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CONSTRUCTION ZONE

For those of you who work in or visit our Department, you know that we inhabit a construction zone. While our research, clinical, and education groups reside in 18 sites at the UCLA campus, West Los Angeles, and across the region, our single largest site is the Center for Health Sciences (CHS). The good news is that after 60 years traveling the seas of science and medicine, CHS is undergoing a comprehensive renovation. The bad news is that we are living in it as around us the storm of construction seethes. Demolition fogs our hallways, building vibrations spasm in our microscope rooms, caged light bulbs swing in the corridors like trenches of the Great War. And for much of this time, the State had engaged in a massive renovation of US405, the major commuter highway in our region, with incredible snarls from home to work and back again. It can only be the influence of USC that got these two projects scheduled at the same time!

Amidst all this, our community has drawn together with a healthy mix of resilience, skepticism, determination, and humor. People have made the construction into a journey, and the journey into a sometimes Odyssean adventure with many good stories to tell. There are measures of greatness, but none surpass what each individual does at a personal level. There is much greatness in our department.

Medicine and science these days are also a construction zone. It is not just the excitement and tumult of uncovering and assimilating new advances. Clinical finance and research finance, and the societal understanding of what medicine and science can or should offer to the larger community, are under ferment unprecedented since the Flexner era at the beginning of the prior century. When will the construction end, and will we like the outcome?

Unlike CHS, there isn’t a simple blueprint or timeline for this construction. In the department, we make this construction also a journey. The strategic plan, now in its second year, sets the goals for this stage of the journey—in research (hematopoietics, genomics); in clinical innovation to reshape regional healthcare (telepathology services, the BURL enterprise, radiology-pathology integrated diagnostics); and to make our department a better place to train and to pursue a career. There is already progress; the annual report is an amazing travel book of the journey this past year. So pursue and read on! Experience this year’s journeys, and imagine where the construction we complete this upcoming year will lead for us and the community we serve.

“MEDICINE AND SCIENCE THESE DAYS ARE ALSO A CONSTRUCTION ZONE.” - Dr. Jonathan Braun

Dr. Jonathan Braun, Professor and Chair Department of Pathology and Laboratory Medicine
Quality – in particular, efforts to ensure and improve patient safety, outcomes, and satisfaction – has become a ubiquitous term in hospitals, accelerated by provisions of the Affordable Care Act. Like many other hospitals’ focus in recent years, UCLA Health places a high premium on quality. Among other things, the hospital’s Quality Council emphasizes data-driven and proactive management of quality improvement efforts, and requires active tracking and management of improvement projects by clinical departments.

The Department of Pathology and Laboratory Medicine has long been a leader in UCLA’s quality assurance efforts. The department has active quality oversight programs to monitor the laboratory test cycle (pre-analytic, analytic and post-analytic phases), as well as the timeliness and completeness of testing. Nearly 70 quantitative metrics are tracked, reviewed, and improved upon by these programs. “These metrics are developed based on the requirements of accrediting agencies, institutional priorities, and quality deficits self-identified by the department, and are compared against national and peer standards,” explains Dr. Romney Humphries, the department’s chief of clinical microbiology. Metrics include monitoring mislabeled specimens, blood cultures contaminated during phlebotomy, pathology diagnoses sent for outside review, and turnaround time of frozen section reporting, to name a few.

While these programs have led to better quality and patient safety, Dr. Humphries notes that more work is yet to be done, “our department is now turning an eye toward moving quality efforts beyond the threshold accreditation standards by taking a leading role in quality improvement in the health system. Quality improvement differs from quality assurance in that it proactively creates improvement rather than reactively correcting deficits in existing quality assurance indicators,” says Dr. Humphries.
Last year the department developed a Quality Improvement Committee, which focuses on identifying departmental quality improvement priorities, aligning these with medical center priorities (Box 1), and monitoring the movement of these priorities toward goals. “Our department is in a unique situation among clinical departments, in that the services offered affect every patient cared for in the health system,” Dr. Humphries says. “As such, quality efforts on our part drive gains in quality, customer satisfaction, and financial performance across the system.”

With that in mind, the department’s current quality improvement priorities focus on two broad categories: test utilization and test reporting. The clinical chemistry program is targeting tests inappropriately used by UCLA physicians for hospital inpatients. As a first step, use of ionized calcium will be standardized for hospitalized patients (Figures 1 and 2). Total serum calcium is routinely performed as part of the metabolic panel and is the appropriate test for most patients. In contrast, ionized calcium requires special sample collection and handling and is required for only a minority of patients.

Pathology’s Dr. Kathleen Kelly, in collaboration with Dr. Paul DiCapua of the Department of Medicine, determined that approximately 45% of ionized calcium tests are likely ordered inappropriately, causing the use of additional instrumentation. Based on total admission in 2011, 43% of all ionized calcium measurements were drawn shortly after a previously normal ionized calcium and 18% were performed on patients that did not have conditions likely to alter calcium status. “We plan to address overuse of this test through educational campaigns and lectures by Department of Pathology and Laboratory Medicine residents, with the goal to reduce this ordering pattern and eliminate the additional instrumentation,” says Dr. Kelly. Microbiology has similarly targeted tests of misuse by evaluating the appropriateness of Clostridium difficile testing at UCLA. C. difficile is a common and serious cause of hospital-associated infection. “Historically, laboratory tests for C. difficile had poor sensitivity (50-70%) and physicians would test patients repeatedly to rule out infection,” Dr. Humphries says. “In addition, many physicians would continue empirical treatment for C. difficile for patients negative for the infection, due to a lack of confidence in the test results.” In 2011, the microbiology laboratory introduced a more sensitive PCR-based test for C. difficile and collaborated with the Division of Infectious Diseases, the UCLA Antimicrobial Stewardship program and UCLA Infection Control on an educational campaign on appropriate testing and treatment for C. difficile infection. In the first year of the campaign, inappropriate testing was reduced from 21% to 5%. This further decreased to 3% in 2012. Unnecessary therapy was also reduced – equating to improved patient care, and more than $275,000 in savings in 2011 alone.

Standardization of reporting in pathology is another priority in 2014. The College of American Pathologists (CAP) produces cancer protocols as a resource for pathologists to aid in effective reporting of surgical pathology findings necessary to provide quality patient care. These “synoptic” reports contain case summaries, background documentation, explanatory notes, and references, ensuring that key findings are clearly and consistently relayed to the treating physician. Standardization of surgical pathology reports will be accomplished using modified CAP protocols for the majority of cancer diagnoses beginning this year.

“Quality improvement is the responsibility of all staff, trainees, and faculty in the department,” Dr. Humphries concludes. “These case studies represent just a small sampling of the culture of continual quality improvement we now foster, with the goal of standardizing care processes and producing better outcomes for patients at UCLA.”

<table>
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<th>Box 1. UCLA Health System Quality Initiatives</th>
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For years, the Gevorkyan family lived with uncertainty about their daughter, Vianna’s condition. Family planning decisions were postponed out of concern that the genetic cause responsible for Vianna’s developmental delays and intractable epilepsy – which had defied diagnosis, despite a seemingly endless series of tests to determine the underlying cause – would be repeated.

Families like the Gevorkyans, whose children are born with rare disorders and no definitive diagnosis, ride a roller coaster of emotions as hopes are raised and then dashed with each new test. “You don’t understand what is happening with your child, what additional symptoms to look for, or what the future holds,” says Eric Vilain, MD, PhD, co-director of the UCLA Clinical Genomics Center.

Through its pioneering efforts putting so-called next-generation DNA sequencing to clinical use, the center is often able to eliminate this uncertainty. For patients suspected of having a rare genetic disease that has eluded diagnosis through conventional means, a single test surveys the protein-coding regions of the genome, where the vast majority of disease-causing variants are believed to lie. Rather than analyzing one gene at a time, the center simultaneously sifts through virtually all of the 37-million base pairs in 20,000 genes in pursuit of the single DNA change responsible for the patient’s disorder. Nearly half the time, the test yields a potential diagnosis for patients whose cases have baffled other specialists. In addition to the catharsis of knowing and being able to move forward, diagnosis can point the way toward potential treatments or the ideal clinical trial.

By the time the Gevorkyans’ diagnostic odyssey reached UCLA’s Clinical Genomics Center, the FDA had finally approved a drug that could better control Vianna’s seizures. The diagnosis confirmed why the drug was effective – and enabled the family to move beyond the nightmare of uncertainty. The Gevorkyans no longer needed to agonize about having more children: Clinical exome sequencing completed at the center determined that the risk is small and they can test for the mutation before going forward with a pregnancy. “Now we can focus on improving Vianna’s health,” says Audrey Gevorkyan, Vianna’s mother.
As a simple, fast, and cost-effective method to screen for cancer and other diseases, cytology is a widely used and invaluable diagnostic tool. Within the UCLA Department of Pathology and Laboratory Medicine, the Division of Cytology offers a comprehensive cytodiagnostic, screening and consultative service, reviewing approximately 38,000 cases each year involving gynecologic, non-gynecologic, and fine needle aspiration (FNA) specimens. “Cytology looks at cells, and often times a single abnormal cell from the body can lead to a very significant diagnosis,” explains Jian Yu Rao, MD, section chief.

