PA-THOL-O-GY (P-THL-J)
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THE SCIENTIFIC STUDY OF THE NATURE
OF DISEASE AND ITS CAUSES, PROCESSES,
DEVELOPMENT, AND CONSEQUENCES.
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EDITORS: KARYN GREENSTONE & SHARON WEBB • WRITER: DAN GORDON • DESIGN: SUSAN LANDES MANN DESIGN

PHOTOGRAPHY: MARGARET SISON • ADDITIONAL PHOTOGRAPHY: TODD CHENEY, REED HUTCHINSON, JIAN YU RAO & KOSAL TAING
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THE QUIET HERO

A FRIEND OF MINE, WHOSE WORK IS PHILOSOPHY, IS ALWAYS READING. Do you know his favorite periodical? It is People Magazine. He explained that it explored each week how fame and wealth do not guarantee a happy or meaningful life! In this annual report, we reflect on my quiet heroes – those who not only bring about real and important change, but also provide the inspiration to bring out what is best in others and make the world that much more of a better place.

Thanks to Dr. Binder and the amazing people who fashion Pathology into a new mode of care delivery, and educate our physician trainees not only in pathology expertise but also in the role of service. With the opening of BURL Laboratories, we are now poised to extend this special amalgam of quality and service to communities throughout the north, west, and south of Los Angeles County.

Extending our boundaries even further, our Department, along with UCLA Health and the Jonsson Comprehensive Cancer Center, has entered into landmark arrangements with the Cancer Institute and Hospital, Chinese Academy of Medical Sciences (CAMS). This builds on our successful partnerships over the past several years in care and teaching with academic health centers and municipal Hangzhou. The new relationship with CAMS will broaden the scope of these partnerships for clinical trials and translational research with leading investigators throughout China.

While we extend our global presence in China and elsewhere, we are also mindful of the needs closer to home, as we begin consultative telepathology services to underserved pathology practices located throughout Southern California. Partnerships with six communities will initiate this program, and will build from there to a network to support community-based practices throughout California.

Even closer to home, our Clinical Genomics Center has implemented the remarkable breakthroughs in high-throughput sequencing and disease-diagnostic genetic bioinformatics as a practical health care service. This is finally bringing closure to families and individuals who have been waiting years for what they once thought were questions without answers. The rapid diagnosis of complex genetic diseases allows patients, families, and their health care team to move onto planning for medical care, and strategies to identify and eventually avert disease in unaffected family members.

Our department is intensely devoted to research, nearly $50M presently in force. What drives this creative enterprise is David Islas and our Fund Managers. They pilot projects through the complex path from inception to funding, and steward these precious funds to assure the greatest value to our investigators and trainee scientists in their challenging experimental work.

It is in the classroom where researchers of tomorrow are inspired by some of the most creative and innovative faculty in the nation. Through the innovation of the “flipped” classroom, Elena Stark inspires future medical leaders to think independently, and Wayne Grody, Steve Bensinger and Chandra Smart encourage fundamental understanding of human processes, and not simple rote learning.

As the path from research to clinical innovation shortens, the distinctions between health care and research diminish as patient biospecimens serve care and research today, and data to guide care of the same patients with improved care tomorrow. This creates conceptual, ethical, and operational challenges for dynamic health systems like UCLA centers. Sarah Dry, William Yong, Justin Perry and their teams in the Translational Pathology Core Laboratory, EngageUC, and the Pathology Portal, have created a new framework to solve these challenges for the UCLA clinical and research communities.

In this annual report, read the stories of these quiet heroes: exceptional people, and the exceptional ways that they enable UCLA to serve the needs and dreams of our community.

Jonathan Braun, MD, PhD

DR. JONATHAN BRAUN, PROFESSOR AND CHAIR, DEPARTMENT OF PATHOLOGY AND LABORATORY MEDICINE
UCLA’s Department of Pathology and Laboratory Medicine has vastly increased its outreach portfolio in recent years, a development that serves the department in several critical ways, according to Dr. Scott Binder, senior vice chair, chief of dermatopathology and medical director of the department’s clinical services and outreach program - the largest university pathology department outreach program on the West Coast.

“The stronger our outreach, the stronger our department will be,” Dr. Binder says. “Our growth in outreach is not only revenue-generating; it also supports our research mission and provides additional teaching opportunities for our residents and fellows. All of these things are interrelated and ultimately dependent on the revenue generated by the outreach-oriented clinical activities of the faculty.”

In a time of economic uncertainty for health systems, Dr. Binder notes, both the quality and quantity of services provided are becoming more paramount to a system’s ability to thrive. As such, by providing high-quality, low-cost laboratory services, the Department of Pathology is playing an integral role in UCLA Health’s ability to grow and prosper by enabling other clinical departments to compete successfully in the Southern California marketplace. Outreach services now comprise more than 60 percent of the department’s clinical activity, says Dr. Binder. He expects that proportion to continue to grow. UCLA Health’s strategic plan is focused on extending UCLA’s reach to cover as many patients as possible in Southern California, spanning from as far north as Ventura County to as far south as Orange County. “That will all be outpatient work, which generates outreach work, because all of those patients in these outlying areas are going to need routine skin biopsies, gastrointestinal biopsies, Pap smears, and other outreach services,” Dr. Binder explains.

The department’s outreach program is several times larger than it was only five years ago, says Dr. Binder, particularly in the areas of dermatopathology, gastrointestinal pathology and urologic pathology. These and other sub-specialties now have a much larger client base and are taking in many more specimens for analysis. The expansion has involved not just more clients, but also a wider variety of services offered. “Essentially we are offering clients a one-stop shop - everything from CBC tests to 21st-century genetic testing for the diagnosis of hereditary disorders,” Dr. Binder explains.

This expansion benefits not only the department, but also the community of clients being served. “They are getting access to UCLA quality with an excellent turn-around time at competitive pricing,” Dr. Binder says. “We are successfully competing with large reference labs in terms of price and turnaround time, and we offer a broader range of services.”

