, class of 2019.
THE PROGRAM, WHICH WON THE STEPHEN ABRAHAMSON AWARD FOR OUTSTANDING INNOVATION IN THE 2014 ..., BENEFITS BOTH THE TEACHERS AND THE STUDENTS

The program, which won the Stephen Abrahamson Award for Outstanding Innovation in the 2014 Innovations in Medical Education Conference at USC, benefits both the teachers and the students, Dr. Stark notes. For the second-year tutors, it helps to reinforce their knowledge of anatomy ahead of Step 1, a test medical students take at the end of their second year as part of the U.S. Medical Licensing Examination process. In addition, the majority of the tutors report the program ignited and/or propelled their desire for being involved in academic medicine and teaching in their future careers. For the first-year students, learning the material through a different approach from the lectures and regular laboratory sessions helps to solidify their knowledge. Equally important, says Dr. Stark, “We have data showing that students report this program helps them become more confident, both in learning anatomy and in their overall feeling about medical school.”

Dr. Elena Stark with a group of Anatomy teaching assistants for academic year 2016-2017, David Geffen School of Medicine students, class of 2019.

--- continued from page 15 ---
A dvancing technology has led to an explosion in the use of point-of-care (POC) testing – clinical tests administered and read directly in the presence of the patient rather than being sent to a laboratory. “POC testing is a helpful addition to ambulatory care, allowing providers to act immediately on medically relevant results,” notes Valerie Arboleda, MD, PhD, a clinical pathology resident. “However, the decentralization of testing across hundreds of sites makes quality assessment challenging.”

Under the leadership of Omai Garner, PhD, assistant professor in the UCLA Department of Pathology & Laboratory Medicine, and in conjunction with the UCLA Department of Nursing, Dr. Arboleda is leading a project aiming to assess the state of ambulatory POC testing in the UCLA Health system, particularly as it pertains to issues of licensing, quality control, training, and adherence to national society guidelines. As part of UCLA’s quality improvement initiative, all pathology residents are tasked with identifying a problem within the hospital system that can be addressed using pathology knowledge and skills.

Dr. Garner, Dr. Arboleda and their colleagues in ambulatory care nursing have conducted site visits at more than 20 UCLA Health outpatient clinics to assess licensure, quality control methods, and training in the point-of-care testing services, as well as how the tests are being used, interpreted and entered into the patients’ records. The overall goal is to ensure that as POC testing continues to grow dramatically across UCLA Health’s more than 300 outpatient clinics and centers, the testing performed in the outpatient setting is comparable to what would be found in the licensed clinical laboratory.

“In many cases, these tests are being used to make important decisions about treatment, for example whether or not to prescribe antibiotics or antivirals,” Dr. Arboleda says. “Even though the tests are relatively easy to perform, it’s important to take all appropriate steps to make sure that we are achieving the highest quality standards so our patients receive the best possible care.”

Dr. Valerie Arboleda
NEW HEMATOLOGIC MALIGNANCY SEQUENCING TEST PROVIDES IMPORTANT TRAINING EXPERIENCE

Trainees in the UCLA Department of Pathology & Laboratory Medicine are gaining a unique and valuable experience working in a multidisciplinary setting to address the newest and most complicated test offered by the department’s Molecular Diagnostics Laboratory.

The hematologic malignancy sequencing panel, which was launched in March, is a comprehensive sequencing test covering 44 clinically relevant genes. The test provides information that can be used in the management of patients with hematologic malignancies, including acute leukemia, myeloid disorders, and lymphoma.

Rena Xian, MD, an assistant professor in the department and a member of the Molecular Diagnostics Laboratory faculty, explains that the test is performed using disease-specific sub-panels capturing genes most appropriate for specific diseases, which needs to be determined by the submitting hematologist/oncologists and the hematopathologist. “Each time a request comes in, we perform requisition reconciliation. We have to review the clinical history, working diagnosis, bone marrow morphologic impression, flow cytometric findings, and any previous molecular testing or pathology review for each patient to determine the disease in question, and the current disease state,” Dr. Xian explains. “Our trainees are playing a key role in integrating all of this information, coordinating with the clinician and hematopathology team, and consulting with them on what would be the best approach for each patient.”

Prior to the launch, Dr. Xian provided in-service education to hematology-oncology faculty and fellows, hematopathology trainees, and pathology residents, with whom she also worked closely on a daily basis in the initial weeks after test launch. A quality assurance study conducted by one of the residents on the impact of the new test found that in the first few weeks it was offered, only 25 percent of the requests were appropriate requests for disease and current disease state, while nearly half were modified in some capacity as a result of the requisition reconciliation process, and the remaining orders were cancelled after further consultation with hematopathology and the ordering clinician.