UCLA’s cytology program has trained and educated numerous cytopathologists, many of whom have become national and international leaders in the field. “I am proud to have trained so many pathologists in the art of cytology,” says Sharon Hirschowitz, MD, a long-time professor in the division. “Cytology can be likened to a tiny golden key that allows us access to a world full of treasures.” Beyond training cytopathologists, the program is one of only two in California that trains cytotechnologists.

UCLA’s cytologists provide high-quality, comprehensive consultation services and direct support for numerous research projects. The division’s reach extends overseas – an international tele-cytopathology program provides second-opinion diagnoses for institutions in countries with limited cytopathology resources. Locally, outreach includes annual participation in the CareNow LA Health Fair to provide free Pap smear diagnostic services.

The division has been a leader in utilizing new technologies to improve cytological diagnosis – for example, UCLA is one of only two centers offering the uCyt method for more precise urine cytology. A state-of-the-art ultrasound-guided FNA clinic includes highly trained cytopathologists who provide rapid on-site assessment.

Faculty members in the division are continuing to advance the field through pioneering work in the development of functional nanocytology. The emerging field combines traditional morphology and molecular analysis at the single-cell level to provide not only more precise diagnostic information, but – even more importantly – to guide the clinical management of patients by predicting drug sensitivity in cancer. The nanocytology approach, developed by Dr. Rao and his cytopathology colleagues along with researchers at UCLA’s California NanoSystems Institute, has been published in high-profile scientific journals and has gained widespread attention.

“Our understanding of human cancer has gone from gross appearance to tissue and cell morphology, and to the current molecular level,” says Dr. Rao. “This may bring cancer diagnosis and management to a stage beyond molecular analysis.”

“Cytology can be likened to a tiny golden key that allows us access to a world full of treasures.”

- Sharon Hirschowitz, MD
THE SINGLE RADPATH REPORT...ALLOWS TREATING CLINICIANS TO MORE QUICKLY AND COMPREHENSIVELY EVALUATE PATIENTS IN CLINICAL PRACTICE, WHILE THE LINKS TO THE IMAGING STUDIES GIVE CLINICIANS AND PATIENTS A BETTER VIEW AND UNDERSTANDING OF THE DISEASE PROCESS...

THE RADPATH REPORTING SYSTEM INNOVATES IN COMMUNICATION AND PATIENT CARE

UCLA RadPath, a new diagnostic reporting system jointly developed by UCLA’s radiology and pathology departments, is moving from the test environment into clinical practice this year. The system, a major clinical improvement project for the UCLA medical enterprise, combines pathology and radiology reports through a dynamic, web-based platform that also links to the diagnostic imaging studies and communication functions such as email and paging.

The single RadPath report brings several advantages. It allows treating clinicians to more quickly and comprehensively evaluate patients in clinical practice, while the links to the imaging studies give clinicians and patients a better view and understanding of the disease process. In addition, the email link facilitates fast and contextualized discussions, optimizing clinician interactions while reducing the misunderstandings or knowledge gaps that can result in suboptimal patient care.

Designed and developed by a team led by Dr. Dean Wallace of the Department of Pathology and Laboratory Medicine and Dr. Corey Arnold of the UCLA Department of Radiology, UCLA RadPath is the most advanced combined radiology/pathology web-based reporting platform in the world, Dr. Wallace says. “By bringing pathology into the radiology environment, the radiologist now has the ability to review the final pathologic diagnosis and correlate it with his or her original impression,” he explains. “This correlation is included in the final diagnostic RadPath report to fully clarify the disease process, potentially preventing misunderstandings as well as delays in diagnosis if the radiologic interpretation differs significantly from the pathologic diagnosis. The correlation may also prompt the clinician to consider repeating the biopsy.”

On the flip side, Dr. Wallace notes, bringing radiology findings into the pathology environment contributes to the pathologist being better informed of the overall disease process and able to render diagnoses with more confidence and accuracy – and in some cases to reconsider the diagnostic comments. The system has earned praise outside of the two departments. Says Dr. Jay Lee, chief of thoracic surgery at UCLA: “This is an extremely valuable project and I am very much looking forward to using it in clinical practice. It will only enhance our integrated practice unit for lung cancer at UCLA.”
DEPARTMENT SERVICES EXPANDING TO NEW LOCATIONS

The Department of Pathology and Laboratory Medicine is joining with the Department of Medicine and UCLA Health in delivering care through newly established and planned future services in the San Fernando Valley, Conejo Valley, and South Bay. To help facilitate the expansion, in March 2013 the pathology department and UCLA Health opened an outreach reference laboratory, BURL, fitted with state-of-the-art equipment and analyzers.

UCLA Health expanded access to primary and secondary care services to the Conejo Valley with the opening of its medical office in Westlake Village – the first of six new UCLA primary/secondary care sites scheduled to open over the next two years in service areas beyond the Westwood and Santa Monica campuses. Soon thereafter, the first of several planned “STAT” laboratories opened at the Westlake expansion site. The BURL Westlake STAT Lab has a patient blood draw station and offers immediate results for many blood and urine chemistries, along with other rapid testing. Additional sites have opened in Porter Ranch and Calabasas. In February, the Community Physician Practice Network moved its laboratory testing to BURL, and two other groups are following imminently.

With the new locations, the department has enhanced its ability to deliver convenient, high-quality care to people who live or work outside UCLA’s traditional primary-care service areas, while providing a gateway to higher levels of care within the UCLA system for patients who need them. Additional practices are scheduled to open in Thousand Oaks, Porter Ranch, Calabasas and Santa Clarita in the next two years. UCLA will also open a new primary/secondary care location in Redondo Beach. These state-of-the-art offices will offer a full range of primary care subspecialties, including internal medicine, family medicine, pediatrics, and women’s health, as well as ancillary and secondary care services.

In addition to bringing highly advanced, integrated care to new communities, the UCLA practices will engage in community education and outreach through mechanisms such as newsletters, physician lectures, and participation at shopping centers, health fairs, and farmer’s markets.
NEW SANTA MONICA BLOOD DRAW CENTER DESIGNED TO PUT PATIENTS AT EASE

The 2011 unveiling of UCLA Health’s rebuilt Santa Monica campus – including a 510,000-square-foot hospital complex and outpatient clinics – has enhanced the ability of UCLA Health to fulfill its mission to “heal humankind, one patient at a time, by improving health, alleviating suffering, and delivering acts of kindness.” The Santa Monica campus provides the technologically advanced care for which UCLA is known in a compassionate, convenient and comfortable setting, replete with ample natural light, trees, and green spaces.

The Department of Pathology and Laboratory Medicine is an integral part of fostering this patient-friendly environment – particularly since the opening last August of a new blood draw center across the street from the 266-bed UCLA Medical Center, Santa Monica inpatient facility.

“The new blood draw center improves our ability to provide outstanding patient care and service,” says Steven Hart, MD, co-director of the pathology lab at UCLA Medical Center, Santa Monica. Previously, he explains, when patients went to one of the clinics and were asked to have their blood drawn, their encounter with UCLA’s pathology staff occurred in a cramped space. “There wasn’t enough room for everyone to wait inside, and as a result, patients often had to wait in the hallway. In addition, waiting times were longer,” Dr. Hart says. “So we made an effort to find a new station.”

The new center, located one floor above the old one, is considerably larger, with a waiting room that includes plenty of comfortable seating. The center also includes dedicated pediatric and maternal blood draw rooms. In many cases UCLA pathologists are able to process specimens at optimum temperatures immediately after the draws.

Pathology’s contribution to the patient-friendly environment extends to the hospital facility, where inpatients are in regular contact with the phlebotomists who visit their rooms to draw blood. UCLA pathologists also work closely with surgeons, providing frozen sections during operations; work alongside interventional radiologists to assess for adequacy during image-guided core biopsies; and work directly with patients in performing bone marrow biopsies in the surgery center.

“This is a smaller hospital campus with a true community feel, while providing UCLA’s world-class care,” says Dr. Hart. Our pathology department is fully integrated in this effort. Through the new blood draw center and our interactions with hospital patients, we are proud to be contributing to patients’ positive experiences.”

“THE NEW BLOOD DRAW CENTER IMPROVES OUR ABILITY TO PROVIDE OUTSTANDING PATIENT CARE AND SERVICE...”
– Steven Hart, MD
The University of California and UCLA Department of Pathology have signed an agreement with Centre Testing International Corp., a Chinese firm, to create a company that will operate a clinical laboratory in Shanghai. The new lab will support clinical trials and enhance medical care for Chinese patients with cancer and other diseases.