Among the notable areas of outreach expansion: the opening this year of the state-of-the-art Bruin University Reference Laboratory (see Page 5 for more about BURL).

The newest area of outreach is in clinical genomics. The department is receiving clinical specimens from all over the country, particularly in California, to conduct next-generation sequencing for Mendelian disorders (those caused by a single gene disruption). The department’s outreach program has also recently expanded significantly into cytogenetics. Working with a large national client, Carlsbad, CA-based Genoptix Medical Laboratory, the department conducts leukemia and lymphoma cytogenetics as part of its outreach to non-UCLA patients.

Other notable departmental outreach activities include: Dermatopathology. In a joint venture between the Department of Pathology and Laboratory Medicine and the Department of Medicine, a lab located at 2020 Santa Monica Blvd. processes and prepares...
the slides for the specimens obtained in the Department of Medicine’s Division of Dermatology for the diagnosis of skin diseases. Those slides are analyzed by trained dermatopathologists under the leadership of Dr. Chandra Smart, the program’s director. The interdisciplinary program, unique in Southern California, represents a direction that Dr. Binder expects to become a significant trend in the outreach program.

LUNG AND MOLECULAR PATHOLOGY. Lung pathology and molecular pathology services now include a large and comprehensive panel of sophisticated molecular tests to better evaluate lung cancers and offer improved guidance for treatment and clinical trial options to patients. The new genetic tests for lung cancer have been developed by UCLA’s Molecular Diagnostics Laboratories to complement the traditional anatomic pathology evaluation of lung cancer. Ultimately, this will enable the pathology team to expand its role from classifying and staging a cancer to reporting the genetic changes that may provide clues to treatment strategies and inform clinicians and patients on the prognosis of the disease.

GASTROINTESTINAL (GI) PATHOLOGY. The GI pathology service is a large-volume, sub-specialty-trained group that incorporates modern diagnostic techniques, maintains an intra-diagnostic divisional conference, participates in clinical research and attends international GI pathology meetings. Devoted to anatomic pathology diagnostics, the service prepared 18,845 diagnostic reports in 2012. It provides additional sub-specialty consultations intra-operatively and on weekends. Advances in the clinical application of the molecular understanding of disease have resulted in the service augmenting reports using molecular genetic and immunohistochemical (IHC) techniques.

The genitourinary pathology section has developed or adopted advanced and sophisticated technologies to further improve the quality of patient care. All cases of prostatectomy are now processed as whole-mount sections, enabling accurate enumeration of tumors as well as the reporting of the pathologic features of each tumor individually. A team consisting of pathologists, radiologists and urologists has developed a targeted biopsy technology that allows improved detection of clinically significant prostate cancers. Many patients with indolent tumors are now enrolled in the active surveillance program instead of receiving radical treatments that carry potentially significant side effects.

Neuropathology. The neuropathology section is now conducting isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2) mutation detection, sequencing tests that can detect common and rare mutations of the IDH1 gene as well as IDH2 mutations – the presence of which in gliomas is associated with a better prognosis and can affect patient management. Tests are offered for FUS and TDP-43, immunohistochemical markers that can assist in the classification of frontotemporal lobar degeneration. In addition to existing muscular dystrophy markers, investigations of rare muscular dystrophies are offered, as are evaluations for epilepsy disorders and rare genetic disorders, the latter using whole genome sequencing.

Hematopathology. The outreach workflow continues to increase for the hematopathology section, with an 8 percent increase in bone marrow cases and a 14 percent increase in flow cases for 2012 vs. 2011. Since 2009, bone marrow volume has increased 34 percent and flow panels to leukemia have increased 31 percent. The hematopathology service’s consultations include evaluation of blood, bone marrow, lymph nodes and hematolymphoid lesions in other body sites that are submitted by pathologists and oncologists throughout the nation as well as from other countries.

Hepatobiliary/Renal Pathology. The hepatobiliary pathology service provides rapid, high-quality diagnostic histopathology for liver disease on both biopsy and surgical material, with extensive experience in hepatitis and biliary disease, neoplastic hepatobiliary disease and transplant pathology. The renal pathology section handles a large volume of diagnostic renal biopsies, and also evaluates and interprets transplant biopsies, nephrectomy specimens and post-transplantation complications.
Bringing UCLA Pathology/Laboratory Services to the Community

The Department of Pathology and Laboratory Medicine has joined UCLA Health and the Department of Medicine in a partnership to deliver additional health services to the San Fernando Valley, Conejo Valley, and South Bay regions of Los Angeles County.

In March, the Department of Pathology and Laboratory Medicine and UCLA Health opened a state-of-the-art outreach reference laboratory, Bruin University Reference Laboratory (BURL), in Panorama City. Laboratory support of new UCLA Health facilities followed, including “STAT” labs (designed to provide quick-turnaround services) serving UCLA Health’s new primary and secondary care facility in Westlake Village. The BURL Westlake Village Patient Service Center has patient blood draw stations and offers immediate results for many blood and urine chemistries, along with other STAT testing.

The Westlake Village office is the first of six new UCLA facilities scheduled to open over the next two years in service areas beyond UCLA’s Westwood and Santa Monica campuses; other sites include Thousand Oaks, Porter Ranch, Calabasas, Santa Clarita and Redondo Beach. The state-of-the-art offices will offer a full range of primary-care sub-specialties (internal medicine, family medicine, pediatrics, women’s health), as well as ancillary and secondary-care services. The new practices will also engage in community education and outreach through newsletters, physician lectures and participation in outreach programs accessible to the community (e.g., in shopping centers, health fairs and farmer’s markets).

By establishing new locations, supporting them with local laboratory facilities, and participating in local programs, UCLA is expanding its ability to provide convenient, high-quality care to people who live or work outside traditional primary care service areas, while providing a gateway to higher levels of care within the UCLA system for patients who need such services.