“This process has been a valuable learning experience for me,” says Sureni V. Mullegama, PhD, a clinical postdoctoral fellow in the department. “As fellows, we are getting a well-rounded training experience – working as consultants to clinicians in ensuring appropriate test utilization, as team players with our technologists and laboratory staff, as variant analysts, and as eloquent writers of clinical pathology reports and effective communicators of the results...” – Sureni V. Mullegama, PhD

Left to Right: Dr. Sheeja Pullarkat, Nora Warschaw, Dr. Wayne Grody, Dr. Samuel Strom, Dr. Rena Xian, Sureni Mullegama, Ashlee Stiles, Annabella Leung, Cora Au
RESIDENT “SUPERUSERS” HELP SHAPE UCLA’S NEW LABORATORY INFORMATION SYSTEM

As one of several UCLA Department of Pathology & Laboratory Medicine residents who volunteered to be “superusers” of Beaker, the hospital’s new laboratory information system, Dr. Alex Nobori saw firsthand the challenges of implementing a new reporting system while gaining a rare opportunity to help shape the system for current and future users.

Beaker is the new computer interface designed to integrate seamlessly with other applications in CareConnect, UCLA’s electronic health record system. Among its functions, Beaker supports workflows for placing orders, collecting and tracking specimens, testing, and reporting results. For residents such as Dr. Nobori, all orders and reports are now supported through Beaker.

Although all of the department’s residents are using the new system, which was implemented beginning in March, Dr. Nobori has been part of a voluntary group designated as superusers. These individuals attended additional training sessions and participated in planning efforts prior to implementation. They held a forum to discuss some of the problems residents were experiencing, then relayed the comments to the team involved in building the system.

“It’s so important that pathology residents be involved in Beaker’s implementation,” Dr. Nobori explains. “Although residents from other fields will interface with the system when submitting specimens, everything that occurs after that is within the domain of pathology, and so we need to make sure that this transition is as smooth as possible.”

Not surprisingly, Dr. Nobori notes, the transition came with challenges, but in the end, Beaker offers important benefits over the previous system. “The big advantage is that Beaker serves as an extension of the electronic health record, with everything integrated into one system,” Dr. Nobori says. “We are continuing to identify features that can be improved, and our hope is to work with the faculty to make this system even better.”

Although all of the department’s residents are using the new system, which was implemented beginning in March, Dr. Nobori has been part of a voluntary group designated as superusers.

Explore the Department of Pathology and Laboratory Medicine, http://pathology.ucla.edu/default.cfm
THE FIVE CORE facilities run by the UCLA Department of Pathology & Laboratory Medicine provide invaluable shared resources and infrastructure for the UCLA research community. “Above all, we strive to enable investigators on campus to accomplish their goals by providing high-quality, low-cost services, and to remain at the forefront of innovation and expertise in the technology,” says Elaine F. Reed, PhD, professor and vice chair of research services for the department, as well as director of the Immune Assessment Core (IAC), one of the labs offering such services across the campus.

But beyond that, the department’s core labs play an important teaching role - educating users about the technologies through seminars, tutorials, courses and individual consultations. “If, as a researcher, you don’t know about the technology, you are unlikely to appreciate any limitations of your data,” Dr. Reed says. “And our core faculty are going to perform better services if they are working with faculty who are knowledgeable about what we’re doing.”

The IAC headed by Dr. Reed is a comprehensive source of immunological testing services for basic, clinical and translational studies that will be central to the campus-wide efforts in precision medicine. With that in mind, the IAC has established assays to measure the human response under various conditions, and to use high-throughput technologies to characterize immune function. “As we recognize how important the immune system is across so many different diseases, we will work closely with researchers and clinicians to develop new assays to help them understand whether patients are responding to therapy in the manner that they should,” Dr. Reed says. “In the future, our vision is to offer a panel of these tests that can be used to assess patients’ immune systems at routine doctor visits.”

One of the strengths of all of the core labs is the expertise of the faculty and staff who run them, and their ability to work well with the researchers who use them. “The core lab directors are all professors in our department and experts not only in the technology, but in guiding the researchers and helping them to ask the right questions,” Dr. Reed says. “This is essential so that the researchers are not wasting valuable resources or time on methods that don’t work for their experiments.”