The new company, CTI-Pathology/UCLA Health, is jointly owned by CTI and the University of California. The 25,000-square-foot facility — the first of its kind in China — will offer genetic and molecular diagnostics and other sophisticated tests that exceed the scope of the average lab in China, and UCLA pathologists will train Chinese lab specialists to accurately interpret the tests. The lab is expected to open in September, 2014.

The partnership is the first between a Chinese company and a U.S. academic medical center to create a specialized laboratory in China. “This joint venture is founded on UCLA's desire to build strong global relationships that, through education, research and service, improve the health of people and communities throughout the world,” said Dr. Tom Rosenthal, chief medical officer for UCLA Health and co-director of UCLA's Center for World Health. “UCLA has a genuine interest in elevating the level of medicine around the world. This is one way we can really make a difference in the quality of the Chinese people's health care and lives.”

“We are extremely pleased that UCLA Health, the UCLA Department of Pathology and the UC Regents agreed to partner with CTI to establish and manage our joint venture laboratory in Shanghai,” said Sangem Hsu, president of CTI. “Our collaboration will offer the people of China oncology, pathology and laboratory medicine services they can trust. Many of these services are not largely available in China and are needed by physicians and health care providers to accurately diagnose and treat their patients.”

The Shanghai laboratory will be electronically and digitally linked with UCLA — enabling physicians and patients to consult with UCLA pathologists — and with hospitals, clinics and other laboratories throughout China.

“CTI will be an outstanding partner in our effort to significantly improve patient care in China,” said Dr. Scott Binder, senior vice chair of pathology and laboratory medicine at the Geffen School of Medicine, and director of pathology laboratory services for UCLA Health System. “Because pathology has a history of being undervalued in China, the country has a shortage of pathologists trained to diagnose and interpret complex test results in specialized fields of medicine,” Binder said. “Our partnership gives CTI and UCLA the opportunity to save lives by changing that.”

“CTI will be an outstanding partner in our effort to significantly improve patient care in China.”

- Scott Binder, MD
For Dawn Ward, MD, UCLA is the ideal place to be practicing transfusion medicine. Dr. Ward recently joined the Department of Pathology and Laboratory Medicine as an assistant professor and member of the UCLA Transfusion Medicine Service Laboratory, which provides standard and specialized blood components for transfusion, compatibility testing for recipients, and diagnostic testing to evaluate for a variety of factors toward ensuring the safety of transfusions.

“UCLA is strongly supporting research in stem cell biology and regenerative medicine,” Dr. Ward explains. “That makes it more important for someone like me to be here to assist these researchers in making sure that patients get access to products with the potential to improve their health.”

Transfusion medicine, often referred to as blood banking, is concerned with all aspects involved in the transfusion of blood and blood components. To help ensure a safe and adequate supply of blood components for UCLA Health patients, the UCLA Blood and Platelet Center collects approximately 30,000 whole blood and platelet donations per year. The center also organizes mobile blood drives throughout the Los Angeles metropolitan area and collects from third-party donors, following strict screening protocols. On the laboratory side, medical technologists test the blood for everything from blood type and compatibility to infectious diseases. About 75,000 blood products are transfused each year at UCLA.

Dr. Ward is interested in one of the newer and more exciting areas of transfusion medicine, involving cellular therapeutics – particularly hematopoietic stem cells derived from bone marrow, peripheral blood, and umbilical cord blood, collected from patients and donors for transfusion. “Within the last few years, researchers have learned to effectively treat a number of different diseases through transplantation of a variety of cell types,” Dr. Ward explains. “That has expanded the role for those of us in transfusion medicine.”
Because of their experience in ensuring the safety of blood, Dr. Ward and her colleagues play a critical role in assisting researchers in meeting good manufacturing practices (GMP) - the procedures that must be followed by all laboratories and companies involved in producing drugs, devices, and other products for patient use. As a transfusion medicine specialist, Dr. Ward is working with UCLA researchers in the development and implementation of additional GMP space. She will also provide integral support in the transfer of cellular therapeutics from the research laboratory to the clinical setting. Dr. Ward will work alongside investigators within the Broad Institute for Stem Cell Biology and Medicine and the Jonsson Comprehensive Cancer Center as they develop their cellular therapies for patient research. She will also participate in training residents and fellows in transfusion medicine and cellular therapeutics.

Transfusion medicine specialists such as Dr. Ward are ideally suited for cellular processing, and Dr. Ward’s background in biotechnology as well as transfusion medicine uniquely prepares her for many aspects of cellular therapy, including not only GMP Phase I/II manufacturing, but also manufacturing of blood and bone marrow for transplantation. “Traditional transfusion medicine and blood banking require quality assurance/quality control [QA/QC] and strict regulatory oversight,” Dr. Ward explains. “In order to produce consistently high-quality products, QA has become a critical part of cellular therapy laboratories. Cellular processing also requires extensive QA/QC and regulatory guidance for the development of products and compliance with FDA regulations. Cell therapies must be safe, pure, sterile, stable, and potent.”

“My ultimate goal in this position is to allow clinical investigators the ability to focus on their research while a dedicated cell processing group is available to perform the scale-up, validation and production of safe and pure products for UCLA patients,” Dr. Ward explains. “It is rewarding to know that I’m helping to make sure patients are receiving the latest cutting-edge therapeutics that are available. Even though I am not directly working with these patients, my part of the process could contribute to a better quality of life or cure for their disease. That’s what drives me to do all of this.”
Each year, tens of thousands of people around the world die of complications from seasonal influenza, while millions more are hospitalized or suffer at home. Children, the elderly and those with compromised immune systems are particularly vulnerable.

Dr. Omai Garner, a member of the UCLA Department of Pathology and Laboratory Medicine faculty, is working with colleagues in UCLA’s engineering school in an effort to fundamentally improve the ability to quickly, accurately and cost-effectively diagnose influenza using a portable telemedicine platform.

Rapid diagnostic tests for seasonal influenza are now available, but lack sensitivity and the ability to differentiate among influenza subtypes, Dr. Garner notes. This has hampered efforts at flu surveillance, prevention, and infection control in clinical settings. ELISA (Enzyme-Linked ImmunoSorbent Assay)-based detection is more sensitive, but automated ELISA-based detection of influenza has proved difficult to adapt for point-of-care testing, Dr. Garner says, in part because it requires a number of manual steps and skilled operators for results to be reproducibly accurate and sensitive.

Along with his engineering school colleagues, Dr. Garner has sought to develop a digital detection system that makes use of flexible and droplet-based microfluidics technologies, as well as cell phone-enabled multi-color fluorescent cytometry and computational microscopy tools. This distributed detection approach aims to improve the efficacy and robustness of ELISA to achieve high-sensitivity field-portable influenza diagnostics by:

- automating sample preparation and analysis processes with flexible electro-adaptive and inertial microfluidic technologies;
- increasing sensitivity and multiplexing using droplet-based signal amplification and a wide-field computational imaging platform running on a cellphone, where a larger field of view results in an improved detection limit and dynamic range;
- reducing temperature and time sensitivities of detection by performing the immunoassay in a digital format (especially important for field testing); and
- providing real-time spatiotemporal statistics to aid in predicting, managing, and analyzing epidemics/pandemics.

“There is an urgent need for rapid, robust, sensitive, and specific influenza surveillance systems worldwide,” Dr. Garner says. He is hopeful that his group’s work will help to fill the void.
The laboratory of Michael Teitell, MD, PhD professor in the department, has discovered how mitochondria (the energy “power-plant” organelles found in all human cells), stem cells, and cancer functionally converge, with potential implications for new treatment approaches.

Their fundamental idea was that a crucial determinant of behavior by stem cells might be their type and amount of energy production. The perplexing clue was that mitochondria of stem cells, unlike differentiated cells, consume oxygen (respire) without generating significant energy. The difference is that stem cells rely on glycolysis – a primitive, oxygen-free way to produce energy that is used similarly by cancer cells. This form of metabolism, while inefficient for energy production, redirects the cell to produce building blocks for rapid cell duplication, a common feature of early stem cells – and of cancer cells.

How are mitochondria retooled to function so differently? Dr. Teitell’s group determined that stem and cancer cells achieve this by producing a modifier protein, UCP2 (for uncoupling protein 2). UCP2 is transported by the stem cell into its mitochondria, where it impairs energy production by inhibiting access of sugar intermediates required for respiration. “Remarkably, UCP2 has emerged as a protein produced by a wide variety of tumors, including cancers of the bladder, esophagus, testis, and breast, along with leukemias and lymphomas – but not in the normal cells from which these cancers arose,” Dr. Teitell explains. “Our studies suggest that cancers may replicate stem cell metabolism and lose features of differentiation at least partly because UCP2 shunts energy-producing substrates away from mitochondria and into glycolysis.”

Dr. Teitell and colleagues are now testing whether blocking the function of UCP2 or similar proteins can reverse this process in stem cells or cancer, and redirect them into cell differentiation. If successful, this offers a new strategy for generating replacement cells for regenerative medicine therapies, or for helping to combat a wide variety of cancers.