“BURL is designed as a price-competitive, quality-driven outpatient laboratory with locations throughout the San Fernando Valley, Conejo Valley, Westside and South Bay regions of Los Angeles.”

- Scott Binder, MD, Medical Director, BURL
THROUGH A GROUNDBREAKING PARTNERSHIP, UCLA Health (including Ronald Reagan UCLA Medical Center and the Jonsson Comprehensive Cancer Center) and the Cancer Institute and Hospital, Chinese Academy of Medical Sciences (CAMS) will develop collaborations in cancer-related clinical services and scientific research. These partnerships will cover a wide range of areas, including diagnostic consultation, biomarker research, telepathology and survivorship.

Plans include the establishment of a joint Cancer Molecular Diagnostic Center providing advanced molecular diagnostic services for use in such areas as early detection, individualized patient management and prognoses, and clinical trial samples. The center stands to benefit patients throughout China, as well as around the world. By linking the expertise of CAMS and other Chinese professionals with the UCLA Department of Pathology and Laboratory Medicine, the new facility will serve as a premier site where authoritative diagnosis can be rendered for difficult surgical, molecular and genetic cases in China through state-of-the-art telepathology methods. UCLA will also work with CAMS to establish a joint tissue/biospecimen repository system that will benefit both entities through cancer biomarker testing and validation studies.

CAMS is a premier academic institution in China. It encompasses 18 research institutes covering five cities, along with six academic hospitals in three cities, including the prominent Peking Union Hospital and Medical College, Cancer Institute and Hospital, and Cardiovascular Hospital. The new cancer-related collaboration is part of a broad, long-term research and clinical partnership between UCLA Health and CAMS.

DEPARTMENT WILL PLAY KEY ROLE IN UCLA HEALTH’S PARTNERSHIP WITH CHINA

INTERCONTINENTAL COLLABORATIONS IN CANCER-RELATED CLINICAL SERVICES AND SCIENTIFIC RESEARCH.
UCLA’s Expanding Global Presence

The UCLA Department of Pathology and Laboratory Medicine has been at the forefront of international telepathology development through its partnership with China, and has now committed a significant effort toward integrating telepathology into daily practice closer to home. Recently, the department received a substantial grant from the State of California to provide consultative telepathology services to underserved pathology practices throughout Southern California. The funding will be used to acquire digital slide scanners that will be installed in remote pathology groups, and will enable the department to begin space remodeling to accommodate telepathology functions.

Once installed and operational, these scanners will allow pathologists working in underserved communities to obtain second-opinion consultations from UCLA specialists on challenging pathology cases. This technology enables rapid transmission of scanned slide data to the consultant pathologist, avoiding delays that occur when glass slides must be transported from one site to another. In addition to improving patient care – particularly for cases with urgent diagnoses – digital imaging will facilitate improved communication and education among pathologists.

The department’s international telepathology program began in 2010 with a collaborative agreement between Ronald Reagan UCLA Medical Center and Second Affiliate Hospital of Zhejiang University (SAHZJU) in China. As part of the agreement, UCLA pathologists provide second-opinion diagnoses to pathologists and other physicians in SAHZJU. Both cytological and histological cases are included, and cases span a broad range of organ systems, including head and neck, lung, gynecological, soft tissue and bone, neurological, and hematological. In addition, periodic multidisciplinary videoconferences are held to discuss interesting cases.

The program has expanded to reach much of China through additional collaborative agreements with two major reference labs (Dian Inc. and Adicon Inc.) and prominent institutions such as Cancer Hospital, Chinese Academy of Medical Science. The program’s success has also stimulated similar collaborations in other areas, including radiology, oncology, and nuclear medicine.
Recent breakthroughs in high-throughput genotyping and sequencing technologies have ushered in an era of large-scale genome-wide disease studies that have identified hundreds of genetic variants associated with risk for many diseases. Studies aimed at unraveling the genetic basis of Mendelian traits (those caused by the disruption of a single gene) have been particularly successful. Technological and computational advances have made it possible to scan DNA in patients that have the disease - revealing, in most cases, the responsible genes. The efficiency of such studies is reinforced by the successful translation of these findings in clinical settings, with UCLA acting as a pioneer in analyzing the entire protein-encoding genome of a patient for diagnostic purposes.

But the most common diseases - including most cancers, type 2 diabetes, and heart disease - do not have Mendelian traits; rather, they are a complex product of many genes that together influence disease risk. Although large-scale genome-wide studies have been highly successful in identifying the loci harboring genetic risk variants for common diseases, the complex correlation structure of the human genome means that the risk variants identified in these studies typically are not themselves causal, but are associated with unobserved causal genetic variants. Thus, although identifying the causal variants is crucial in understanding the functional basis of a disease, for most common diseases the true causal variants have yet to be discovered.

In an attempt to bridge this gap, Dr. Bogdan Pasaniuc and colleagues in the UCLA Department of Pathology and Laboratory Medicine are conducting studies using sophisticated genotyping or sequencing approaches for tens to hundreds of thousands of individuals of different ethnicities. Dr. Pasaniuc’s lab has found a great benefit to studying multi-ethnic populations. “Not only is it important to study the genetic basis of disease across a wide range of ethnicities for the benefit of a larger group of people, but computational and statistical approaches can leverage genetic diversity across populations to strengthen our ability to find causal variants,” Dr. Pasaniuc explains.