The IAC provides high-throughput immunological testing services for researchers throughout the UCLA research community and the greater Los Angeles region. It is one of the five core facilities run by the UCLA Department of Pathology & Laboratory Medicine. The lab offers comprehensive services for immunological studies, including the measurement of immune responses to various stimuli and the characterization of immune function using high-throughput technologies. The IAC is intended to be a central resource for researchers interested in understanding the role of the immune system in various diseases and conditions, with the ultimate goal of developing new therapies and treatments.
questions in the context of the technology to accomplish their research goals,” says Dr. Reed. “They essentially become part of the research team, helping the researchers at all levels, from developing hypotheses and aims to the execution and analysis of the research. And they stay on the pulse of the field so that we are always able to offer researchers the most up-to-date technologies and expertise.”

Part of the labs’ mission is also to disseminate that knowledge. Educational events include “wet” workshops that provide hands-on lessons in the fundamentals of the technology to data-analysis workshops, along with presentations by UCLA-based users and industry partners on the technologies’ applications and utilities.

For the last nine years, the CMC has offered a week-long genomics education course that consistently attracts far more applicants than it can accommodate. Participants include UCLA faculty and staff from all over campus, as well as people from industry and other institutions across the country and abroad. The course includes lecture, wet-lab and bioinformatics components. “This course is very important to us,” says Xinmin Li, PhD, professor in the pathology department and CMC director.

The Human Genome Project, which sequenced and mapped every human gene, was considered an enormous accomplishment. Launched in 1990, it took 13 years to complete and cost more than $3 billion. “Today, we can complete one human genome within three days, at a cost of less than $1,000,” Dr. Li notes.

With all of the next-generation sequencing platforms and a staff of experts, the CMC provides comprehensive as well as flexible services with a quick turnaround time. But unlike most core labs outside of UCLA, CMC goes beyond performing the service. “If you were to outsource to another facility, you would have a longer turnaround time, higher cost, and you would miss out on the support,” Dr. Li says. “Here, before the experiments the researcher can sit in my office to discuss the design and understand the technologies, then come back afterward to discuss the data analysis. If you go somewhere that doesn’t provide that support, the outsourcing comes at the expense of the science.”

ESTABLISHED IN 2015, THE IAC IS THE DEPARTMENT’S NEWEST CORE. OTHERS INCLUDE:

- The Brain Tumor Translational Resource (BTTR), a biorepository and resource supporting brain tumor research at UCLA, other academic centers, brain tumor consortia, and industry.
- The Clinical Microarray Core (CMC), a fully automated, high-throughput genomic facility equipped with all major next-generation sequencing and microarray platforms.
- The Pathology Research Portal (PRP), part of the department’s Center for Pathology Research Services, which functions as a biospecimen liaison between researchers and clinical testing.
- The Translational Pathology Core Laboratory (TPCL), which provides pathology-related services and expert consultations to investigators in pathology-related study design, tissue selection, microscopic interpretation, immunohistochemistry/in situ hybridization, laser-capture microdissection, digital image analysis, and IRB-related tissue questions.
MULTIPLEX IMMUNOFLUORESCENCE OFFERS UCLA RESEARCHERS MAJOR BENEFITS OVER TRADITIONAL IMMUNOHISTOCHEMISTRY

The UCLA Department of Pathology & Laboratory Medicine is bringing immunofluorescence, digital scanning and digital image analysis – including multiplex staining – to the UCLA research community via the Translational Pathology Core Laboratory (TPCL), a state-of-the-art approach that the lab’s director and associate director call “a huge step forward.”

Traditionally, researchers have relied on immunohistochemistry to identify specific proteins or biomarkers within cells of interest. The problem, notes Sarah Dry, MD, professor in the department and TPCL director, is that at the most, only two antibodies can be used on the same slide. “That means researchers have had to cut a series of slides in order to use all of the antibodies of interest, and as they are examining those slides it can become difficult to determine whether a particular cell is staining for multiple antibodies,” Dr. Dry says. “That cell might disappear on the different sections that are cut, and it is sometimes very difficult to know whether or not you’re looking at the same cell.”

With multiplex immunofluorescence, as many as six different stains can be placed on the same slide, and all can be imaged using immunofluorescence and digital slide scanners. “These scanners will allow us to capture the immunofluorescence image and then look at each marker separately or in any combination to see if cells of interest are expressing multiple biomarkers,” explains Dr. Sam French, TPCL associate director. “From the perspective of the researcher, it is very exciting to see this type of cellular detail.” Beyond that, he notes, multiplex immunofluorescence represents an advance in that under the traditional immunofluorescence approach, the signal tends to fade within about two days. By using the scanners, the image can be captured as a digital file and retained indefinitely.