UCP2-regulated mitochondria function. Early human stem cells (left) express UCP2, which prevents sugar intermediates, like pyruvate, from entering mitochondria. Aberrant UCP2 re-expression has been identified in cancers (left), where it may reprogram energy metabolism back to a stem cell-like state. On the right is a UCP2-negative differentiated normal cell. Key: ETC, electron transport chain; OXPHOS, oxidative phosphorylation (e.g. respiration); ROS, reactive oxygen species; TCA, tricarboxylic acid cycle; UCP2, uncoupling protein 2.
A surprising new frontier in medicine is the discovery of the human microbiome— the enormous but invisible communities of microorganisms that cohabit our body’s gut, skin, lungs, and genitourinary tract. The awareness of the microbiome came from two advances—pioneering molecular ecology concepts established during the previous decade, and technologies emerging from the recent human genome project. The challenges at this frontier are to identify the composition of the microbiome, how it differs between individuals, what roles it plays to protect or induce disease, and how to garden the microbiome to our benefit.

In the Braun lab, the microbiome work centers on two diseases—Crohn’s disease and cancer (lymphoma) susceptibility. Crohn’s disease and the related syndrome, ulcerative colitis, result from altered interactions between gut microbes and the intestinal immune system, but how intestinal microbiota contribute to IBD remains to be elucidated. Recent work by the Braun lab and a national consortium led by Dr. Braun established that disease-associated microbiome changes involve critical microbial biochemical pathways and metabolic products that may directly affect the health of the intestinal mucosa. It also has begun to map these microbiota and products with IBD genetic variants, thus perhaps opening the path to a “Rosetta stone” between the microbiome and IBD genetics. In the work ahead, the group is identifying microbial products important to mucosal health that can be therapeutically targeted—by blocking the production of deleterious ones, and restoring beneficial ones that are deficient in Crohn’s disease patients.

A collaboration of the Braun lab with Dr. Robert Schiestl and an international group of scientists, discovered that specific types of bacteria that live in the gut are also major contributors to lymphoma, a cancer of the white blood cells. In mice genetically at risk for lymphoma, they discovered that certain compositions of the microbiome allowed mice to live much longer. Mechanistically, this was due to microbiota whose products reduce or augment gene damage (genotoxicity) activity in white blood cells that cause lymphoma. This work is the first to show a relationship between intestinal microbiota and the onset of lymphoma. Since the composition and products created by microbiota is a modifiable trait, these results hold considerable promise for intervention of B cell lymphoma and other diseases.

“[The Braun lab] has begun to map these microbiota and products with IBD genetic variants, thus perhaps opening the path to a ‘Rosetta stone’ between the microbiome and IBD genetics.”

— Jonathan Braun, MD
Duchenne muscular dystrophy is the most common lethal genetic muscle disease of childhood, causing profound loss of skeletal muscle function. With advanced diagnostic techniques, including whole genome sequencing, doctors can identify the mutation in the dystrophin gene that causes Duchenne in almost all boys. However, even with that information, boys with Duchenne can have dramatically different disease courses. For instance, the average boy with Duchenne loses the ability to walk independently by age 10; however, some boys with the disease never walk and have a more severe progression – dying from complications before the age of 10 – while others can still walk past the age of 18.

In an effort to determine why the disease can be so variable, Parent Project Muscular Dystrophy provided $100,000 to Dr. Stanley Nelson, Director of the Clinical Genomics Center at UCLA, to examine the entire genomes of boys with Duchenne muscular dystrophy who are either very mildly affected or very severely affected. “The goal is to identify changes in genes other than dystrophin that may affect the course of the disease,” Dr. Nelson explains. “DNA variants in other genes may play a key role and highlight new ways to treat the disorder. It is also likely that some of the changes identified will be relevant to other forms of muscular dystrophy and muscle disease.”

Dr. Nelson is using a relatively new technique, known as exome sequencing. Because the exons of the genome make up less than 1% of the total genetic material, this method provides a cost-effective way to look at all genes that encode all 20,000 human proteins. For this project, Dr. Nelson is obtaining blood samples from boys and men throughout the world who have a known Duchenne diagnosis based on genetic data or muscle biopsy, along with an unusual course of the disease. The work is being conducted within the Center for Duchenne Muscular Dystrophy at UCLA, with additional analyses supported by the Genomics and Bioinformatics Core of the UCLA Muscular Dystrophy Core Center.

Information generated from the project has the potential to serve a number of important purposes, including providing critical insight into biological functions that affect Duchenne muscular dystrophy progression; allowing clinical trial sponsors to select participants with more similar disease courses based on genetic data (to design smaller, faster, and more powerful trials); and identifying new protein targets for drug development.
For many students, medical school represents the introduction to pathology – or at least a first opportunity to correct misconceptions they may have had about what it means to be a pathologist. A number of innovative courses are available to medical students at UCLA’s David Geffen School of Medicine that provide an authentic look at the diverse and vibrant opportunities available in pathology and laboratory medicine. These courses are designed to interest students at different stages in their training, through both selectives (offered to first- and second-year medical students) and electives (offered to third- and fourth-year students).

Intro to Pathology

“Intro to Pathology,” a first-/second-year selective, aims to provide students who are still deciding on their specialty with an accurate view of pathology. Dr. M. Fernando Palma-Diaz, assistant clinical professor of pathology and laboratory medicine, began teaching the introductory course this year. His goal is for each student to leave with a real-world view of what a pathologist does on a daily basis.

The course’s integrative approach exposes students to many of the basic areas of pathology, balancing their time between anatomic and clinical pathology rotations. During the seven-session, two-hours-per-week program, students are introduced to some of the department’s anatomic pathology and clinical pathology facilities in order to get a better understanding of the workflow of specimens once they reach the department. Students are also scheduled for rotations through cytopathology, surgical pathology, molecular pathology, and microbiology. As part of the surgical pathology rotation, students spend a session covering the gross room and the frozen section service, with the goal of giving them a practical view of a career in pathology.

For students who ultimately choose a specialty other than pathology, the course provides an important opportunity to better understand the role of pathology in nearly every facet and stage of medicine. Students learn to appreciate pathology’s role in diagnosis, detection, monitoring, and management, and leave with more realistic expectations about pathology’s
Nicole Dawson, MD and M. Fernando Palma Diaz, MD

capabilities — and its limitations. Dr. Palma-Diaz emphasizes that patient care is enhanced when colleagues understand all that is involved — including, for example, reasons a biopsy report may take longer than anticipated. The course consistently receives high marks from students, and its reputation is growing. This year, an unprecedented six students are participating — a dramatic change from the average of two students per session in previous years.

**Multidisciplinary Breast Oncology**

An example of an innovative, immersive elective offered to fourth-year students is “Multidisciplinary Breast Oncology.” This pioneering course, taught at the UCLA Breast Center in Santa Monica, is designed to expose medical students to the multidisciplinary approach to breast cancer, incorporating pathology, radiology, surgery, and oncology. The course highlights pathology’s critical role, as students follow specimens out from surgery through to pathology and into the gross room, where they experience how specimens are handled. They also have the opportunity to participate in frozen section and to attend a tumor board meeting.

Associate Professor Nicole Dawson of the Department of Pathology and Laboratory Medicine spends approximately three afternoons every three weeks with students in the breast elective, reviewing slides in depth and mentoring students. She values how this unique educational model follows patients from diagnosis to surgery to treatment. Students often stay with the same patient through each stage — an experience that resonates. This approach provides trainees with a sense of the multidisciplinary nature of medicine, and how each area works together as a team — a concept that is difficult to convey in a classroom environment.

Key to the success of the course is UCLA Breast Center coordinator/patient navigator Robin Dvorak, who schedules and coordinates the program to ensure that each student has an opportunity to rotate within every specialty. Participants give the course high praise. “The UCLA Santa Monica Breast Center exemplifies the type of patient care that makes me proud to be a UCLA medical student,” says one. Adds another: “...by far the most educational clinical rotation that I have taken...it achieves the goal of exposing the student to each phase of breast cancer diagnosis and treatment.”

The holistic, hands-on approach to training that these courses exemplify is so well received that it is being expanded to other areas within the medical school. For students with an interest in pathology, it is an invaluable opportunity to experience the range of opportunities within the discipline, and to appreciate pathology’s fundamental role in medicine.
THE PATHOLOGY INTEREST GROUP (PathIG), initiated for the 2013-14 academic year, is designed to inspire and educate the next generation of leaders in pathology and laboratory medicine. The program highlights the various roles in pathology and their impact on the medical field, as well as offering a venue for UCLA medical students interested in pathology to further explore the field.

PathIG includes informative sessions with guest speakers, microscope review sessions, shadowing opportunities, research fairs, and mixers. Medical student coordinators Jason Scapa (the program’s founder), Sara Mottahedan, Richard Morgan, and Kevin Yang organize and manage the program, which is under the leadership of Dr. Elena Stark, vice chair for medical and dental education in the department.

