



The IMED Seminar Series: The place to be on Wednesdays

Not sure where to go Wednesdays at noon? Just follow the stream of faculty, students, postdocs, residents and staff heading towards the Institute for Molecular Medicine (IMED) Seminar Series. Under the direction of Lee Goodglick, Heather Christofk, Hong Wu, Sam Chow and Lynn Gordon, the series has become one of the most dynamic and electrifying lectureships on campus.

"Our goal", says Goodglick, "is to re-define the concept of the 'seminar', of 'community gathering' and of networking here on campus. We wanted to create the most exciting seminar series at UCLA in order to promote education and awareness, but also to foster both inter- and cross-disciplinary mingling of faculty, students, postdocs, residents and staff."

The exciting and eclectic roster of guests includes

Nobel Prize winners (e.g., Timothy Hunt, Joe Goldstein,



Tom Steitz, Michael Bishop, Stan Prusiner, Elizabeth Blackburn), game-changing researchers and physicians (e.g., Jeff Bluestone, Todd Golub, Marc Kirshner, Janet Rowley, Michael Karin, Frank McCormick, Barry Bloom, Fred Alt, Sean Morrison), policy leaders (e.g., Ezekiel Emanuel, Joycelyn Elders, Temple Grandin, Laurie Levenson), experts in communication (e.g., Nancy Snyderman, Robert Bazell), pioneers of technology (e.g., Nathan Myhrvold), authors (e.g., Oliver Sacks, Jared Diamond, Samuel Shem, Natalie Angier) philanthropists (e.g., Eli Broad, Don Listwin) and our own community leaders (e.g., Gene Block, Eugene Washington, Ben Howland, Owen Witte).

The seminar series is primarily sponsored by IMED, a UCLA interdepartmental partnership co-led by Pathology and Lab Medicine. The goal of IMED is to provide the infrastructure and environment needed to drive bench discoveries towards clinical relevance.

"The series really exemplifies the mission of IMED to promote cross-disciplinary discussion and pollination," Goodglick says. "As the huge crowds each week can attest, we not only have a little bit of something for everyone, we have a lot of everything for all."

More information and a complete schedule listing can be found at www.IMEDseminar.com.



The Most Human Human

he 2009 winner of the international competition for the Most Human Human was Brian Christian. (http://www.theatlantic.com/magazine/archive/2011/03/mind-vs-machine/8386). A philosopher, journalist and comedian, Christian participated for the Loebner Prize, an annual competition on the Turing Test of computers and humans to overcome the greatest challenge of our time—meaningful conversation. As he observed, living in our technology world provides "... a healthier view of human intelligence—an understanding, not so much that it is complex and powerful, per se, as that it is reactive, responsive, sensitive, nimble..." The computation theorist Hava Siegelmann once described intelligence as "a kind of sensitivity to things."

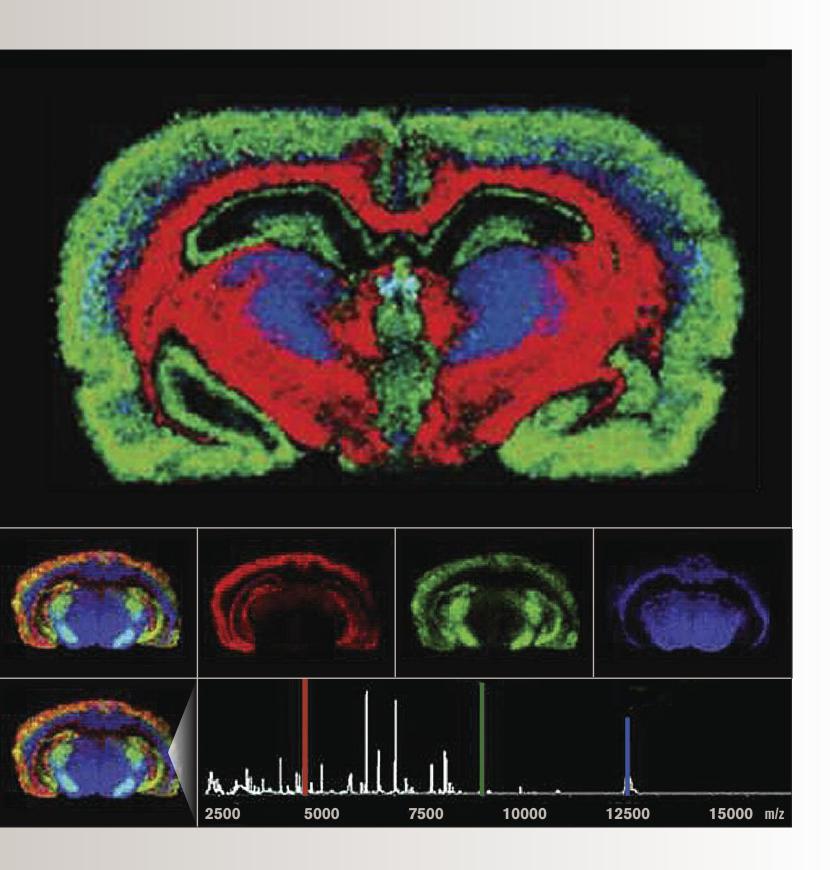


Buffeted by technologic and social change, who doesn't struggle to harness the tumult to benefit, rather than diminish, the welfare of those we care for? This struggle was at the heart of the works of artists from Mark Twain to Bruce Springsteen, and John Dewey to Modest Mouse. More than most disciplines of medicine, pathology is immersed in technology. Our anatomic pathologists dive deep into cell biology to diagnose cancer and inflammatory diseases. Our laboratory medicine staff array thousands of biochemical and molecular features to monitor disease course and guide treatment. Our researchers, probing molecular metabolism, immunity, and stem cell biology, struggle for new insights from cancer to Alzheimer's disease, and as well as heart disease to the control of HIV. And together, we train our students so that they can do better than us to understand and treat these diseases for the generations ahead.