For researchers who have access to a limited amount of tissue, the need to use 12 slides in order to conduct 12 stains with traditional immunofluorescence might have led them to use up all of their tissue, whereas now only two slides would be required. “We are now able to get much more information in fewer tissue sections,” says Clara Magyar, PhD, TPCL manager. “This means that researchers can learn how different markers may interact in the cells. When you’re trying to uncover mechanisms for a disease, and you can see more of the players in the same image, you can come to more insightful conclusions.” Dr. Magyar notes that multiplex immunofluorescence is an expensive investment for an individual lab, but as a core facility the TPCL is able to make it accessible to the UCLA research community.

Multiplex immunofluorescence was made possible not only by the advent of digital slide scanning, but also by advances in the scanners themselves, which can now be more finely tuned to the resolution at which lab members see fluorescent signals coming off the tissue. “With immunofluorescence you’re looking for light that’s being emitted at certain wavelengths, and in the past there was quite a bit of signal overlap from one antibody to another – making it difficult to discriminate between antibodies,” Dr. French says. “Now, the wavelengths at which these antibodies are emitting light and being excited are much smaller and narrower, which allows us to use multiple antibodies on the same slide.”

While multiplex immunofluorescence is currently confined to the laboratory, Dr. Dry believes it is likely to move into the clinical setting in the near future. “We need more experience with it in the research arena to make sure that we can get results consistently, and although the scanners have become more precise, further work needs to be done to ensure that the images are even cleaner to read and more accurate,” she says. “But once we get there, this will be a very important clinical tool that make more tissues available for molecular testing.”

EXPLORE Translational Pathology, http://pathology.ucla.edu/tpcl
The UCLA Immunogenetics Center (UIC), which has a long record of leadership in human leukocyte antigen (HLA) typing and cross-match testing for tissue and organ transplants, is continuing to apply new technological advances in histocompatibility and immunogenetics testing toward better and more cost-effective care for transplant patients.

One of the most exciting UIC initiatives involves the first use of next-generation sequencing (NGS) to achieve a higher resolution in HLA typing. Since the 1970s, the technology employed to match blood and bone marrow donors with compatible recipients has relied on methods for sequencing HLA genes that have significant limitations.

“They are relatively expensive and low-throughput, and the results can be ambiguous,” says Jennifer Zhang, PhD, associate professor in the Department of Pathology & Laboratory Medicine and associate director of the UIC. “This has been the major barrier in blood and marrow transplantation.”

Dr. Zhang and her colleagues have developed and scientifically validated a technique that harnesses the power of NGS – which allows for billions of DNA fragments to be sequenced at once – for HLA typing. Since 2014, the UCLA team has used the automated technology to report full-gene sequences of more than 20,000 donors through a partnership with the National Marrow Donor Program. In addition to significant improvements in accuracy and reductions in cost, obtaining the full-gene sequence speeds up the process by which patients can be transplanted. “Because no additional testing needs to be done, the donor selection goes very quickly, and faster transplantation leads to better outcomes,” Dr. Zhang notes.

The UIC is also moving toward automation of routine laboratory procedures for virtual crossmatch and deceased donor workups to improve accuracy and reduce cost. Virtual crossmatch is the process by which information on the patient’s antibody sensitization is used to determine the compatibility of a potential donor without performing a physical crossmatch test such as a flow cytometry or complement dependent cytotoxicity crossmatch. “In the past, we have done this manually through a review of the case, a workup of the patient and a consultation,” says Michelle Hickey, PhD, assistant professor in the Department of Pathology & Laboratory Medicine.

---continued on page 24---
Medicine and assistant director of the UIC. "By automating the system, we increase accuracy, reduce cost and tech time, reduce manual-entry error, and potentially increase the turnaround time to the organ procurement organization and transplant programs, which should result in faster allocation of the organ." A similar effort is under way to develop a fully automated system that integrates all of the analysis instruments and computing programs involved in deceased donor crossmatching.

Dr. Hickey and her UIC colleagues are also studying the role of non-HLA antibodies in adult heart transplant patients. Patients who receive a ventricular assist device (VAD) – a mechanical device implanted to serve as a bridge until the time when a donor can be found – have recently been shown to have a higher rate of experiencing a primary non-functioning graft after their transplant. The UIC researchers have discovered that the cause may be an antibody the AT1R receptor. Using a new test for AT1R, they have begun a study to determine the connection between development of the AT1R antibodies, VAD placement, and transplant outcomes.