The inaugural PathIG Speaker Series sessions, which explored the field of pathology clinically, as well as its importance in research and education, proved to be an overwhelming success. The first session, “Pathology as a Specialty,” was led by Drs. Linda Baum, M. Fernando Palma-Diaz, Dinesh Rao, Peggy Sullivan, Dawn Ward, and Elena Stark. This was followed by “Introduction to Dermatopathology,” presented by Drs. Scott Binder and Peter Sarantopoulos. Both events were attended by more than 50 first- and second-year medical students. The inaugural Pathology Review Series, focusing on examining the histopathology pertinent to Block 7 of the medical school curriculum, was so successful that the session had to be doubled when 30 students turned up for an anticipated 12 openings. Additional sessions held during the year included “Collaboration Between Pathology and Radiology,” “Surgical Pathology,” and multiple microscopic sessions.

“During our first year of medical school, we learn about the normal and abnormal histological findings; these talks are helping me understand how to translate my enthusiasm in histology lab to a future career,” shared first year medical student Sina Rabi. Delila Pouldar - also a first year medical student - adds, “Through the shadowing opportunities provided by PathIG, I was introduced to the clinical applications of our histopathology coursework and it also cultivated my interest in the field as I witnessed it’s vital role in whichever field I ultimately choose.”

Says Dr. Stark: “The success of these initial Pathology Interest Group programs both ensures its continuance and provides a mechanism to spread the word about pathology’s broad, diverse, and integral role in nearly every facet of medicine.”

...THESE TALKS ARE HELPING ME UNDERSTAND HOW TO TRANSLATE MY ENTHUSIASM IN HISTOLOGY LAB TO A FUTURE CAREER.”
- Sina Rabi, first year medical student
PROGRAM MEETS MAJOR NEED BY TRAINING CLINICAL LABORATORY SCIENTISTS

Each year, nearly 300 clinical laboratory scientists perform more than 6 million clinical tests in the 11 UCLA Health laboratories located throughout Los Angeles County. The demand for highly skilled clinical laboratory scientists will only escalate as UCLA’s Department of Pathology and Laboratory Medicine expands its outreach program.

Since 2002, the department, in affiliation with California State University Dominguez Hills, has provided training to 48 post-baccalaureate clinical laboratory scientist students. The focus of the one-year clinical training is to impart the technical skills as well as the theoretical background required to interpret and analyze test results performed in a multitude of clinical disciplines. Clinical rotations include chemistry, toxicology, hematology, coagulation, bacteriology, virology, serology, and blood banking. Emphasis is placed on working interactively alongside a licensed clinical laboratory scientist. This interaction enhances the understanding of the diagnostic theory of testing and its association with disease, as well as developing the groundwork for thinking outside the box.

Statewide, the need for highly skilled clinical laboratory scientists is expected to continue rising because of a rapidly retiring workforce. To meet this challenge, and to augment the generalist clinical laboratory scientist program, one-year clinical laboratory scientist limited license programs were established. Limited license program opportunities are offered in clinical laboratory disciplines that include cytogenetics, genetic molecular biology, immunohematology, and microbiology. During the intensive one-year clinical training in their chosen discipline, students are exposed to all aspects of their specialty, including research, management, and quality assurance.

Utilizing the abundant educational, technical, and research expertise within UCLA Health, the Department of Pathology and Laboratory Medicine aims to develop and mentor the next generation of highly skilled laboratorians who will perpetuate a tradition of excellence.

EXPLORE the UCLA Clinical Laboratory Scientist Program pathology.ucla.edu/cls
Anatomy Academy, a school-based health intervention program offered by the Department of Pathology and Laboratory Medicine’s Division of Anatomy since June 2012, satisfies a selective course requirement for David Geffen School of Medicine (DGSOM) students while educating community middle school students about the importance of developing and maintaining healthy lifestyles.

Under the directorship of Naomi Schmalz, an associate in the department, and through the continued support of Dr. Elena Stark and the passion of DGSOM medical students Vartan Tashjian and Erica Tukiainen, Anatomy Academy provides an interactive and engaging opportunity for students from a low-income middle school in the local community to take an active role in their own health. The program supplements existing physical education curricula with an interactive learning experience that teaches biological concepts about human anatomy and physiology, as well as nutrition and physical activity.

Medical and undergraduate students, called mentors, engage students through exercises using anatomical models, as well as a variety of hands-on, recreational and sports activities. The fall-semester program is held an hour a week for six weeks, focusing on the basic anatomic, physiologic, and health-related features of a different body system each meeting.

Everyone benefits. Middle school students gain knowledge and tools designed to help them lead healthier lives and decrease their risk for developing chronic diseases, and they are enriched by excellent role models who in some cases inspire them to pursue a college education. Undergraduate mentors appreciate their interaction with medical student mentors, who in some cases motivate them to pursue degrees in medicine. For their part, medical student mentors enhance their understanding of anatomical concepts and are challenged to translate complex anatomical and medical concepts to middle school students— an invaluable and often overlooked skill crucial to effective patient and colleague communications.

Equally important is the hands-on community experience that the program encourages. “Anatomy Academy gave me the opportunity to [teach] stress-relieving exercises so that students can deal with problems in the community and home in order to achieve well-being. The exercises were a success and I felt like I really made a difference,” says second-year medical student and fall 2013 program coordinator Vartan Tashjian, who taught a session on stress relief and stress’ impact on digestive and mental health.

While the goals of Anatomy Academy lie primarily in improving middle school students’ knowledge of anatomy, health, exercise, and nutrition to encourage healthy lifestyles, the impact of the program is multifaceted, shaping the personal and professional development of all involved.
Long recognized as a pioneer in human leukocyte antigen (HLA) typing and cross-match testing for tissue and organ transplants, the UCLA Immunogenetics Center is expanding its purview into non-transplant areas while continuing to serve as an invaluable resource in HLA research and the development of accompanying diagnostic testing.

“The Immunogenetics Center is devoted to the study of the human immune system and the genes that regulate that system,” says Dr. Elaine F. Reed, director of the center, which is part of the Department of Pathology and Laboratory Medicine. “These are important concerns for HLA disease association and histocompatibility — particularly for solid organ and stem cell transplantation, but also for other areas related to health and disease.”

The newest addition to the center’s expanding portfolio is the Immune Assessment Core, a comprehensive source for immune assessment testing services needed in basic, clinical and translational studies. The laboratory develops and performs a variety of immunological tests using cutting-edge high-throughput technologies to evaluate the immune status of study subjects. Through non-invasive blood tests, the new lab is bringing the work the center has done in transplantation to a wider scope of patients. “Immune inflammation is now known to be a component of many different diseases, including cancer, heart disease and autoimmune diseases,” notes Dr. Reed. “Understanding what inflammation does and knowing when it’s present or absent can help guide the management of patients.”

Immune assessment testing services developed within the laboratory will be applied to seeking a better understanding of tumor immunology and therapies used to fight cancers through the immune system, determining whether drugs are effective for patients with rheumatologic disease, and identifying when older patients’ compro-
mised immune systems point toward the need for altered therapies, to name a few.

While the Immune Assessment Core will initially focus on patients with known immune system concerns, Dr. Reed suspects that ultimately the tests the lab is developing could become routine aspects of primary care. The Immune Assessment Core team hopes to establish criteria for a healthy immune system across different human subpopulations and age groups, and to use these metrics to identify patients at risk for immune and inflammatory diseases. “We envision that patients might get an immune assessment panel as part of going to their doctor for an annual physical, just like you have your cholesterol checked,” Dr. Reed says.

The mainstay of the Immunogenetics Center continues to be in matching organ and stem cell transplant donors and recipients, assessing recipients’ histocompatibility and immune status at the time of the transplant, and weighing the transplantation risk. The center is a World Health Organization reference laboratory for HLA typing and has trained many laboratory and scientific personnel across the nation and globally in HLA typing. And here, too, the center’s role is growing, as it becomes increasingly involved in the post-transplant period through efforts to prevent chronic rejection.

To help guide care after the transplant, the center has developed tests that can measure the patient’s response to the donor tissue and the development of anti-donor HLA antibodies. For example, patients found to have developed a donor-specific HLA antibody may receive augmented immunosuppression. By identifying donor-specific antibodies that are markers for a patient being at high risk for transplant graft loss, the center has paved the way for tests to prospectively determine which patients undergoing heart, lung or kidney transplants are at high risk for rejection. The center has also worked closely with UCLA’s transplant programs to develop protocols to monitor patients’ response to therapy.

Researchers at the center are exploring a new paradigm in the transplant field – the role of non-HLA antibodies involved in graft rejection. “These are antibodies that cause chronic rejection, but don’t involve the major histocompatibility antigens,” Dr. Reed explains. “Rather, they are antigens expressed on the endothelial cells of the donor organ.” Her team is working with an industry partner to develop new tools for identifying these non-HLA targets in an effort to enhance the ability to prevent chronic rejection.