Of particular interest in studying disease across ethnicities are admixed populations (populations with recent ancestry from different continents) such as African Americans and Hispanic Americans, who are often medically underserved while carrying a disproportionately high burden of disease. Because of the diversity of their genomes, admixed populations offer the promise of capturing additional genetic diversity compared with studies of homogeneous populations such as Europeans. This poses particular technical challenges and opportunities.
Of particular interest in studying disease across ethnicities are admixed populations... such as African Americans and Hispanic Americans, who are often medically underserved while carrying a disproportionately high burden of disease.

challenges, since in admixed populations, correlation among genetic variants exists both at a fine scale in the ancestral populations and at a coarse scale, due to chromosomal segments of recently shared ancestry. By jointly modeling both types of genetic structure in African American genomes, Dr. Pasaniuc and colleagues showed that a combined approach achieves greater statistical power to identify risk loci than what can be achieved in studies of homogeneous populations such as Africans or Europeans.

The vast amount of data currently being generated by sequencing technologies increases the need for accurate yet computationally efficient methods of performing disease scans in multi-ethnic cohorts to decipher the genetic basis of disease in various populations. Such efforts will go a long way toward translating genetic findings for common diseases to the clinic, improving diagnostics and treatment decisions.

EXPLORE Dr. Pasaniuc’s lab bogdanlab.pathology.ucla.edu
It is estimated that as much as 10% of the U.S. population suffers from a Mendelian genetic disease. More than 4,000 Mendelian genetic diseases have been described, with the precise genetic mutation identified. These discoveries have contributed significantly to our understanding of biology, as well as the mutations that lead to human diseases. However, an even larger set of genes remains to be discovered. Dr. Stan Nelson’s research has led to the successful implementation of genomic sequencing approaches that enable researchers to efficiently and economically search the entire human genome in individuals for disease-causing mutations. Using this approach, Dr. Nelson’s group has identified the genetic cause for more than 17 Mendelian genetic diseases in the last three years.

Based on these successful efforts, Dr. Nelson and colleagues have launched the UCLA Clinical Genomics Center, featuring a new and powerful diagnostic test called clinical exome sequencing. Under Dr. Nelson’s guidance as the center’s director, this genome sequencing test is not only proving to be much more sensitive at finding the root cause of many serious human diseases, but it is also resulting in novel gene discovery and leading to new approaches to the development of therapies. In the past year, Dr. Nelson’s group has been able to specifically diagnose children with developmental delay, autism, seizure disorders, muscular dystrophy, and other disorders. Many of these children have mutations in previously unrecognized genes; providing the specific diagnosis ends a patient’s medical odyssey and often points health care providers toward more tailored medical interventions.

EXPLORE Clinical Genomics
pathology.ucla.edu/genomics
Next-generation sequencing (NGS) offers the promise of significantly enhancing our understanding of how genetic differences affect health and disease. Compared with conventional Sanger sequencing (considered “first-generation” technology), these new methods can inexpensively yield large volumes of sequence data. The contrast is stark: For example, NGS technology can produce 600,000 megabytes of data at a cost of four cents per megabyte, whereas first-generation technology produces 0.06 megabytes at a cost of $1,500 per megabyte of data.

The second-generation sequencers, such as the HiSeq 2500 and Ion Proton, have already realized what was once only a dream: the ability to sequence one human genome in one day for $1,000. Now, third-generation sequencers, such as those produced by Oxford Nanopore Technologies, have the potential to achieve what was once unthinkable: sequencing a human genome in 15 minutes.

The ability to sequence an entire human genome quickly and cheaply will profoundly affect the way we think about scientific approaches in basic, applied and clinical research. With further improvement of the bioinformatics infrastructure and more detailed clinical annotation of the human genome, NGS-based personalized medicine is on the way to revolutionize disease diagnosis, prognosis and treatment.
Supported by nearly $47 million per year in extramural research funding, faculty in UCLA’s Department of Pathology and Laboratory Medicine conduct groundbreaking studies that are advancing our understanding of disease causes, improving diagnosis, and contributing findings with the potential to improve treatments and ultimately lead to cures for major diseases.

But without the work of a group of behind-the-scenes administrators, the researchers’ work would be far more difficult. Led by David Islas, manager of research administration, six research fund managers working for the department provide invaluable assistance to faculty, assisting those who are awarded grants as principal investigators (PIs) in the fine details of pre-award and post-award administration.

Their work includes helping PIs secure funding by ensuring that their grant proposals meet the agency’s requirements, and then managing the grant account once the application has been awarded. The fund managers’ post-award work includes making sure expenditures follow agency policy and procedures, and helping the PI’s spending remain within the approved budget. Monthly reports prepared by the fund managers keep PIs updated on financial issues; if the fund manager foresees any problem, he or she works with the PI toward its resolution.

“We know that our PIs are very busy with their research, and our role is to manage their money and help them worry as little as possible about issues of financial compliance and reporting,” says Trung Phan, one of the group’s senior fund managers.

The group manages approximately 100 accounts at any one time, including all contracts and grants as well as unrestricted, endowment and other gift funds. The work requires a strong financial background, good communication skills and close attention to detail. “Every time a PI gets funded and we are able to assist in that PI’s work, we are contributing to research that can lead to cures for humanity,” says Phan. “To be part of that effort is very rewarding.”
THE TRADITIONAL LECTURE SETTING is going by the wayside in some academic arenas, replaced by a new method of teaching that better engages students, increasing their enthusiasm and sparking their curiosity. The interactive learning environment of the “flipped classroom” is sometimes called “inverted instruction” because the majority of teaching is by students to students. It’s a platform that elevates students’ intake, processing, and recall of data.

The flipped-classroom concept has been gaining momentum in a variety of educational institutions, including the classrooms at UCLA’s David Geffen School of Medicine, where the Department of Pathology and Laboratory Medicine strives for this enriched level of teaching by flipping the first-year histopathology laboratory sessions. The approach is not to be confused with problem-based learning (PBL), in which, for example, groups of students analyze a case study that reflects lectures by one or more professors. While PBL is also a form of active learning, it requires a base knowledge specific to the topic – i.e., the case study demonstrates the information that was previously taught traditionally.