UIC researchers are also developing new algorithms for the transplantation of highly sensitized patients. Their donor histocompatibility calculator scans the HLA antigen information on all donors in the United Network for Organ Sharing database to predict the likelihood of finding a donor match for the patient based on the patient's immuno-phenotype. An extremely low likelihood of a match suggests that an intervention other than transplantation is indicated.

Another UIC research effort focuses on measuring immunosuppressed patients' ability to respond to various stimuli to assess their level of immune competence. "One of the biggest risks after transplant is acquiring infections, because the immunosuppressed patient is unable to respond in the same way as a healthy individual can," says Elaine F. Reed, PhD, professor in the department and UIC director. In developing tests designed to measure the patient's post-transplant immune response, Dr. Reed and her colleagues are focusing on cytomegalovirus and BK, two viruses that are commonly associated with transplantation, and are highly pathogenic. "With the assays we have developed, we will be able to gauge whether patients will be able to clear these infections, which will help to determine if they need continued therapy," Dr. Reed explains.

Precision medicine, or individualized approaches to treatment, is seen as the future of healthcare, but Dr. Reed points out that for the UIC that future has already arrived. "We practice precision medicine on a daily basis," she says. "Through complex algorithms and a number of innovative strategies, we determine how to optimize the patient's chance of getting transplanted, and to achieve the best possible outcome."
UIC continues to lead the way in standardizing tests for organ transplantation

Now in its fifth decade as an international leader in standardizing human leukocyte antigen (HLA) typing and histocompatibility testing worldwide, the UCLA Immunogenetics Center (UIC) continues to be a pioneer in refining and ensuring the quality of the testing that is critical to the success of organ transplantation.

“In the early 1960s, after it was determined that a person’s HLA type was important for tissue compatibility, most of the testing was being done by a handful of labs, and there were many discrepancies between these labs,” says David Gjertson, PhD, a professor in the UCLA Department of Pathology & Laboratory Medicine and member of the UIC faculty.

That changed in 1974, when the UIC (then known as the UCLA Tissue Typing Laboratory), under the direction of Dr. Paul Terasaki, established the UCLA International Cell Exchange program. On an annual basis ever since, UIC sends approximately 24 cells to participating laboratories around the world, which proceed to type the cells and report the results back to the UIC. “The discrepancy rates were as high as 90 percent when we started, and now they are less than 2 percent across a wide variety of components of the HLA system,” Dr. Gjertson says.

Beginning in the early 1990s, the UIC began to expand its programs to tackle other challenges. As laboratories shifted from a serological-based test to molecular testing, the UIC began sending out not just cells, but also DNA extracts to the participating labs for testing. Since the late 1990s, under the leadership of Elaine Reed, PhD, the UIC has added other charges to its core mission of standardizing the practice of HLA typing. That includes standards for typing of the HLA-associated genes KIR and MICA, class I and class II antibody identification, and proficiency testing services. Most recently, with the increased recognition of the importance of monitoring the immune response post-transplant, UIC began adding a cross-match component to the survey it sends to participating laboratories.

More than 150 labs currently participate in UIC’s reference program, and individual laboratories use UIC materials for their accreditations. “We are well recognized and continue to perform an important service,” Dr. Gjertson says.

More than 150 labs currently participate in UIC’s reference program, and individual laboratories use UIC materials for their accreditations. “We are well recognized and continue to perform an important service,” Dr. Gjertson says. ▲

EXPLORE Immunogenetics, http://pathology.ucla.edu/uic-hla

Dr. David Gjertson
As the volume of research involving human subjects – and thus requiring pathology services – continues to grow at UCLA and study designs become more complex and sophisticated, the UCLA research community is increasingly relying on the coordination and expertise of the Center for Pathology Research Services (CPRS), established within the UCLA Department of Pathology & Laboratory Medicine in 2013.

CPRS serves as a centralized resource for UCLA investigators seeking to access and utilize the extensive services of the pathology department’s clinical labs and core facilities. CPRS director Dr. Sarah Dry and co-director Dr. Dawn Ward work closely with the CPRS manager, Michelle Li, PhD., to ensure CPRS provides timely and high quality services. In the last year, the center has dramatically enhanced its IT infrastructure.

The changes include:

- OnCore, a new project-management software platform, is now being introduced to all UCLA clinical research projects. “Since more than 80 percent of projects use pathology services, this increases the transparency between CPRS as an ancillary service provider and our users,” Dr. Li explains. “It’s a great way to link pathology with the users so that we can communicate about project needs and customize our services to fit users’ needs.”

- CPRS has been heavily involved in the implementation process of ResearchConnect, which is the research module used in CareConnect, UCLA’s electronic health record program. While this has meant making changes in the ordering, billing, budgeting and other aspects of clinical research administration, it is contributing to a more centralized approach to managing clinical research throughout the campus.