This year's annual report tells some of these stories. There is much about them at the edge of colorful science and awesome technology. However, what lingers with me are the underlying stories—to find the broken and incomplete, and to repair and make whole. Rosario Saavedra and her experience with liver transplant. Wesley Chu and his journey with prostate cancer. And how, for patients with failing tissues, Gay Crooks and Lisa Kohn discover the molecular ecology to make stem cell therapy and regenerative medicine a reality.

So, I invite you to read these stories of amazing people, wrestling to harness powerful technologies on behalf of our patients and community, and to all while mentoring our students and fellows in "sensitivity to things".

—Dr. Jonathan Braun, Chair, Department of Pathology and Laboratory Medicine



MALDI-TOF instrument that is capable of detecting proteins directly from thin tissue sections mounted to conductive glass microscope slides. We will be capable of compiling mass spectra across the tissue with 10–20 um resolution and converting them to heat maps based on protein or lipid abundance.



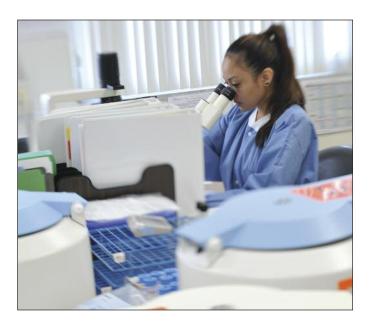
"Our future success is increasingly dependent upon philanthropic support for essential investments in cutting edge technologies and infrastructure improvements that nurture promising young scientists and investigators" — KENNETH DORSHKIND, PhD

he Department of Pathology and Laboratory Medicine is home to scientists internationally renowned for their expertise in areas of biomedical research that include bioinformatics, cancer cell biology, immunology and inflammation, metabolomics, neurobiology and stem cell biology. The department's research goals are twofold. First, we seek to determine how cells, tissues and organs function normally in order to better understand the changes that occur in disease. Second, we endeavor to apply the information obtained to enhancing diagnostic capabilities and developing new therapies.

The building of the Department's research enterprise has been a major emphasis over the past decade and the continued successes of our faculty members provides strong evidence that we have been successful.

Work in the laboratory of Gay Crooks, MB, BS, FRACP, focuses on the expansion and manipulation of hematopoietic stem cells, the population from which all blood cells derive, for therapeutic purposes. Jiaoti Huang, MD, PhD, typifies the role played by departmental faculty in both research and diagnostics. The Director of Urologic Pathology, Dr. Huang works with surgeons and other physicians in the diagnosis and treatment of prostate cancer. He also directs an active research laboratory that recently reported groundbreaking results about the origins of that disease.

Obesity, diabetes and cardiovascular disease are the leading causes of morbidity and mortality in industrialized societies. The common thread that links these disorders is a dysregulation of lipid metabolism. Peter Tontonoz, MD, PhD, an investigator with the Howard Hughes Medical Institute, has led the way in determining how genes that regulate this process, turn on and off.

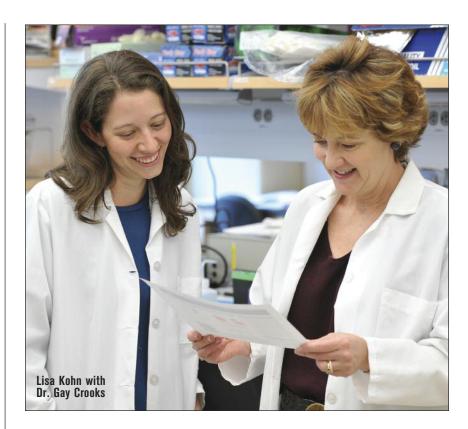


The work of Drs. Crooks, Huang and Tontonoz typifies the cutting-edge research being conducted at UCLA as well as our commitment to sustaining the infrastructure that will allow us to retain research leaders while attracting rising stars to the department.

Continued success of these investigators and the research enterprise overall is dependent on sufficient funding. Our faculty and trainees are highly competitive for NIH funding, the traditional source for most biomedical research support. However, with mounting pressure on the federal budget, it is clear that we will increasingly depend on philanthropic support as we move forward, particularly for investing in cutting edge technologies that benefit many investigators and for supporting the promising young students and investigators who represent our future.

Team Science

A new era of personalized medicine requires an unprecedented integration of many disciplines including chemistry, pathology, engineering, biology, physics, imaging and clinical sciences. Integration of these disciplines requires a new model of collaborative interaction between basic and clinical scientists with different backgrounds working together on common problems to an end result of proven benefit to patients. This "Team Science" focuses on problem solving in patient care founded on new science and new technologies. The Institute for Molecular Medicine (IMED), a UCLA interdepartmental partnership co-led by Pathology and Lab Medicine, is the coming together of these disciplines in a common space with a common mission that is to build the molecular tools for linking new molecular diagnostics and molecular therapeutics based on a new systems biology view of disease. The ultimate measure of success is in improving the care of patients.



Stem Cell Research Leads to Innovative Cures

he early clinical work of Gay Crooks, MBBS, as a bone marrow transplant physician, caring for children with leukemia and genetic diseases of the blood and immune system, initiated her interest in stem cell research as well as the challenges confronting bone marrow transplant physicians and their patients. Seeking new ways to produce and transplant hematopoietic stem cells that can rapidly restore normal blood and immune function, she arrived at UCLA in 2009 where she is supported by grants from the NIH, NHLBI, NIAID and the California Institute of Regenerative Medicine (CIRM).

Here in Westwood she has continued her internationally known research on how human hematopoietic stem cells can be isolated and manipulated to improve the results of transplantation. The remarkable self-renewing ability of the blood-forming stem cells in bone marrow and umbilical cord blood, allows physicians to reconstitute a complete blood and immune system from healthy donors in patients after high dose chemotherapy and radiation.

Dr. Crooks' work has led to discoveries on how stem cells produce a new immune system as they develop in the thymus and how this process might be improved. In addition, she endeavors to develop ways to make blood and immune cells from human embryonic stem cells to overcome shortages of matched adult stem cells. Her study of these rare and intriguing cells continues to guide the science of stem cell biology and lead to innovative cures through gene and cell therapy.