In a flip-teaching/inverted-classroom scenario, the authority to introduce and explain primary information becomes the responsibility of the students. Students research, gather and evaluate the subject from various sources – instructor-created supplements (e.g., PowerPoint modules), the internet, and textbooks – prior to class. After such preparation, they teach it to each other in the classroom/lab setting. This material integration, also known as hybrid learning, promotes many perspectives on a subject, raising questions or making connections that might not have been revealed from simply listening to a lecture.

It’s a win-win structure for both the professor and the students: The professor gains time to observe the students and communicate with them, while the students gain a wider field of cognition as the flipped classroom adapts to different forms of comprehension. The students master the information because they are forced to explain the material to their peers.

In the histopathology laboratory for first-year students at UCLA’s David Geffen School of Medicine, Dr. Elena Stark conducts a flipped classroom. Dr. Stark’s lab classroom in the 1P corridor has eight tables hosting seven students each, the groups having been assigned at the beginning of the year. At the head of each table is a computer monitor with access to a shared folder containing 3-6 Aperio virtual slides.

First up: the Assessment Quiz. Starting off with a test may sound unorthodox, but because the students have prepared the material on their own, it is their responsibility to arrive at the laboratory already in an active state of mind. This way, from minute one of the lab session, their knowledge can be molded, sharpened, challenged and strengthened.

Since the quiz isn’t for grading purposes, the evaluation gives the professor a good sense of the degree of studying, explaining and understanding taking place each week. By eliminating any anxiety over a grade, students benefit by focusing on their own knowledge,
THE APPROACH SUPPORTS CRITICAL THINKING, SINCE STUDENTS NEED TO COMPREHEND THE SUBJECT BOTH FOR THEMSELVES AND TO BE ABLE TO TEACH IT TO OTHERS.

comparing it to the knowledge held by others, and learning what is expected of them up to that point. What’s noteworthy is that although the students know that the quiz is not for a grade, the average score is about 80%, with a mode of 90%-100%; proof that the majority of students come to the lab session prepared and ready to teach.

The second phase begins once the quiz Scantron forms are collected. Now it is time for the students to discuss their answers with their peers.

“Why did you pick ‘A’ over ‘B’?”
“Because ‘B’ identifies both characteristics...”

Meanwhile, Dr. Stark circulates and confirms the person(s) with the correct answer(s), asking them to expand on their thought processes surrounding the question. After the entire quiz has been scrutinized within each group, the class connects as a whole for another review. Dr. Stark asks the questions to all:

“The answer to #5 is?”
“And why is this important to recognize?”

(Assessment quizzes are later posted to Intranet/ANGEL as a supplement for reference. The students can email the professor with more queries.)

The third stage employs a handout, which serves as a teaching guide. The students open the first Aperio slide. Today, the lesson is on the histopathology of the mucosa of the stomach, and the first slide is “Stomach Fundus.” The teaching guide consists of multiple pages containing directions (“find,” “locate,” “identify”) along with probing questions (“What are the components of the lamina propria?” “Does the structure and location of GALT make sense in terms of its function?”); a comparison chart; and fill-in-the-blank sentences (Describe, to your peers, the cell populations that are found in the gastric glands). Together, these prompts cover the vast data that the students had to explore prior to class.

Dr. Stark notes that “the same information is packaged in different ways” in the flipped classroom. Different students in a group emphasize different pieces of information, and each explains the material in his or her own way. “This is how you study,” asserts Dr. Stark. “This is how you learn.” The students listen to one another, interrupting with astute questions, seeking more knowledge from each other. It is an active and rich conversation – the opposite of the passive note-taking (or checking one’s text messages) that occurs in the lecture hall.

A brief overview presented by Dr. Stark introduces the Aperio slide to which the handout/teaching guide refers, orienting the students for their investigation. With the ability to navigate and magnify the image on monitors, each group consults with its members on the issues prompted by the handout/teaching guide. A give-and-take discussion ensues.

Again, Dr. Stark circulates and confirms. She reminds everyone that when learning from each other, “emphasize thinking your way through the material vs. memorizing tidbits of information.”

A summarization session follows, conducted by Dr. Stark, who again redirects any applied notions or inquiries from one student to them all.

“How good question! Who has a possible answer?”

As time and subject matter progress, so does the flip teaching process, with three more Aperio slides. The lab period concludes with the students applying their knowledge on two case studies, presented by a guest lecturer.

Many professors and instructors are praising the flipped classroom approach, but does this alternative learning process make for more enriching education? According to some first-year medical students, it certainly does. One student notes that working in groups presents a less intimidating environment for inquiring about misunderstandings and delving into challenges. Another declares that the approach supports critical thinking, since students need to comprehend the subject both for themselves and to be able to teach it to others. It was none other than Albert Einstein who agreed: “If you can’t explain it simply, you don’t understand it well enough.”
Pathology is considered a descriptive discipline dealing with the morphology of diseases in different organ systems. As a sub-specialty within both pathology and dermatology, dermatopathology is unusual in that various cutaneous diseases can be visualized by the naked eye and further characterized microscopically. Since the building blocks of pathology include inflammation and neoplasia (the formation of new abnormal tissue), both of which affect the skin, dermatopathology serves as the perfect vessel for introducing students to these core pathological concepts.

Interactive dermatopathology laboratory sessions are used to introduce UCLA medical students to pathology. During these sessions, instructors present a mixture of case vignettes, accompanied by descriptions of the histopathologic features corresponding to specific diseases. While reviewing the vignettes, students are shown a variety of descriptive clinical photographs that highlight the importance of clinico-pathologic correlation. The students leave these sessions with a wealth of information, giving them a solid foundation upon which to build their subsequent medical education.
MED SCHOOL PUTS MOLECULAR GENETICS FIRST

With the advent of the “block” curriculum several years ago, instruction of UCLA medical students in the field of genetics moved from the last quarter of the second year, at the close of their preclinical studies, to Block 1 of the first year—and indeed, starting in the very first week of that block. This reflects the understanding that we have entered the era of genomic medicine. Principles of inheritance and molecular genetic mechanisms underlie all fields of medicine—from surgery to psychiatry and everything in between. Patient care in all fields will increasingly rely on a thorough understanding of these concepts in order to provide optimal state-of-the-art tests and treatments, while avoiding inappropriate use of molecular diagnostic tests with the potential to harm the patient, both medically and psychosocially.