- CPRS is also using Beaker, which went live in March as part of the CareConnect system, to manage all research specimens. The laboratory information system integrates seamlessly with other applications in CareConnect to support workflows for placing research orders, collecting and tracking specimens, testing, and reporting results.

While implementing all of these improvements, CPRS has continued to grow dramatically. The user base roughly doubled from 2014-15 to 2015-16, and first-time users nearly tripled during the same period. Dr. Li says the center intends to step up its efforts to educate potential users about CPRS services as a strategy to promote further growth inside as well as outside the UCLA campus.

Explore Pathology Research Portal, http://pathology.ucla.edu/ctrl
**Facilities**

Total Space in Square Feet = 270,105

Total number of square feet of Clinical, Research, and Teaching space

- Clinical: 165,961
- Core Lab: 8,442
- Research: 40,045
- CLINICAL SPACE AWAITING TENANT IMPROVEMENTS: 8,334
- EDUCATIONAL, ACADEMIC, & ADMINISTRATION: 45,587
- DEPARTMENT SPACE AWAITING TENANT IMPROVEMENTS: 1,736

**Department of Pathology**

Total = 1234

- Faculty: 89
- Residents/Fellows: 61
- Postdoc Researchers: 11
- Grad Student Researchers: 20
- Professional Research Series: 14

- Staff: 1,039

**Research Funding**

Total = $38,600,210

- NIH Funding: $34,981,705
- OTHER GRANTING AGENCIES: $3,618,505

**Department Inventions in 2016**

6,000 Molecular Pathology Cases

360 Microarray Cases

45,840 Cytology Cases

11,000 Surgical Pathology Cases Santa Monica

32,600 Surgical Pathology Cases Westwood

56,136 Anatomic Pathology Cases Outreach

20,242 Cytogenetics Cases

680 Exome (Genomics) Cases

5,702,828 Clinical Lab Tests
Care Harbor is a major opportunity for our department volunteers to reach the people most important to their mission – all under one roof at one time. The men and women attending this free clinic are an accessible and eager audience as they wait, often for hours, for the health services they request. Charities, organizations and government agencies can connect with their publics on a large scale with great efficiency and impact.

Care Harbor provides free medical, dental and vision care to the uninsured, underinsured and underserved in our communities. For those who live without access to the care they need, our clinic events are a destination for help and hope.

There is space for exhibits and presentations that educate and inform patients or provide them with a needed service. Our goal is to promote the wellness and wellbeing of the people we serve who are among our most vulnerable populations – with prevention and education resources.

Care Harbor & UCLA
• brings medical, dental and vision care to the uninsured, underinsured and underserved in our communities.
• transforms arenas and other large venues into working clinics treating thousands of people in the space of a few days.
• connects patients to medical homes - local clinics and practices that can provide ongoing primary and specialty care.


NATIONAL MEDICAL LAB PROFESSIONALS WEEK
APRIL 24-30, 2016
The Department of Pathology & Laboratory Medicine celebrated National Medical Laboratory Professionals Week by acting as “Diagnosis Detectives”. Ronald Reagan had games like a Crime Scheme photo contest and Code word scramble contest based on common laboratory items. There was even a Whodunit Mystery where Core Lab staff had to solve the case of missing Mr. Meditech.

The 2016 Lab Gives Back Initiative was the People-Animal Connection. The UCLA People-Animal Connection (PAC) program has grown from a single-pet therapy team in 1994 to more than 60 volunteer human and canine teams, which makes UCLA one of the most comprehensive Animal-Assisted Therapy programs in the nation. The Ronald Reagan Core Clinical Laboratory donated over $1000 to the program. Two of the PAC dogs, Finn & Remey, brought their owners to say thank you to the laboratory staff.

L to R: Cristina Hilado, Kathleen Siplon, Lilian Baldwin, Khanh Andrews, Gabriela Ware (Support Services), Lavita Boyd, Nathan Okawa, Diana Crary, Diana Tanaka-Mukai Front: PAWS- Finn and Remey

THE SOCIAL JUSTICE LEARNING INSTITUTE (SJLI)
The Social Justice Learning Institute (SJLI) continues to expand its educational and health equity programs to deepen its impact on youth and communities of color. Among our 40 high school graduates, 93% are headed to college this fall. To provide continued support to these young men, SJLI launched an Alumni Program to promote access and persistence in college. During the academic year, SJLI youth leaders were invited to speak to the Los Angeles Unified School District Board on restorative justice and school climate. In September of 2015, SJLI also launched the Inglewood Certified Farmers’ Market to provide access to fresh, affordable and healthy food to the Inglewood community. For more information about our programs or to get involved, visit www.sjli.org.