Research laboratory studies with hematopoietic stem cells such as those headed by Dr. Crooks, have revealed much of the remarkable biology behind all types of stem cells and can provide clues on how to move stem cell biology into clinical care.

Strategies to Cut the Risk of Atherosclerosis

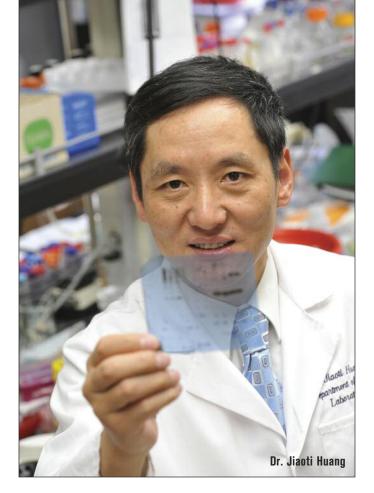
eter Tontonoz, MD, PhD, is working to understand how lipids regulate cellular physiology and influence the development of metabolic disease. His work has uncovered fundamental mechanisms involved in the control of cholesterol homeostasis and helped to define new connections between lipids, their metabolism and immune responses. The dissection of these pathways is not only advancing the understanding of basic biological processes, but also highlighting potential opportunities for therapeutic intervention in human diseases.

Dr. Tontonoz's research has uncovered a new pathway for regulation of blood cholesterol levels that may lead to new strategies to treat heart disease. High levels of plasma LDL cholesterol (bad cholesterol) are a strong risk factor for atherosclerosis. A major indicator that determines the levels of LDL circulating the blood is the level of expression of the LDL receptor (LDLR). LDLR on the plasma membrane of cells binds to circulating LDL facilitating the clearance of LDL from the blood. Thus, higher levels of LDLR expression lead to less LDL in the blood and reduced risk of cardiovascular disease. Statins, a well-known class of lipid lowering drugs, act by increasing LDLR expression in the liver. Tontonoz's study of the nuclear receptor LXR, has discovered a new mechanism by which the level of cholesterol in a cell's feedback inhibits the expression of LDLR. Identification of a protein called IDOL (Inducible Degrader of the LDLR) that targets the LDLR for degradation, thereby blocking LDL uptake, may lead to the development of new drugs to lower cholesterol levels.

Dr. Tontonoz is currently working to determine whether inhibiting IDOL activity with small molecules or molecular biological approaches may reduce LDL levels and risk for cardiovascular disease.

Below: (left to right) Peter Tontonoz, MD, PhD, Claudio Villanueva, Anna Calkin, and Cindy Hong





Targeting Prostate Cancer While Preserving Normal Tissue

iaoti Huang, MD, PhD, came to UCLA in 2008 where he serves as the Director of Urologic Pathology. Both a physician and scientist, Dr. Huang is in the unique position of being able to translate laboratory discoveries into useful modalities that benefit patients. Treating patients with tumors of the urinary system, Dr. Huang routinely provides histologic diagnosis, including classification, grading and staging of the tumors of the urinary system seeking the most appropriate therapies for patients.

Focused on advancing the diagnosis and treatment of prostate cancer, Dr. Huang's research is funded by the American Cancer Society, the National Cancer Institute, the Prostate Cancer Foundation and the Department of Defense Prostate Cancer Research Program.

Dr. Huang's current research seeks the basic mechanisms responsible for the development and progression of prostate cancer, biomarkers for the diagnosis of prostate cancer and novel therapeutic agents that specifically target cancer cells without adverse effects on normal tissue.

His collaboration with clinicians and scientists throughout the medical community has proven essential in improving the radiologic diagnosis of prostate cancer, researching ways to spare patients of radical treatments and the identification of certain stem cells known to give rise to cancer as well as isolation of circulating tumor cells from the blood of patients with advanced cancers for the purpose of targeted and personalized therapies.

Wayne Grody Pioneers DNA-based Testing

ne of the first facilities of its kind, the UCLA Diagnostic Molecular Pathology Laboratory has pioneered applications of diagnostic DNA-based testing for a wide variety of genetic and neoplastic diseases as well as DNA fingerprint analysis. In addition, the laboratory has emerged as a leader in the development of quality assurance and ethical guidelines for molecular genetic testing.

Operating under the direction of Wayne Grody, MD, PhD, one of the primary authors of the College of American Pathologists Inspection Checklist, the lab's role is not limited to clinical service and includes activity in basic and

applied clinical research. Some of the innovations emanating from the lab include the first documentation of HIV infection of the heart in AIDS, development of a highly sensitive method for detection of cell-specific gene expression and micrometastatic tumor cells, population genetic studies of the allele frequencies of the clotting factor V-Leiden mutation, and CCR-5 polymorphism of HIV resistance and early diagnosis of pancreatic carcinoma.

The facility offers a host of testing including differentiation of donor from recipient cells after a bone marrow or organ transplant by DNA polymorphisms; detection of Philadelphia chromosome and other translocations in leukemias and lymphomas; detection of clonal immunoglobulin and T-cell receptor gene rearrangements in lymphomas and leukemias; identification of mutations in cystic fibrosis, Fragile X syndrome, familial breast/ovarian cancer (BRCA1/2 genes), hereditary thrombophilias, Huntington disease and other genetic disorders; oncogene mutation analysis in solid tumors as companion diagnostics for targeted molecular therapies; determination of paternity, twin zygosity and surgical specimen identity by DNA fingerprinting.

Recently, the lab was the site of a Human Genome Project funded pilot study on population screening for cystic fibrosis mutations, which led to the recommendations that all couples nationwide be offered such a screening.

Consistent with its cutting-edge

tradition, the laboratory is working with Stanley Nelson, MD, of the Department of Human Genetics, as well as members of the Department of Pediatrics, embarking on whole genome analysis for diagnosis and discovery of inherited disorders and acquired mutations in tumors. The project will build on the lab's strengths and reflect a unique mix of state-of-the-art molecular diagnostics with expert clinical interpretation of the data produced. With plans in place to make this powerful new technology available to selected patients unable to obtain a precise diagnosis using standard genetic testing approaches, the Diagnostic Molecular Pathology Laboratory has established itself among the preeminent facilities of its kind globally.