The Department of Pathology and Laboratory Medicine is responsible for the content in Block 1, making it the first discipline and first cohort of medical school faculty that the new students encounter. While the students can’t be expected to have any clinical context for these concepts as they start the curriculum, many are surprised and excited to learn that there are clinical applications to the molecular biology content they studied as undergraduates, according to Dr. Wayne Grody, professor and director of UCLA’s Molecular Diagnostics Laboratories, who presents most of the lectures and laboratory exercises during that first week.

An important component of Dr. Grody’s approach to the course, and to the entire “Genetics Thread” that stretches through all four years of medical school, is to convey to the students that molecular genetic tests do not exist in a vacuum. These tests carry tremendous consequences for the person being tested, as well as for that individual’s blood relatives. Dr. Grody’s lectures and lab exercises stress these ethical issues just as strongly as the technical aspects, delving into such philosophical dilemmas as genetic privacy, informed consent, insurance and employment discrimination, inequity of access to expensive genetic tests, and the burdens of exclusive gene patents. Student evaluations over the years demonstrate that they greatly appreciate this side of the story and find it interesting and challenging, providing much food for thought and discussion both in and outside the classroom.
Inflammation is a complex, multi-component response that protects the host from a harmful invader or tissue destruction. It represents an early defense warning system of the body, designed to minimize danger, mitigate damage and start the repair process. To achieve this essential task, the inflammatory system relies on an intricate series of molecular sensors stationed on high alert throughout the body. Once these sensors sound the alarm, the body activates an ever-growing array of molecular and cellular effectors tasked with protecting the host from dangerous foreign invaders or minimizing tissue damage from traumatic injury. Without the full armamentarium of this system, people can experience a myriad of problems, ranging from life-threatening infections to an autoimmune disease such as lupus. If left unchecked, excessive inflammatory responses can cause significant disease and death, likely contributing to atherosclerosis, diabetes and obesity, to name a few.

Dr. Steven Bensinger, who has been studying the inflammatory response and the immune system for nearly 15 years, teaches first-year medical students about the principles of inflammation. “The goal is not to memorize details, many of which will ultimately fade from their memory,” he explains. “Rather, I want the students to fundamentally understand how the inflammatory system works.”

Dr. Bensinger starts with anatomy so that students can see the tissues that are involved, then introduces the cellular players of the inflammatory system: neutrophil and macrophage. Next, he covers the myriad molecular effectors dedicated to rapidly responding to danger signals. Finally, students learn about the resolution of the inflammatory response — including the brakes of the system, keeping the host from the ever-escalating response. “The principles of inflammation, including how it functions in health and contributes to disease, will serve as a foundation throughout students’ medical education,” Dr. Bensinger notes.
The growing emphasis on translational research (converting laboratory findings to clinical gains) and personalized medicine has increased the importance of high-quality human tissue and fluid samples to identify potential therapeutic targets, find prognostic biological markers, and recognize markers that will facilitate tailoring of individual therapies for cancer patients. The biobanking practices associated with storing such samples have changed significantly over the past decade. A leader in this changing arena is Dr. Sarah Dry, director of the UCLA Department of Pathology and Laboratory Medicine’s Translational Pathology Core Laboratory (TPCL), which includes the UCLA Institutional Biobank.

In August 2012, TPCL became the fourth biorepository in the United States to be accredited by the College of American Pathologists (CAP). Similar to laboratory accreditation, CAP biorepository accreditation is a rigorous process designed to ensure that biorepositories have standard operating procedures in place that conform to current best-practice standards; processes for continual quality control monitoring and improvement; and appropriate initial and ongoing staff training processes. TPCL is now in the process of obtaining Clinical Laboratory Improvement Amendments (CLIA) certification, as more patients want their samples banked for future personalized-medicine clinical use.

Given the storage costs (space, freezers, electricity) involved with traditional biosample storage, biobanking researchers are exploring alternative storage methods. One technique being studied by Dr. William H. Yong, UCLA neuropathologist, involves room temperature storage of lyophilized samples (see page 25).

Two innovative additions to UCLA/TPCL biobanking are being introduced this year. One involves linking whole-slide digital images to samples in the biobank database. The quality control slide for each biosample is scanned on TPCL’s Aperio AT scanner and stored. A thumbnail image of the scanned slide appears in the database, and a link to the full image enables staff or researchers to immediately determine if the biosample satisfies research needs. The second innovation involves the installation of Daedalus Crimson software at UCLA. Crimson permits identification of soon-to-be-discarded clinical samples for use in research. This technology will make it easier for researchers to obtain (with appropriate informed consent) both patient-specific and disease-specific samples.

An important effort underway at UCLA involves instituting global informed consent for the use of remnant biosamples in research. Recent federal and state concerns about patient privacy given current genomic testing capabilities suggest that continued use of
"anonymous" or coded samples may not be considered sufficient protection for human research subjects, and that informed consent may be required. Dr. Dry has been leading a UCLA group that is evaluating this issue and determining how to implement appropriate changes at UCLA. This effort parallels and complements Dr. Dry’s efforts on her recent National Institutes of Health grant for biobanking and informed consent.

Pioneering biobanking practices ensures that UCLA will continue to lead the way in translational research and personalized medicine.