MOVEMBER HEALTH FAIR
The Core Lab performed glucose and lipid screening for 160 UCLA staff and students at the November 19, 2015 Movember Health Fair held in Pauley Pavilion. This was the third year that the Core Lab has participated in this event.
CITY OF ANGELS FUN RIDE PRESENTED BY VOLKSWAGEN

The 19th annual City of Angels Fun Ride presented by Volkswagen was held on May 22nd at Dickson Plaza on the UCLA Campus. With over 700 participants including: riders, LAPD police officers, along with spectators, volunteers, staff and other support personnel. Two rides were offered, an advanced metric century of 62 miles and a recreational 32 mile ride with a complete LAPD rolling traffic closure. After the ride there is a lunch, blood drive and huge raffle. Six bikes and thousands of dollars in other prizes were given away during the raffle, with all ticket sales going to the event charity.

Profits and donations from the event are going toward purchasing the UCLA Blood & Platelet Center a new, larger and much needed Bloodmobile. Funds from last several years were used to purchase a new box truck for the UCLA Blood & Platelet Center. The event producer, Peter Heumann said, “We are very close to having the funds necessary to purchase the bloodmobile... but not quite there and hope to meet the goal by next year’s ride.

The City of Angels Fun Ride is produced by Peter & Deborah Heumann (Heumann Powered Productions) and each year their daughter flies to LA to help with this family run event. Title sponsored by the Southern California Volkswagen Dealers who make a very generous donation each year along with sponsoring the event. Other Sponsors include Pace Sportswear who donates 10% of their sales from event merchandise to the cause and KHS Bicycles of Rancho Dominguez who donates bikes and other great prizes.

Photos of the start line and the UCLA campus. Photo by Chris Hatounian

Greater Los Angeles County Heart Walk
Saturday, September 26 2015 | Rose Bowl

The Department of Pathology & Laboratory Medicine touches virtually each and every patient in the hospital, assisting in their diagnosis and treatment. A total of 63 Team members raised $6837.00 for the American Heart Association’s research and education programs.
**2016 PATHOLOGY FAREWELL CELEBRATION**

The 2015-16 Pathology Farewell Reception and Dinner took place on June 15 at the UCLA Faculty Center. Once again, graduates were honored on a beautiful Southern California evening which began with hors d’oeuvres and an art exhibit featuring faculty, graduate, and staff talent. Dinner and presentations followed, hosted by Department Chair, Dr. Jonathan Braun.

**PATHOLOGY ALUMNI UPDATE**

The faculty of the Department of Pathology and Laboratory Medicine at UCLA value their relationship with alumni and would like to keep their ties strong, even after the training period is over. The pathology alumni committee provides the opportunity for alumni to keep and make new and valued connections through social and educational events, with the support and resources of the department. The clinical Pathology alumni committee is currently made up of three departmental alumni, Dr. Pouneh Beizai, Dr. Celina Nadelman, and Dr. Rubio Punzalan. The committee is currently organizing an alumni reception which will be held in Los Angeles.

**KEEP IN TOUCH!**

- [UCLA Pathology Alumni](#)
- [Pathology Research Alumni](#)

To learn more or subscribe to our newsletter, explore pathology. ucla.edu/alumni

**AWARDS & RECOGNITION**

- **Anatomic Pathology Staff Members** — UCLA Health CICARE Team award
- **Elaine F. Reed, PhD** — Daljit S. and Elaine Sarkaria Chair in Diagnostic Medicine
- **Elena Stark, MD** — 2015 David Geffen School of Medicine Excellence in Education Award
- **Gregory Fishbein, MD** — Recipient of the Brigham and Women’s Felix M. Brown, MD Pathology-in-Training Award
- **Hanlin Wang, MD** — Distinguished Pathologist Award from the Chinese American Pathologists Association (CAPA)
- **Janet Hindler, CLS** — Clinical and Laboratory Standards Institute Award.
- **Jeffrey Goldstein, MD** — Trustee of the American Board of Pathology
- **Jonathan Zuckerman, MD** — Department of Pathology and Laboratory Medicine 2015-2016 Daljit S. and Elaine Sarkaria Fellowship
- **Kenneth Dorshkind, PhD** — Interim Director, Jonsson Comprehensive Cancer Center
- **Neda Moatamed, MD** — Roberta K. Nieberg Anatomic Pathology Faculty Teaching Award
- **Omai Garner, PhD** — Faramarz Naeim Clinical Pathology Faculty Teaching Award
- **Rena Xian, MD** — Neil and Carol Ruzic Award for Cancer Innovation.
- **Ritchie J. Mendoza** — Clinical Pathology Technical Staff Teaching Award
- **Robyn Parks, MD** — Cardiovascular Achievement Award
- **Roya Hariri** — Administrative Staff Appreciation Award
- **Sophia Apple, MD** — 2016 College Outstanding Alumni Award, Wright State University.
- **Zhongyi Zhang** — Roy Bailey Anatomic Pathology Technical Staff Teaching Award
## ENDOWED CHAIRS