Bench to Bedside: Easing a Child's Suffering

CLA's Molecular Diagnostic Services are unique from those obtained from commercial reference labs and most other academic-based laboratories, in the degree of integration with the clinical aspects of the patient and our laboratory directors' ability to provide consultation to ordering physicians on that basis.

Wayne Grody, MD, PhD, an attending physician in the Medical Genetics Clinic within the Department of Pediatrics, recently saw "Eddie," a 2-year-old boy with recurring high fevers and abdominal pain. While it is easy to write off such symptoms as merely the usual pediatric viral infections, the periodic nature of the episodes and the family's Armenian background, suggested a likely diagnosis of familial Mediterranean fever (FMF), a disorder for which we have extensive experience at UCLA. Dr. Grody also attends in the monthly FMF clinic at the Department of Medicine, the largest clinic dedicated to this disease in the Western hemisphere.

FMF is readily treatable with a very old and inexpensive drug, colchicine. However, the patient must take the drug every day for life in order to prevent the recurrent fever and possible renal failure. Despite the relatively low incidence of side effects, Eddie's parents did not want to begin the drug treatment without a definitive laboratory diagnosis of FMF, potentially prolonging the child's suffering. While a number of serum inflammatory markers can be elevated in this disorder, the only specific laboratory test is the detection of mutations in the causative gene, designated MEFV.

The laboratory directed by Dr. Grody is one of only a few in the world offering this DNA test for the 12 most common MEFV mutations in Middle Eastern populations, as well as by complete sequencing of the entire gene to detect virtually all possible mutations. Eddie was found to have two mutated copies of the gene and the delivery of this definitive diagnosis to the parents convinced them to begin the colchicine therapy right away.

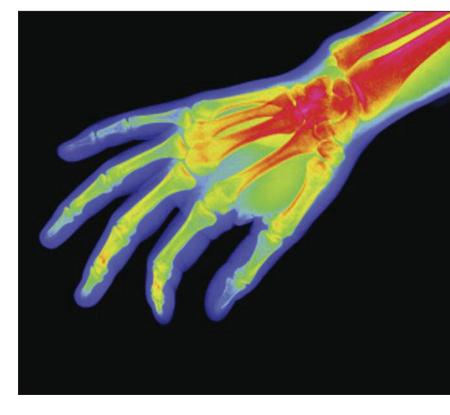
The laboratory tests many other suspected FMF patients on blood specimens sent in from all around the country and Dr. Grody offers similar clinical consultation on diagnosis and management by phone to many of the referring physicians making the lab a comprehensive service covering all aspects of the disease.

PATHOLOGY'S ROLE IN HAND TRANSPLANT'S SUCCESS

World renowned as pioneers in the field of transplant, UCLA recently performed its first limb transplant with great success. The delicate surgery offers the recipient a life free from prosthetics as well as a promising vision of the future where patients who have lost one or both hands will have the opportunity to regain functionality with a transplanted limb.

With only a few transplants of this type ever performed, Scott Binder, MD, and Chandra Smart, MD, are leading the pathology team in this exciting new area of transplant pathology helping to restore a semblance of a normal life to victims of accidents or warfare.

With very little in the literature regarding the immunology of limb acceptance and rejection, Dr. Smart is collaborating with Elaine Reed, PhD, in immunogenetics and colleagues in plastic surgery, transplant medicine and immunology, on numerous studies designed to learn the immunologic basis for rejection of these specialized transplanted limbs.



Providing the Tools For Effective Research

Offering expertise and services impossible for the individual researcher to perform cost-effectively, the Translational Pathology Core Laboratory (TPCL) provides a broad range of pathology services to UCLA researchers.

Directed by Sarah Dry, MD, since 2004, the laboratory has seen tremendous growth in core activities, with a greater than 250 percent increase in services performed and a greater than 150 percent increase in researchers using the facility. Equally successful at fundraising, Dr. Dry recently collaborated with the Directors of the Advanced Light Microscopy Systems Core to bring the latest generation laser microdissection unit to UCLA. Prior successes include procuring over a million dollars of funding to purchase new state-of-theart technologies. Eleven new or upgraded instruments have been added to the Core, including highly sophisticated quantitative digital analysis software. Perhaps the most exciting purchases are two digital high throughput whole slide scanners which convert a traditional glass slide into a digital image file, which can be viewed at different magnifications and promises to transform pathology's clinical and research activities.

One of the first core laboratories in the country to provide high-throughput digital slide scanning services, the TPCL now performs more than 10,000 slide scans and 1,000 automated digital analysis projects annually.

Pathology and Radiology Join Forces to Provide Comprehensive Diagnoses

he UCLA Radiology-Pathology project is a joint venture by the UCLA departments of Radiology and Pathology to develop a single integrated report encompassing all diagnostic modalities for evaluation of a disease process. Working to combine state-ofthe-art imaging diagnostics, including minimally invasive image-guided biopsies with sophisticated analysis of tissue specimens, Scott Binder, MD, W. Dean Wallace, MD, and Kingshuk Das, MD, designed the service to have the capacity to combine clinical staging, pathologic diagnoses, molecular prognoses and response prediction in patients for evaluation and treatment of their malignant disease. Initial focus will be on lung, breast, pancreas, liver and kidney organ systems. The report will be designed to allow for easy access to all pertinent imaging or pathologic diagnostic information in one place. The electronic report will be accessed through a secure website and allow the end-user to view the diagnostic studies easily and without the need to wade through burdensome information. Utilizing an electronic web-based report will enable informatics technology to maximize the end-user's capabilities. Ultimately, the treating clinician will benefit the most by this report format. Diagnostic errors will be recognized before the reports are signed out thus reducing false negative findings. The clinician's workflow will be streamlined by having a single site for all pertinent diagnostic studies. The availability of the information through a secure web based reporting system will provide greater flexibility to clinicians who work in multiple locations or who may be temporarily absent from their primary place of practice.