EXPLORE Translational Pathology Core Laboratory pathology.ucla.edu/tpcl
The new Center for Pathology Research Services (CPRS), under the leadership of Justin Perry (manager) and Dr. Sarah Dry (director), will serve as a centralized and comprehensive resource for investigators looking to access services offered by the department’s core facilities. These facilities include:

- Clinical Microarray Core Laboratory
- Clinical and Translational Research Laboratory
- High-Throughput Clinical Proteomics Core Laboratory
- Translational Pathology Core Laboratory
- UCLA Immunogenetics Center

Rather than investigators spending valuable time and resources determining whom to contact about a particular question, all inquiries can now be directed to a single location. The CPRS is staffed by a group of research coordinators and located on the A-level of the Center for Health Sciences building, enabling researchers to contact a single office or website for all of their study needs. This includes basic inquiries about services offered, protocol reviews, pricing, budget development, Institutional Review Board support, invoicing, result reporting and specimen handling, among other operational and logistical services.

With the CPRS, researchers can expect increased access to the available services, improved coordination and processing speed for service requests, and significant cost savings through greater use of shared resources. The CPRS aims to facilitate and expand utilization of the department’s core facilities while supporting UCLA researchers in their efforts.  

EXPLORE Research Services  
pathology.ucla.edu/rs
A three-year, $2 million National Institute of Health grant has been awarded to UCLA Department of Pathology and Laboratory Medicine’s Sarah Dry, MD, PhD, and two colleagues at UC San Francisco. This effort to inform debate on the issue of informed consent practices in the use of biosamples for genomic research, is in response to concerns expressed by both federal and state government funding agencies.

“EngageUC,” has three objectives:

- Develop harmonized biobanking operations and governance practices among the University of California’s (UC’s) five biomedical campuses (Davis, Irvine, Los Angeles, San Diego and San Francisco);
- Create uniform administrative practices for inter-UC research activities by working with the institutional officials at each campus; and
- Conduct a randomized clinical trial of different types of informed consent forms for use of biosamples in research.

The researchers will solicit community participation and advice on biobanking and informed consent issues using a process known as Deliberate Community Engagement during weekend-long meetings in both Northern and Southern California. Ultimately, their goal is to have a standing community advisory board to UC on issues of biobanking and the use of biosamples in research.

EXPLORE EngageUC
pathology.ucla.edu/engageuc
Using a freezer to store tissue and blood is arguably the most effective approach to modern pathological analysis. But there are drawbacks, including the cost of freezing the biospecimens and their vulnerability to thawing as a result of freezer failure or other events. Securing funding and space for banks of freezers can be challenging for biomedical institutions. On the other hand, formalin fixed paraffin embedded tissues – the most common biospecimens stored – can remain relatively stable at room temperature over the long term, but these tissues contain fragmented and cross-linked nucleic acids, limiting their value. Now a group headed by William H. Yong, MD, director of the Brain Tissue Translational Resource, is seeking to achieve the best of both worlds – developing better ways to store tissues at room temperature while preserving nucleic acids and proteins.

Dr. Yong’s group has conducted studies showing that when brain tumor tissue is freeze-dried (lyophilized) and stored in vacuum-sealed vials for a year at room temperature, nucleic acids and proteins are suitable for histology, mutation detection, and protein analyses, including enzymatic assays. Ribonucleic acids (RNA), though amenable for genetic analyses, show some evidence of degradation in such conditions, so Dr. Yong and colleagues are exploring ways to better stabilize RNA in the freeze-dried tissue as they move closer to their ultimate goal. A variety of factors, including light, oxygen, humidity and peroxidation, can degrade nucleic acids, so Dr. Yong’s group is evaluating additives that might mitigate their effects. The researchers have also lyophilized samples that are 2-4 years old to determine their characteristics.

While the investigation into the freeze-dried storage approach continues, Dr. Yong and colleagues are also looking at ways to protect precious frozen samples from being lost as a result of extended loss of power from earthquakes or other events. They believe diversified storage, in both location and modality, may be the answer. Samples can be stored in freezers in different rooms or buildings so that if there is damage in one location, all will not be lost. In the future, the group hopes that stabilized tissues storable at room temperature will lower the monetary, labor, space and environmental costs necessary to support biobanks, which are critical for propelling personalized molecular therapy research.
FACILITIES
Total number of square feet of Clinical, Research, and Teaching space
TOTAL SPACE IN SQUARE FEET = 254,980

- Clinical: 146,485
- Research: 41,543
- Core Lab: 12,568
- Educational, Academic, & Administration: 45,997

AWAITING TENANT IMPROVEMENTS: 10,387

DEPARTMENT OF PATHOLOGY
TOTAL = 1,226 PEOPLE

- Staff: 984
- Faculty: 117
- Residents/Fellows: 45
- Postdoc Researchers: 37
- Grad Student Researchers: 25
- Professional Research Series: 18

CLINICAL METRICS 2013 (projected)

- Outreach Cases: 59,500
- Cytology Cases: 41,000
- Surgical Pathology Cases: 31,000
- Molecular Pathology Cases: 7,100
- Cytogenetics Cases: 21,000

RESEARCH FUNDING
TOTAL = $46.7 MILLION

- NIH Funding: $30.7M
- Other Granting Agencies: $16M

DEPARTMENT INVENTIONS IN 2012
- 15

CLINICAL LAB TESTS
- Nearly 6 MILLION

OTHER GRANTING AGENCIES: $16M

NIH FUNDING: $30.7M

STAFF: 984

FACULTY: 117

RESIDENTS/FELLOWS: 45

POSTDOC RESEARCHERS: 37

GRAD STUDENT RESEARCHERS: 25

PROFESSIONAL RESEARCH SERIES: 18

CLINICAL METRICS 2013 (projected)

OUTREACH CASES

Cytology Cases

Surgical Pathology Cases

Molecular Pathology Cases

Cytogenetics Cases

DEPARTMENT INVENTIONS IN 2012

15
Raymond Barnhill, MD: Founders’ Award of the American Society of Dermatopathology

Kingshuk Das, MD: 2012 Daljit S. & Elaine Sarkaria Fellowship

Gregory Fishbein, MD: 2013 Daljit S. & Elaine Sarkaria Fellowship

Samuel French, Sr., MD: 2014 American Society for Investigative Pathology Gold-Headed Cane Award