<table>
<thead>
<tr>
<th>Chair Type</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Executive Endowed Chair</td>
<td>$3,000,000</td>
</tr>
<tr>
<td>Permanent Endowed Chair</td>
<td>$2,000,000</td>
</tr>
<tr>
<td>Professional Development 5-Year (renewable) Term Chair</td>
<td>$1,000,000</td>
</tr>
<tr>
<td>Recruitment/Distinguished Service/Teaching (1-5 year) Term Chair</td>
<td>$500,000</td>
</tr>
</tbody>
</table>

## EDUCATION

<table>
<thead>
<tr>
<th>Position</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postdoctoral Researcher/Fellow</td>
<td>$1,000,000</td>
</tr>
<tr>
<td>Endowed Fellowships</td>
<td>$500,000</td>
</tr>
<tr>
<td>Graduate Student Researcher</td>
<td>$500,000</td>
</tr>
<tr>
<td>Clinical Resident Trainee</td>
<td>$500,000</td>
</tr>
<tr>
<td>Lectureships</td>
<td>$100,000</td>
</tr>
<tr>
<td>Teaching Awards</td>
<td>$100,000</td>
</tr>
<tr>
<td>Summer Youth Trainee</td>
<td>$10,000</td>
</tr>
</tbody>
</table>

## CLINICAL INNOVATION

- Pathology Translational Core Laboratory
- Clinical Genomics Core Laboratory

## DEDICATED RESEARCH

- Pathway Diagnostics
- Finding New Treatments for Brain Cancer
- Personalizing Treatment for Sarcomas
- Molecular Therapy of Obesity and Diabetes
- Women’s Health Studies
- Biology of Aging
- Advances in Transfusion Medicine
- Inflammatory Bowel Disease (IBD)
- Controlling Inflammation-Mediated Atherosclerosis

## GIFT DONORS

- Albert & Frances Piansky
- Arline Young Trust
- Armgenia
- Broad Stem Cell Research Center
- Carol And Howard Anderson Family
- Caroline V. Saltzman
- Clark Frank W Jr
- Claude N Cohn Memorial Research Fund
- Daljit S. And Elaine Sarkaria Endowment
- Dehgani-Fard Estate
- Dr. Elaine Sarkaria
- Dr. George N. Papanicolaou Endowment
- Dr. Richard Braun And Mrs. Barbara Braun
- Dunford Albert E Research Fund
- Eric Lax, M.a.
- Geleris Cancer Research Fund
- Genoptix Research
- Georgina Adams Medical Research Fund
- Gloria R. Malkin
- Haddad Jaye Concern Fellowship
- Lya Cordova Latta
- Henry Brandler Memorial Fund
- Henry E. Singleton Brain Cancer Research Fund
- Heumann Powered Productions
- Hibm Fund
- Hickey Family Foundation
- Hirshberg Foundation For Pancreatic Cancer Research
- James & Laura Maslon
- Jill & Martin Hyman-Moss
- Joanne W. Heumann
- John & Patricia Nickoll
- John &Wendy Henning
- Judith Carol Survivors Trust
- Judith Zolan Miller
- K H Burkholder
- Karen A. Sulzberger
- Kris & Judith Nakasu
- Lou & Melinda Spitz
- Mary Louise Honberger Fund

Michael M. Erman
Pace Sportswear, Inc
Peter & Deborah Heumann
Prostate Cancer Foundation
Rebecca Smith Endowment
Roy Walford Endowed Lectureship
Ruzic Research Foundation, Inc
Southern California Volkswagen Dealers
Spitzer Family Foundation
Stop Cancer
Stotter Revocable Trust
The Pritzker Family Endowed Chair
Thomas & Ann Martin
Vilma Peterson Estate
Volup Nathan & Zara Fund
William & Lynn Heumann

Explore opportunities for giving and make donations online at pathology.ucla.edu/giving.