Bench to Bedside: Outsmarting Rejection

here are many patients who await a kidney transplant in this country, roughly 80,000 at last count. For some, the challenge is lack of a living kidney donor where the wait for deceased donor transplantation can be 10 years in this region for certain blood types. For others, the challenge can be the presence of antibodies against HLA molecules, essentially antibodies against other people that prevent them from receiving a kidney from a family member or friend because of immune sensitization. In many, but not all cases, these patients can be desensitized to receive that transplant. However, the greatest challenge is for the patient who does not have a living donor kidney candidate and also has substantial immune sensitization. These patients, more than likely, have no chance of receiving a cross-match acceptable kidney transplant.

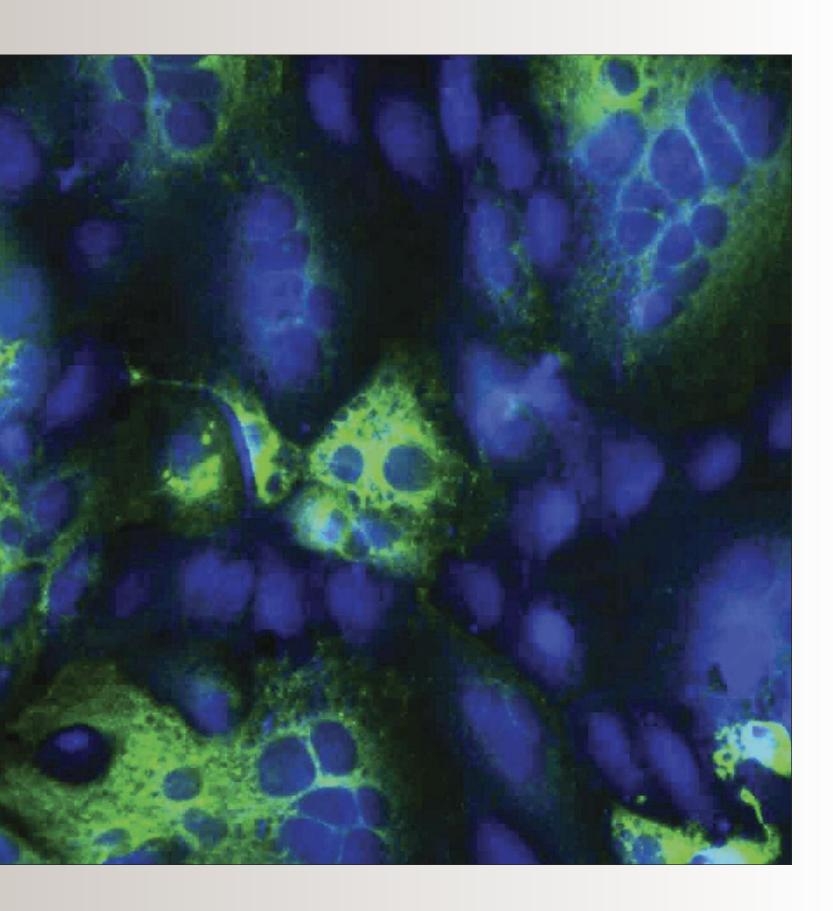
About 25 percent of kidney transplant candidates test positive for HLA antibodies which are proteins that will attack the foreign donor organ and cause rejection of the transplant. Pregnancy, blood transfusions and previous transplantation can cause a patient to develop HLA antibodies. Often patients who are sensitized have to wait many years to find a donor organ that they will not reject. Until recently, there has been little hope that patients with high HLA antibody levels would ever receive a transplant and get off dialysis. Here at UCLA, we have established a program called Deceased Donor Desensitization (DDD) for patients who have immunological sensitization and no living donor candidates. This program is made possible through collaboration between our Department's Immunogenetics laboratory under the leader-

ship of Elaine Reed, PhD, and her team, Rajalingam Raja, PhD, and Jennifer Zhang, PhD, and Kidney Transplantation physician, Gerry Lipshutz, MD. Novel plasmapheresis and IVIG therapeutic strategies are used to lower the levels of HLA antibodies in patients like Mr. M, a 62-year-old man with renal failure from diabetes and substantial immune sensitization. Mr. M. was waiting for a transplant for more than 10 years. Shortly after starting the desensitization therapy, Mr. M.'s HLA antibody levels began to decline and he received a deceased donor kidney transplant. To date, we have performed more than 50 HLA incompatible kidney transplants after desensitization therapy with high-dose IVIG or a combination of high-does IVIG/anti- CD20 and plasmapheresis therapy.

The success of the DDD program is hinged on the close collaboration between the transplant physicians, nurses and the Immunogenetics laboratory. The Immunogenetics laboratory provides rapid testing of HLA antibody levels using sensitive solid phase assays to measure the patient's response to therapy. This information is used by Dr. Lipshutz to determine each phase of the patient's desensitization treatment. The Immunogenetics laboratory also identifies the "acceptable" HLA mistmatches that the patient can be transplanted with–called the "virtual crossmatch." The "virtual crossmatch" facilitates transplantation of sensitized patients by enabling the patient to be matched with donors from all geographic areas around the United States.

Research at UCLA is underway to determine if other therapeutic strategies can increase the success of the desensitization protocol to improve outcome and prevent the antibodies from coming back.





Nipah virus, a deadly emerging human pathogen, is studied in the laboratories of Dr. Benhur Lee and Dr. Linda Baum. The Nipah virus fusion protein (here labeled green) causes fusion of infected cells (shown by coalescence of blue-labeled nuclei), with subsequent cell breakdown and eventual loss of organ function.



"Utilized by a broad segment of the UCLA biomedical research community, the five core laboratories of the Research Services Division provide highly innovative and specialized services."

— ELAINE REED, PhD

CLA Research Services Division is composed of five core laboratories serving the research community by offering innovative instrumentation, technologies and specialized services, which are utilized by a broad segment of the UCIA biomedical research community.