Dennis Goldfinger, MD: The Suzanne Ledin Lectureship And Award, Suzanne Ledin Memorial Foundation, Presented By The California Blood Bank Society, April 3, 2012

Wayne Grody, MD, PhD: President, American College of Medical Genetics Arno Roscher Endowed Lectureship, International College of Surgeons Bowes Award Lectureship in Medical Genetics, Harvard Medical School Golden Apple Award, UCLA Intercampus Medical Genetics Training Program AMP Leadership Award, Association for Molecular Pathology

Elaine Reed, PhD: ASHI Rose Payne Distinguished Scientist Award & 2012 Rachel McKenna Memorial Lecturer

Elena Stark, MD, PhD: UCLA DGSOM Class of 2015 Golden Apple Award for Excellence in Teaching

Mike Teitell, MD, PhD: 2013 Harrison Latta Chair in Pathology

Robert Trelease, PhD: appointed Associate Editor, *Anatomical Sciences Education* (official journal of American Association of Anatomists).

Jonathan Wisco, PhD: American Association of Anatomists 2013 Basmajian Award

Voted BEST DOCTORS® 2013:

Scott Binder, MD

Alistair Cochran, MD

Galen Cortina, MD, PhD

Charles Lassman, MD, PhD

Sheeja Pullarkat, MD

Jonathan Said, MD

Hanlin Wang, MD, PhD
The Clinical and Research Alumni Committees are a vital part of the Department of Pathology and Laboratory Medicine at UCLA. 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, is Chair of the Clinical Research Committee; Josh Deignan, PhD, FACMG chairs the Research Alumni Committee.

The Pathology Clinical and Research Alumni Committees are delighted to represent our former trainees and ensure the link between them and the UCLA Department of Pathology and Laboratory Medicine remains strong. To learn more, or to subscribe to our newsletter, please visit our website.

Recent Highlights:

- The first Clinical Alumni Newsletter is introduced
- Clinical and Research Alumni Web pages launched: pathology.ucla.edu/alumni
- New Clinical Alumni Facebook Page (search “UCLA Pathology Alumni”)
- Active Research Alumni LinkedIn Page (search “UCLA Pathology Research Alumni”)
- Alumni Mentoring and Teaching Programs:
  - Mohammad Kamal, MD and Valerie McWhorter, MD address career issues
  - Kimberly Mislick, MD, PhD addresses medical directorship of the community laboratory

DEPARTMENT IN DEPTH

explore...
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

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

NAMING OPPORTUNITIES

For support of a dedicated research institute or center, including capital improvements and/or programmatic support: $10,000,000
• University Immunogenetics Center

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

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

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

2012 VOLKSWAGEN CITY OF ANGELS FUN RIDE, benefitting the UCLA Blood & Platelet Center.

L to R: Dr. Linda Baum, Dr. Scott Binder, Dr. Alyssa Ziman, Peter Heumann, City of Angels Fun Ride Founder; Maria Marsh, owner of Pace Sportswear; Howie Neftin, owner of Neftin Volkswagen; and Pamela Bumerts.
A Closer Look

The Crohn's & Colitis Foundation of America, and The Leona M. and Harry B. Helmsley Charitable Trust

Through a competitive grant to Jonathan Braun, MD, PhD, The Crohn's & Colitis Foundation of America, and The Leona M. and Harry B. Helmsley Charitable Trust, generously support the Department of Pathology and Laboratory Medicine in research on the role of intestinal microbes in Crohn's disease. This multi-center national study aims to uncover the disease-significant microbes and their products, and to determine how to target them for treatment and prevention of this common intestinal disease. CCFA has been a longstanding partner of the Department, advancing its research on Crohn's disease and colorectal cancer, and the career development of young scientists and doctors devoted to these health concerns of our community.

Ms. Agi Hirshberg and the Hirshberg Foundation for Pancreatic Cancer Research

The Department of Pathology and Laboratory Medicine is grateful for contributions from Ms. Agi Hirshberg and the Hirshberg Foundation for Pancreatic Cancer Research in support of innovative research under the direction of David Dawson, M.D. His work focuses on genetic modifications that have shown potential to slow or stop the cancer's progression.

The Foundation also has long-sustained key partnerships with the UCLA Center for Pancreatic Diseases, UCLA Division of Digestive Diseases, Simms/Mann UCLA Center for Integrative Oncology, UCLA Department of Chemistry and Biochemistry, and others and has been instrumental in the University's efforts to find a cure for pancreatic cancer, an aggressive and deadly disease.

Joseph Drown Foundation

In the past year, the Joseph Drown Foundation renewed its support of important research in ataxia-telangiectasia (A-T) under the direction of Richard Gatti, M.D. Private contributions have helped UCLA become a leader in this area, and such vital funding helps to ensure continued progress toward improved treatments for DNA repair-deficiency disorders. The Department is appreciative of the Foundation’s commitment to preserving excellence in A-T and related investigations.

We Thank Our Generous Supporters, Including:

American Cancer Society, Inc.
American Society of Hematology
Dr. Richard Braun & Mrs. Barbara Braun
Crohn's & Colitis Foundation of America
Joseph Drown Foundation
The Leona M. and Harry B. Helmsley Charitable Trust
Lya Cordova Latta
Mizutani Foundation for Glycoscience
Drs. Elaine and Daljit Sarkaria

“IT IS A PRIVILEGE TO SUPPORT A DEPARTMENT THAT TRAINS PEOPLE OF SUCH HIGH CALIBER AND INTEGRITY, WHO GO OUT AND DO SO MUCH FOR THE COMMUNITY.”
- Lya Cordova Latta