The Immunogenetics Center is also embarking on using a simple blood test to measure for signs that cancer patients are responding to anti-tumor therapies – yet another on an expanding list of efforts to assist UCLA researchers and clinicians in improving patient care. “In all of these activities, our goal is to help identify immuno-phenotypes associated with health and disease,” says Dr. Reed. “Understanding the immuno-phenotype helps us to better understand the patho-physiology of disease, and to direct patients toward the best therapies.”

“We envision that patients might get an immune assessment panel as part of going to their doctor for an annual physical, just like you have your cholesterol checked.”

- Elaine Reed, PhD
Through a partnership with the National Marrow Donor Program (NMDP) to assist in the matching of donors and recipients for life-saving transplantation, the UCLA Immunogenetics Center is advancing the field of human leukocyte antigen (HLA) typing through innovative new technologies.

The NMDP is a nonprofit organization that has facilitated more than 55,000 marrow and cord blood transplants since it was established in 1987. As one of three laboratories in the country contracted with the NMDP to perform HLA testing for prospective bone marrow donors, the UCLA Immunogenetics Center – based in the Department of Pathology and Laboratory Medicine – is spearheading efforts to help the NMDP provide the low-cost, high-volume HLA typing that will help to save more lives.

Because the HLA system is extremely variable, NMDP must retain a massive national registry of volunteer unrelated donors in order to ensure that appropriate matches are available for patients who require marrow transplantation. Given the fluidity of the donor pool – many move and become difficult to locate, or pass the cutoff age of about 50, after which donation is usually not viable – there is a constant need for new volunteers to be added to the registry. Through its contract with the NMDP, the center provides HLA typing for approximately 1,000 donor samples a week.

Conducting this kind of high-volume testing requires ever-advancing technology. “NMDP needs us to be efficient, both at the level of resolution – so that we can more precisely predict the matches – and in developing high-throughput, rapid-turnaround, low-cost methods,” says Dr. Elaine F. Reed, director of the UCLA Immunogenetics Center. “That is driving our efforts to constantly improve the sequencing technology.”

To meet NMDP’s needs, the center’s state-of-the-art lab has upgraded its automation capabilities. Two LABXpress robotic systems have improved the high-throughput sample processing capacity. The center is developing next-generation sequencing technology platforms under the leadership of Dr. Jennifer Zhang (see page 24). Led by Dr. Ping Takemura and her team in the lab’s molecular section, the center is also developing new automated strategies using classic Sanger sequencing methods, with the goal of producing high-resolution typing with fewer ambiguities and at a reduced cost.

“The need to adapt to this volume of work has really upped the overall capabilities of our lab,” says Debra LaCava, manager of the Immunogenetics Center. “It has forced us to constantly look at ways to not only advance our technology, but also to work more efficiently.”

L to R: Chen Ling, Jacqueline Monreal, Mary Lin, Ping Ge Takemura, Sadaf Qureshi, Ying Wang, Linda Nguyen and Nicole De la Fuente
The UCLA Immunogenetics Center, based in the Department of Pathology and Laboratory Medicine, is developing a first-of-its-kind next-generation sequencing method for human leukocyte antigen (HLA) typing, the genetic tests that help to determine how closely the tissues of a potential transplant donor and recipient match.

Deciphering DNA sequences – our genetic blueprint – is a fundamental aspect of biological research, and is increasingly making its way into clinical practice. Since the 1970s, research and clinical laboratories have relied on the Sanger method, named after the technique’s inventor, Nobel Prize-winner Frederick Sanger. But that technology, which is still widely used, has inherent limitations in throughput, resolution, cost and turnaround time.

In recent years, fundamentally new DNA-sequencing technology has been introduced, enabling scientists to run the tests at a wildly accelerated clip. Under the traditional Sanger method, researchers will typically sequence an average of 600 to 800 nucleotides in length, yielding a maximum of 6 megabytes (Mb) of DNA sequence per day at a cost of $500 per Mb. With so-called next-generation (also called massively parallel) DNA-sequencing technology, they can sequence millions of fragments of DNA from a single sample in unison – resulting in a much higher throughput, a faster turnaround time and a lower cost.

“Next-generation sequencing addresses many of the limitations that have hampered traditional Sanger sequencing,” says Dr. Jennifer Zhang, assistant professor of pathology and laboratory medicine and associate director of the UCLA Immunogenetics Center. “The entire genome can be sequenced for ten cents per Mb.”

Given the wide variability among HLA genes, it has been particularly challenging to determine complete HLA gene sequences using the conventional approach, Dr. Zhang notes. That, along with the center’s partnership with the National Marrow Donor Program (NMDP) to provide high-volume HLA testing for potential marrow donors (see page 23), has driven Dr. Zhang’s group to seek to develop an HLA testing method on the next-generation sequencing platform, both for single-patient typing and for batches of thousands at a time such as those necessitated by the NMDP partnership.

Using two of the most common next-generation sequencing approaches, Dr. Zhang and colleagues have developed a method that has yielded encouraging results in a pilot study indicating less ambiguous and higher resolution typing. These promising outcomes could mean faster donor matching and better patient survival. The center continues to develop the technique, with an eye toward using it for patient care in the near future. ▲

developing next-generation sequencing test to improve transplant donor matching

...new dna-sequencing technology has been introduced, enabling scientists to run the tests at a wildly accelerated clip.
The Spring 2013 opening of the Center for Pathology Research Services (CPRS), under the leadership of Sarah Dry, MD (director) and Justin Perry (manager), was lauded by the UCLA research community. Well aware of the high-quality services offered by the pathology core labs, UCLA investigators welcomed the administrative infrastructure provided by CPRS as a way of improving access to and use of these cores, which include:

- Brain Tissue Translational Resource (William Yong, MD)
- Clinical Immunology Research Laboratory (Anthony Butch, PhD)
- Clinical Microarray Core (Xinmin Li, PhD)
- Immune Assessment Core (Elaine Reed, PhD)
- Translational Pathology Core Lab (Sarah Dry, MD)
- UCLA Institutional Biorepository (Sarah Dry, MD)

Consolidating the business and administrative functions of the core labs into a centralized CPRS office provides many advantages to researchers. The office, located on the A-level of UCLA’s Center for Health Sciences, is staffed by research coordinators who work closely with each lab. Familiar with the services, technology, and instrumentation used in each unit, the research coordinators provide comprehensive, hands-on support to individual researchers for elements that are critical to successful research: test ordering, result reporting, budget development, and invoicing. Throughout the life of any research project, the CPRS office serves as the primary contact for the investigator.

CPRS has enabled a streamlining and standardization of many of the administrative processes researchers encounter when they utilize a core lab. Leadership looked closely at these processes and, in turn, created more efficient and transparent policies and procedures for customers and pathology staff. For example, the CPRS overhauled how researchers request clinical laboratory tests. Processes that had been inefficient and time consuming – budget development, study setup, sample handling, result reporting, and invoicing – were standardized and simplified. Simple improvements to the request form, requisition, and lab website allowed researchers to access these services more quickly and easily. As a result of these changes, investigators have been able to devote more of their time and resources to their research.

Throughout the next year, the CPRS will continue to focus on providing robust services to the research community, as well as improving the overall customer experience.

Justin Perry
A member of the department had a brush with history in 2013, playing a role in a landmark U.S. Supreme Court case that forever changed the nature of ownership of one's genetic makeup and intellectual property rights in the biotechnology industry.

Most people are shocked when they learn that substantial portions of the human genome – the DNA content of our cells that constitute all of our genes – have been “owned” exclusively by a large number of biotech companies and commercial reference laboratories, essentially granting these entities a “monopoly” over the diseases associated with those genes. Yet, Dr. Wayne Grody, director of molecular diagnostics for the UCLA Department of Pathology and Laboratory Medicine, notes that this has been the case since the mid-1970s, when the U.S. Patent and Trademark Office began granting exclusive licenses to those making discoveries of genes, and even human DNA fragments.

“As enunciated by Thomas Jefferson in Article 1 of the U.S. Constitution, the purpose of patent law is to provide some protection to inventors in order ‘to promote the progress of science and useful arts,’” Dr. Grody says. “But in the area of healthcare, it can be argued that gene patents have had the opposite effect, barring access for patients to needed and affordable genetic tests and discouraging competitors from advancing the field.”

Several years ago, Dr. Grody was approached by the leadership of the American Civil Liberties Union (ACLU), which was considering mounting a legal challenge to the constitutionality of gene patents. The ACLU chose as the test case one of the most visible – and, to opponents of the gene patents, distressing: the patents granting exclusive ownership of the BRCA1 and BRCA2 genes, responsible for familial breast and ovarian cancer, to Myriad Genetics in Salt Lake City. Dr. Grody notes that the company’s charge for DNA sequencing of both genes was $4,000, and that any other laboratories attempting to offer the same test were quickly shut down by legal action, creating longstanding problems of access for patients at risk and no place to turn for a “second opinion.”