The Clinical Microarray Core (CMC), under the direction of Xinmin Li, PhD, provides a wide range of clinical and translational research-based genomic services including differential gene expression assay, gene alternative splicing assay, copy number variation assay and high-throughput genotyping.

The Clinical Immunology Research Laboratory (CIRL), under the direction of Anthony Butch, PhD, provides research and clinical services for biomarkers identifying early signs of immunity related to disease activation and monitoring responsiveness to drugs in management of organ and stemcell transplantation, HIV infection as well as a variety of chronic inflammatory diseases.

The High-Throughput Clinical Proteomics Core (HTCP), under the direction of James LeBlanc, PhD, is a mass spectrometry core facility designed to profile large numbers of clinical samples for changes in protein content by high-resolution MALDI-TOF mass spectrometry.

The Immunogenetics Center (UIC), under the direction of Elaine Reed, PhD, is a World Health Organization reference laboratory for HLA providing immunogenetics and histocompatibility clinical and research services including molecular HLA, MICA and KIR genotyping, HLA and non-HLA antibody testing, multiparameter immunophenotyping, quantitative gene and protein expression as well as cellular immune function assays.

The Translational Pathology Core Laboratory (TPCL), under the direction of Sarah Dry, MD, and Jonathan Said, MD, provides pathology services critical to the success of modern biomedical research including remnant human tissue procurement and distribution, histology services, immuno-histochemistry/fluorescence services, state-of-the-art digital pathology services and pathology consultation services.

Working with an eye toward the future, the division is laying a foundation to increase services including whole genome next generation sequencing, the creation of a state-of-the art digital imaging core lab, novel MALDI tissue imaging services, expanding chemistry, hematology, coagulation and endocrine testing for clinical trial work and growing the immune assessment laboratory services for clinical trials.



Minimizing Toxicity of Anti-Rejection Therapy

ransplantation is one of the most exciting areas of modern medicine that allows the replacement of a failing organ with a functioning one from a living or deceased donor. UCLA offers the most comprehensive transplant service for a variety of tissues and organs including kidney, heart, liver, lung, pancreas, intestine and stem cells. The fundamental problem of organ transplantation is rejection during which the recipient's white blood cells turn against the new organ, potentially leading to transplant failure. White blood cells recognize the allograft by sensing highly specific histocompatibility proteins (HLA antigens) that are usually different between an unrelated donor and recipient. The vast majority of transplants are performed between unrelated individuals that have disparate HLA antigens. Therefore, transplant recipients must take immunosuppressive drugs to keep their white blood cells from rejecting the transplanted organ. Unfortunately, the immunosuppressive drugs cause serious side effects including infection and graft failure. Therefore, tapering or even withdrawing immunosuppression in transplant recipients may be required provided this is not accompanied with graft loss.

The risk of transplant rejection can be reduced by identifying the most appropriate donor-recipient match through HLA typing of the recipient/donor pair and by determining recipient sensitization to the HLA and non-HLA antigens of the organ donor. Elaine Reed, PhD, Michael Cecka, PhD, Raja Rajalingam, PhD, and Qiuheng Zhang, PhD, at the UCLA Immunogenetics Center have pioneered molecular HLA typing methods to improve matching





between the recipient and donor for solid organ and stem cell transplantation. The team also developed several noninvasive blood tests targeting subsets of white blood cells (B and T cells) and their products to assess the risk of transplant rejection and guide immunosuppressive treatment. Single HLA antigen-based antibody testing was developed to precisely measure antibodies, the products of B cells that directly engage HLA antigens expressed on the endothelium of the graft leading to antibody-mediated rejection. Data from this test is used in conjunction with the detection of the complement split product C4d in the transplant biopsy to diagnose antibody-mediated rejection. Michael C. Fishbein, MD, Charles Lassman, MD, PhD, Dean Wallace, MD, and Chi Lai, MD, developed sensitive and specific immunohistochemistry methods to detect C4d deposition in the graft for the diagnosis of antibody mediated rejection. The Immunogenetics team also developed an assay to measure antibodies targeting non-HLA antigens on the graft endothelium that are linked to rejection of renal and heart transplants.

Limiting the administration of immunosuppressive medications when the immune response is not detectable could minimize the toxicity of the treatments. The UCLA Immunogenetics research team's mission is to develop cutting-edge immune assessment assays to guide immunotherapy. The Immune Cell Function assay (Cylex, ImmunKnow) measures the recipient's T cell immune response against the transplanted graft. This is a powerful tool to help tailor chronic immunosuppressive therapy to prolong graft survival and decrease the risk of infection. Researchers at the Immunogenetics Center have recently reported novel methods for detecting acute renal allograft rejection by measuring the expression level of one or more genes and proteins in the blood.

Bench to Bedside: A Blood Donor Reunion

ue to confidentiality laws, most blood donors and recipients never know who receives their blood. Recently, a rare reunion was organized by the UCLA Blood & Platelet Center, changed all that as a UCIA liver-transplant patient met with 18 blood and platelet donors who sustained her life with their generous donations.

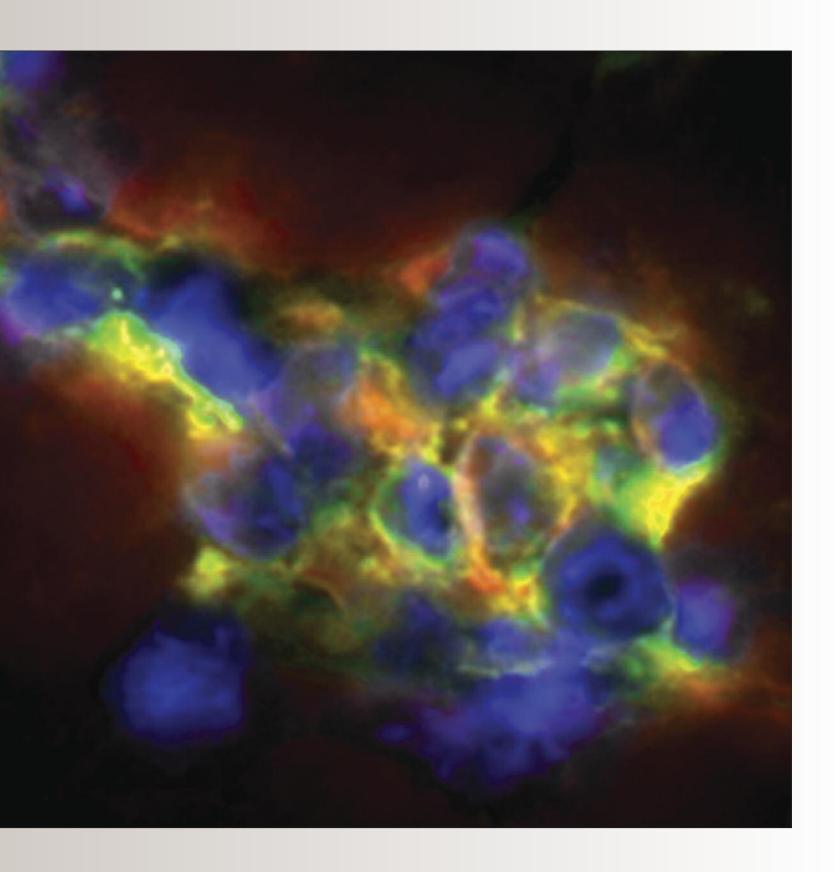
Peruvian born, Rosario Saavedra, 66, suffered liver failure and massive blood loss in early 2010, requiring extensive transfusions just to stay alive. After waiting several months, the mother of eight underwent a liver transplant at Ronald Reagan UCLA Medical Center.

The impact was heavy on the Saavedra family as her sons sold their comfortable home at a loss to pay for her 30-plus daily anti-rejection drugs and post-surgical expenses. Eldest son, Mario, gave up everything to save his mother's life. When the hospital required a full-time caregiver for Rosario to qualify for a liver transplant, he moved into his parents' tiny Newbury Park home and sold belongings for gas money to drive Rosario the 40 miles to her medical appointments. After Rosario's surgery, Mario left school and quit his job in order to stay by her hospital bedside during her recovery. Now he sleeps on the couch of his parents' two-bedroom apartment, which they share with three other children.

Rosario and Mario attend a UCLA support group for liver patients and their caregivers and hope to educate the Hispanic community about the importance of blood and organ donations. Hispanics are more prone to diabetes, hypertension, obesity and types of hepatitis, which can lead to chronic liver disease and the need for a new organ and nearly 41 percent of the almost 7,000 people waiting for liver transplants at UCLA are Hispanic. To complicate matters, much of the general population, including 53 percent of Hispanics, share type-O blood, creating a longer wait and more competition for the same liver.

In a process that takes one to two hours at a time, blood donors can donate every two months and platelet donors can donate every eight days. UCLA was fortunate to find 18 individuals willing to donate, many for just for a cookie and the knowledge of helping someone in need. L.A. Unified School District employee Benny Ng and UCLA student Minerva Esquivel were among the 18 donors who gave Rosario a warm hug at the reception. For Jeff Nerdin, a UCLA attorney, the donation was his way of helping his sick mother who lives far away. "When someone you love is suffering, you want to do something, but when they're not near you, I think it's not uncommon to try to help people near you in the hopes that other people will help your loved one and it will all work out," Nerdin said. True to his words, his mother and Rosario are now recovered from their respective illnesses. The group spans the spectrum in terms of ethnicity, religion, gender, age and career with some having donated platelets and blood hundreds of times, twice a month for more than 15 years.





Inflammatory Lesion in Dystrophic Muscle



"Pathology is the driver of innovation in molecular diagnostics and development in human genetics"

— SCOTT BINDER, MD

athology is the driver of innovation in molecular diagnostics and development in human genetics. Under the guidance of Scott Binder, MD, and Linda Baum, MD, PhD, UCLA Clinical Services continues to remain at the cutting edge of this healthcare revolution. Over the past few years, Clinical Services has expanded its outreach services and devoted considerable resources to our Radiology/Pathology initiative. Our department launched an integrated report that provides physicians across all disciplines with patient results, including the diagnosis of a tumor and its radiologic staging. Clinical Services is now focusing on a prospective research database in an effort to create a highly interactive combined report that will allow pharmaceutical companies to design clinical trials and to generate outcome data that will drive the development of companion diagnostics.

Clinical Service's relationship with the Radiology Department continues to prosper with both departments exploring creation of a shared "Diagnostic Institute" which would offer greater integration of the diagnosis and management of certain cancers.

The future will see the resources of Clinical Services extending far beyond the Los Angeles area as we implement our telepathology network to connect underserved pathology groups around the State with the subspecialty expertise of the UCLA Pathology Clinical Group. Furthermore, this technology will allow for commercial and research opportunities as wells as augment the education of residents.

Research continues to play an important role with the focus on the Clinical Translational Project, a combined molecular and genomics core tasked with clinical testing as well as research and development of new clinical tests. Work is in place to create the necessary infrastructure and to provide scientists with the equipment and support required to perform effective research and development.

In addition to these innovations, the department is strengthening its commitment to outreach services in clinical



labs and anatomic pathology. We are creating innovative ways to collaborate with physician groups and hospitals to expand their menu of services. The goal is to make the department the sole resource for anatomic pathology and clinical esoteric testing and innovation.

Financial resources are needed to hire the brightest scientific and clinical leaders, and to purchase sophisticated equipment for the development of these novel technologies. Funds devoted to these areas of growth and development will be investments in the future and part of a dramatic shift in healthcare delivery and diagnosis. The management of patients with a variety of diseases will depend significantly on results of testing that will take place in the UCLA Clinical and Anatomic Pathology Laboratories.



Critical Shortage of Laboratory Professionals

As demand for laboratory testing increases dramatically, the nation faces a critical shortage of clinical laboratory scientists (CLS) and other laboratory professionals. The Balanced Budget Act of 1997 caused the closure of 32 of the 40 active training programs in California. Currently, only two new clinical laboratory scientists enter the field for every seven who retire.