Dr. Grody recruited plaintiffs for the case – major medical organizations such as the Association for Molecular Pathology, the College of American Pathologists, and the American College of Medical Genetics – and served as an expert for the ACLU in crafting its arguments. The suit against Myriad Genetics was filed in 2009 and ultimately was taken up by the U.S. Supreme Court in April 2013.

With Dr. Grody sitting in the “VIP Gallery” of the Court chambers, oral arguments were held on April 25. “I was on pins and needles the whole time, but it seemed to go well for our side,” Dr. Grody recalls. His optimism was well founded. On June 13, the Court ruled unanimously that genes are products of nature and therefore not patentable under the Constitution – invalidating Myriad’s patents as well as those covering all other genes. The case – AMP et al. v. Myriad Genetics – will now be a permanent part of law school textbooks. 

...it can be argued that gene patents [bar] access for patients to needed and affordable genetic tests and discourag[e] competitors from advancing the field.”
- Wayne Grody, MD, PhD

WHO OWNS YOUR GENES?

Read more about the Supreme Court’s decision at articles.latimes.com/2013/jun/13/science/la-sci-sn-supreme-court-gene-patent-brca-celebrate-20130613
HEART WALK
Path and Lab faculty, staff and family members came out en masse in support of Heart Walk 2013
Back: Dawn Stene, Salpi Janetsian, Dr. Lu Song, Nathan Okawa, Abdur Alioua, Amie Ludovico.
Front: Ofelia Cartagena, Teresa Siojio, Cristina Dunn, Emmy Von Seyfried

CODE BLUE AT 41,000 FEET
Dr. Jonathan Braun and Lynn Gordon, MD, PhD, professor of ophthalmology and associate dean for academic diversity at the David Geffen School of Medicine at UCLA, are among three UCLA physicians who came to the rescue of an airplane passenger who experienced a heart attack during flight.

MOVEMBER
Path and Lab sports fledgling mustaches in support of “Movember,” an annual, worldwide event to raise awareness of men’s health issues
Pathology and Laboratory Medicine fellows Philip Scumpia, MD, PhD, Serge Alexanian, MD, and Matthew DeNicola, MD

VOLKSWAGEN CITY OF ANGELS FUN RIDE
Path and Lab faculty, staff and students gave their support to the UCLA Blood and Platelet Center on May 4, 2014, either as volunteers or riders on the 32 or 62 mile course for this 17th annual event.

2014 BRUIN RUN/WALK
Over 60 UCLA Pathology and Laboratory staff, faculty, family and friends participated in the 2014 Run/Walk benefitting UCLA’s Mattel Children’s Hospital, in support of Kadin (pictured above), a multiple kidney transplant patient.

CARE HARBOR
The Department is a proud participant in Care Harbor, an annual, free, four-day health care event serving the Los Angeles Community.
UCLA Pathology’s Jessie DeLaCruz (far left), Lavita Boyd (center), and Lynne Ford (far right) with Care Harbor volunteers

EXPLORE the Bruin Run/Walk at www.bruinrunwalk.com
EXPLORE City of Angels Fun Ride at coafunride.com
EXPLORE Heartwalkla.kintera.org/af/home/default.asp?ievent=1091086
EXPLORE U Magazine at magazine.uclahealth.org/body
WHO’S WHO IN PATHOLOGY

Oliver Hinkson, PhD
Sharon L. Hirschowitz, MD
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Kathleen A. Kelly, PhD
Charles R. Lassman, MD, PhD
Stephen Lee, MD
Ximin Li, PhD
Robert Moran, MD
Cynthia Nast, MD
Scott D. Nelson, MD
Nora Ostrzega, MD
Jian Yu Rao, MD
Naphef P. Rao, PhD, FACMG
Elaine F. Reed, PhD
Nora Rozengurt, DVM, PhD
Jonathan W. Said, MD
Robert H. Schiestl, PhD
Elena Stark, MD, PhD
Michael A. Teitell, MD, PhD
Peter J. Tontonoz, MD, PhD
Robert B. Trelease, PhD
Harry V. Vinters, MD
Hanlin L. Wang, MD, PhD
Haodong Xu, MD, PhD
William H. Yong, MD
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Marcelo Couto, DVM
David W. Dawson, MD, PhD
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Samuel W. French, MD, PhD
Xin Liu, MD, PhD
Qun Lu, MD
Claire Lugassy, MD
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Neda A. Moatamed, MD
Sheja T. Pullarkat, MD
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Sophie X. Song, MD, PhD
Peggy S. Sullivan, MD
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Ahlysa Ziman, MD
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Bita Behjatnia, MD
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Kingstok Das, MD
Joshua L. Deigman, PhD, FACMG
Joel Gamo, MD
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Steven D. Hart, MD
Haijiang Hu, PhD
Romney Humphries, PhD
Sibel Kantarcii, PhD, FACMG
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David Lu, MD
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M. Fernando Palma-Diaz, MD
Bogdan Parsian, PhD
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Chandra N. Smart, MD
Lu Song, PhD
Samuel Strom, PhD
Emiris T. Taylor, MD
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Yaela Keren, MD
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Yaela Keren, MD
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Slavash K. Kurdistani, MD
Jasmine Kwok, MD
Michael E. Phelps, PhD
Charalabos E. Pothoulakis, MD
Gary Schiller, MD
S. Andrew Schwartz, MD
Ram R. Singh, MD
James S. Tiedball, PhD
Anna Wu Work, PhD
Hong Wu, MD, PhD
Endowed chairs
Scott W. Binder, MD
Pritzker Family Endowed Term Chair in Pathology
Gay M. Crooks, MBBS
Rebecca Smith Chair in A-T Research
Michael C. Fishbein, MD
Frances and Albert Pianky Chair in Anatomical Pathology
Benjamin J. Glasgow, MD
Wasserman Professor of Ophthalmology
Jerzy W. Kupiec-Weglinski, MD, PhD
Joan S. and Ralph N. Goldwyn Chair in Immunology and Transplantation
Michael E. Phelps, PhD
Norton Simon Chair in Biophysics
Charalabos Pothoulakis, MD
Eli and Edythe L. Broad Foundation Chair in Inflammatory Bowel Disease Research
Michael A. Teitell, MD, PhD
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houser staff residing
Michael Alberti, MD, PhD
Ramir Arcega, MD
Yaela Bebbahedian, MD
Shelly Chang, MD, PhD
Sue Chang, MD
Vanda Farahmand, MD
Gregory A. Fishbein, MD
Julie Hiss, MD
Aaron James, MD
Michael E. Kallen, MD
Christopher J.X. Kim, MD
Nam K. Ku, MD
Peehee Lee, MD, PhD
Thomas D. Lee, MD, PhD
Lawrence H. Low, MD, PhD
Shino D. Magaki, MD, PhD
Jeremy M. Petersen, MD
James Rankin, MD
Eric Swanson, MD
Dawn Ward, MD
Jennifer Woo, MD
Annie Wu, MD
fellows
Elizabeth Akiyama, MD
Serge Alexanian, MD
Jeffrey Antoniu, MD
Mehnashi Bhasin, MD
Durha Cherukuri, MD
Brian Cone, PhD
Rachel Conrad, MD
Taherbeh (Maryam) Dadfarinia, MD
Matthew M. DeNicola, MD
Negar Ghaemahmani, PhD
Donina Gui, MD, PhD
Michelle Hickey, PhD
Jianling Ji, PhD
Rina Kancsl, MD
Jamee Koo, MD
James Lan, MD
Leila Langston, MD
Michael Lee, MD
David Lin, MD
Eric Loo, MD
Ashad Mahmood, MD
Ian McIerdy, MD
Zhiqiong Mo, MD, PhD
Denise Ng, NP
Beth Palla, MD
Khaled Sarantopoulos, MD
Philip Scumpia, MD, PhD
Atsuko Seki, MD
Nora C. Sun, MD
Mitsu Sugimoto, MD
Julien L. VanLancker, MD
Elizabeth Wager, MD
assistant associate investigators
David Casero, PhD
Lily Chao, MD
Cynthia Y. Hong, MD
Rong Rong Huang, MD
Jinna Jiang, PhD
Yiping Jin, PhD
Yael D. Korin, MD
James F. Leblanc, PhD
Hane Lee, PhD
Fan Li, PhD
Claire E. Matfer, PhD
Yei Hsien Mah, PhD
Encarnacion Montecino-Rodriguez, PhD
Amelie Montel-Hagen, PhD
Kotoko Nakamura, PhD
Ping Rao, PhD
Zorica Scuric, PhD
Hong Yu, MD, PhD
post-doctoral scholars
Jinkuk Choi, PhD
Steph Cocheonne De-Barros, PhD
Eszter Deak, PhD
Ling Dong, PhD
Thilini Ranna Fernando, PhD
Negar Montakhab Ghaemahmani, PhD
Ayaka Ito, PhD
Jianling Ji, PhD
Marius Coprin-Jones, PhD
Ronik Khachatourian, PhD
Yoko Kidaiki, PhD
William Sang Kim, PhD
Stephen David Lee, PhD
Zhen Li, PhD
Lin Lin, PhD
Brett Eugene Lemenick, PhD
Ian H. McIerdy, PhD
Jeffrey Thomas McNamara, PhD
Shelley Anne Miller, PhD
Kiyoko Miyata, PhD
Shabnam Mohandesani, PhD
Rani Samih Naji, PhD
Mahtta Nili, PhD
Jayanth Kumar Palanichamy, PhD
Christina M. Priest, PhD
Prashant Raghunadi, PhD
Salem Sandoval, PhD
Katrin Schafer, PhD
Nwe Nwe Soe, PhD
Balu T. Suterwala, PhD
Minh Thai, PhD
Sandrine Thie mann, PhD
Kimberly Anne Thomas, PhD
Bo Wang, PhD
Ning Wang, PhD
Kevin Jason Williams, PhD
Max Wu, PhD
Yuxin Yin, PhD
Thomas Andrew Zangle, PhD
Li Zhang, PhD
graduates and residents
Joseph P. Arquy
Robert Brown
Dana Case
Chee Jia Chih
Jennifer Pong Chou
Michael Dawson Arensman
Jeffrey Nels Dock
Amy Helene Henkin
Jason Seung Pyo Hong
Kathleen M. Kershaw
Giel Kichav
Ying Kong
Brian McDonnell
Xin Rong
Sahar Salehi
Jaspreet S. Sandhu
Eiko Christine Shimada
Tara Ann Tse Lee
Maomeng Tong
Nicole C. Walsh
Jieixin Wang
Lynnea R. Waters
Autumn Gabrielle York
**METRICS**

**DEPARTMENT OF PATHOLOGY**

**Total Department Inventions in 2013**

- Faculty: 109
- Residents/Fellows: 45
- Postdoc Researchers: 41
- Grad Student Researchers: 23

**Total Staff:** 971

**Research Funding**

- NIH Funding: $33,976,333
- Other Granting Agencies: $12,986,250
- Total: $46,962,583

**Facilities**

- Total Space in Square Feet: 278,228
- Clinical Space: 161,697
- Core Lab: 11,345
- Research: 43,802
- Educational, Academic, & Administration: 40,249
- Clinical Space awaiting Tenant Improvements: 17,945
- Department Space awaiting Tenant Improvements: 3,190

**Metrics**

- In the previous twelve month period, pathology.ucla.edu website has had...
  - Nearly 6 million page views
  - 117,890 visits
  - 78,215 unique visitors
  - 335,971 page views

**Clinical Lab Tests**

- 32,164 Surgical Pathology Cases
- 24,576 Cytogenetics Cases
- 28,000 Cytology Cases
- 45,100 Outreach Cases

**Other Granting Agencies**

- Other Granting Agencies: $12,986,250

**Research Funding**

- NIH Funding: $33,976,333

**Facilities**

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- Educational, Academic, & Administration: 40,249
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- Department Space awaiting Tenant Improvements: 3,190
Gay Crooks, MBBS
Appointed UCLA Department of Pathology and Laboratory Medicine
Rebecca Smith Chair in A-T Research

Rita Effros, PhD
Elected President of the Gerontological Society of America (GSA)

Dennis Goldfinger, MD
Francis S. Morrison Memorial Lecture Award from the American Society for Apheresis

Wayne Grody, MD, PhD
Public Address, Smithsonian Institution, Washington, DC, for the exhibit “Genome: Unlocking Life’s Code”

Plaintiffs’ Expert and Invited Guest for Oral Arguments at U.S. Supreme Court for landmark gene patent case “Association for Molecular Pathology et al. v. Myriad Genetics Laboratories, Inc.”

Appointed National Research Advisory Council, U.S. Department of Veterans Affairs, Veterans Administration Health System

Oliver Hankinson, PhD
Elected Fellow of the American Association for the Advancement of Science

Robert Schiestl, PhD
President-Elect Carcinogenesis Specialty Section of the Society of Toxicology
President-Elect Council of the Environmental Mutagen Society

Ram Raj Singh, MD
37th Michael Einbender Distinguished Lectureship in Medical Research of Lupus from the University of Missouri, Columbia, MO

Peter Tontonoz, MD, PhD
Gerald D. Aurbach Award from the Endocrine Society

Nicole Valenzuela, PhD
2014 UCLA Chancellor’s Award for Postdoctoral Research

Anna Wu, PhD
Elected President of the World Molecular Imaging Society
The Pathology Clinical and Research Alumni Committees are an active and vital part of the Department of Pathology and Laboratory Medicine, and are committed to ensuring the link between them and the UCLA Department of Pathology and Laboratory Medicine remains strong. Coordinating the needs of the alumni with the resources of the department, the committees provide educational and mentoring opportunities, encourage activity and philanthropy, and provide an opportunity for alumni to keep and make new and valued connections. Valerie McWhorter, MD, chairs the Clinical Alumni Committee; Josh Deignan, PhD, FACMG chairs the Research Alumni Committee.

UCLA Pathology Alumni

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Pathology Research Alumni
## OPPORTUNITIES FOR GIVING

### ENDOWED CHAIRS

Executive Endowed Chair: $3,000,000
Permanent Endowed Chair: $2,000,000
Professional Development 5-Year (renewable) Term Chair: $1,000,000
Recruitment/Distinguished Service/Teaching (1-5 year) Term Chair: $500,000

### EDUCATION

Graduate Student Researcher: $500,000
Postdoctoral Researcher/Fellow: $1,000,000
Clinical Resident Trainee: $500,000
Summer Youth Trainee: $10,000
Teaching Awards: $250,000
Lectureships: $250,000

### CLINICAL INNOVATION

Core Laboratories: $2,000,000
- Clinical Genomics Laboratory
- Translational Pathology Core Lab
- Clinical Microarray Core Lab
- High-throughput Clinical Proteomics Core Lab
- Clinical Immunology Research Lab

### DEDICATED RESEARCH

Research Funding: $250,000
- Stem Cells in Prostate Cancer
- Finding New Treatments for Brain Cancer
- Personalizing Treatment for Sarcomas
- Molecular Therapy of Obesity And Diabetes
- Women’s Health Studies
- Restoring the Aging Immune System
- Advancing Transfusion Medicine
- Inflammatory Bowel Disease (Crohn's and Ulcerative Colitis)
- Controlling Inflammation-Mediated Atherosclerosis
- Rapid Diagnosis of Congenital Mendelian Disease

### GRANT SPONSORS

- Action for A-T
- American Heart Association - National
- American Heart Association - Western States Affiliate
- Amgen
- Becton Dickinson and Company / BD Biosciences
- BioMérieux Vitek, Inc.
- BioMérieux, Inc.
- BioTheranostics
- Broad Institute
- California Institute for Regenerative Medicine (CIRM)
- California Institute of Technology (Caltech)
- Cedars-Sinai Medical Center
- Cepheid
- Charles R. Drew University of Medicine and Science
- Clavis Pharma ASA
- Crohn's & Colitis Foundation of America
- Cubist Pharmaceuticals
- DxTerity Diagnostics, Inc.
- Gen-Probe
- Intalytix
- JMI Laboratories
- John Wayne Institute for Cancer Treatment and Research
- Kaiser Foundation Research Institute
- Leidos Biomedical Research, Inc
- Luminex Corporation
- Moral Effort Limited
- Muscular Dystrophy Association of America
- NIH/National Cancer Institute
- NIH/National Eye Institute
- NIH/National Heart, Lung and Blood Institute
- NIH/National Institute of Diabetes and Digestive and Kidney Diseases
- NIH/National Institute of Allergy and Infectious Diseases
- NIH/National Institute of Environmental Health Sciences (NIEHS)
- NIH/National Institute of Neurological Disorders and Stroke (NINDS)
- NIH/National Institute on Aging
- Novartis Pharmaceuticals / Novartis AG
- Oklahoma Medical Research Foundation (OMRF)
- Prometheus Laboratories, Inc.
- Quidel Corporation
- Science Applications International Corporation (SAIC)
- Siemens
- True North Foundation
- UC/Cancer Research Coordinating Committee (CRCC)
- University of California, San Diego
- University of California, San Francisco
- University of Southern California
- University of Virginia

### GIFTS

- A-T Ease Foundation, Inc.
- Balancefrom Products
- Barbara and Richard Braun
- Cold Genesys, Inc.
- Peter and Deborah Heumann
- Hirshberg Foundation for Pancreatic Cancer
- Dr. Geraldine Kurz
- Lya Cordova Latta
- Dr. Douglas McGregor
- Dr. Valerie McWhorter
- Ruzic Research Foundation, Inc.
- Drs. Elaine and Daljit Sarkaria
- Dr. Changgao Yang
- Ziman Family Gift to support the Loni Calhoun Educational Scholarship

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