UCLA Clinical Laboratories are working in partnership with California State University
Dominguez Hills to train six CLS students per year.
Clinical Laboratories also has programs to train students for specialty licensure in Transfusion Medicine, Microbiology, Molecular Diagnostics and Cytogenetics. In addition, UCLA has affiliated with Santa Monica College and College of the Canyons to train students through their Medical Laboratory Technician (MLT) programs. UCLA trains 20-25 laboratory professionals per year.

This effort, however, is insufficient to meet the growing need for UCLA Health System and the surrounding community. Investment in additional training programs is necessary to insure a sustainable number of medical laboratory professionals in the future. Unfortunately, budget constraints in the state of California preclude development of any new educational programs.

Above: (left to right) Linda Baum, MD, PhD, with Brian McMorran, Biomedical Engineering grad student, and Sandra Thiemann, post-doctoral fellow

Comparing Biological Neighborhoods of Patients with IBD

umans and other animals live in a symbiotic relationship with millions of bacteria on our skin, in our mouths, our intestines and elsewhere. Researchers have recently come to appreciate that alterations in this relationship may be the cause of disease.

Michelle Li, graduate student in the lab of Jonathan Braun, MD, PhD, is working to understand how the balance between bacteria in the gut and the cells lining the surface of the human intestinal tract is changed in inflammatory bowel disease (IBD), which affects millions of patients. She studies this by analyzing the bacterial population using state-of-theart genomic techniques combined with high-throughput analyses of the proteins present in samples taken from the mucosa of patients during endoscopy. Ms. Li has found that the composition of bacterial populations and the proteins present vary depending on which region of the gut is examined. In other words, this was like looking at different neighborhoods in a city. She hypothesized that changes in the bacteria and proteins of these "neighborhoods" in the gut could be altered under different physiological or pathological conditions and were related to IBD. To test this hypothesis, she compared mucosal biological "neighborhoods" in areas along the intestine between healthy individuals and those with IBD. Using sophisticated mathematical methods, she showed that certain "neighborhoods" differed between normal individuals compared to those with IBD and were highly correlated with disease. These findings supported the concept that there are dynamic interactions between the host and microbes suggesting this type of analysis could aid in the diagnosis and monitoring of patients with IBD and provide deeper understanding of the basic biology underlying this disorder.



Novel Methods for Pathogen Detection

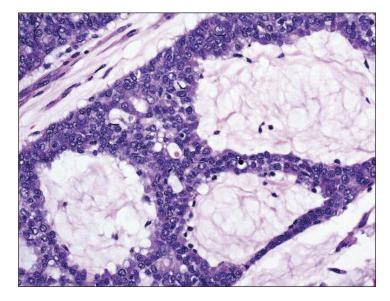
Humphries, PhD, the core objective of UCLA's Clinical Microbiology Laboratory is to isolate, identify and report pathogens in a timely manner. This process has been made all the more possible via novel nucleic acid based "molecular" methods which have become the new gold standard for sensitive and accurate pathogen identification. This remarkable technology has led to turn-around times of hours instead of the days or weeks required by traditional methods.

In 2010, UCLA Microbiology bridged the use of molecular assays into bacteriology and mycology diagnostics by implementing three new assays for routine testing: bacterial identification by 16s rDNA sequencing, yeast identification by AdvanDx PNA-FISH and bacterial strain typing by Diversilab® repPCR.

16S rDNA sequencing is a powerful tool for the identification of bacteria grown in culture. The assay targets a region of DNA common to all bacteria, the 16s rRNA gene; sequence determination of the gene then provides the identification. This method is particularly useful for identification of slow-growing, fastidious and usual bacteria. Similar to 16s rDNA sequencing, PNA-FISH allows the identification of yeast when grown in blood culture. This technology utilizes fluorescent-based probes that differentiate common Candida species based on fluconazole resistance allowing the laboratory to report same day results that are relevant to the choice of antifungal therapy.

Finally, Diversilab repPCR was introduced as a tool for epidemiological investigations by which to generate fingerprints on bacterial and fungal isolates. The technology evaluates unique repetitive DNA sequence patterns in order to distinguish isolates at the subspecies and strain level.

With its focus on patient care at UCLA and beyond, the Clinical Microbiology Laboratory continues to evaluate and implement new molecular diagnostics in 2011 for use in all areas of the laboratory.



Crossing Borders with Digital Pathology

Digital images have been used by Radiologic Sciences/ Imaging to make diagnoses on a global basis for some time. Until recently, pathology had not been able to perform similar analyses because of the unsuitability of images for definitive diagnostic purposes. The development of new, scanning device technology which produce high-quality digitized images have enabled pathologists to use these images to make many, though not all, diagnoses. Scott Binder, MD, and Sarah Dry, MD, are looking beyond UCLA's borders as they guide the implementation of new digital technology to improve the standard of care for pathologists in underserved areas of California. Their vision includes a network of 20-25 remote hospitals which can benefit from UCLA's diagnostic expertise for more challenging cases. Digital images scanned from slides and sent to UCLA pathologists over a secure internet access will enable small groups of pathologists without subspecialty expertise to consult with our expert team of pathologists for diagnostic purposes.

This exciting and dynamic model will significantly influence healthcare in California by providing accurate diagnoses in a timely manner, thus patients will receive appropriate therapy sooner. The additional benefit includes a windfall of educational opportunities for residents as well as providing UCLA with material for research and esoteric testing. The future is now as the department is already successfully engaged in a telepathology exchange with a prestigious health center in China, which has been developed and fostered by Dr. Jian Yu Rao.

Above: Mucinous carcinoma-nests of basaloid tumor cells take on a cribriform appearance and often float free in pools of mucin.

Future Physician/ Scientist Works to Reduce Transplant Rejection

The immune system is amazingly complex, and like a national defense network, it has to monitor for both internal and external potential threats. Maggie Chang's research in Benhur Lee, MD's group studies the specialized cells of the immune system that perform this function. Dendritic cells are the guards of the immune system and patrol the peripheral tissues of the body for signs of inflammation or injury. They sense the environment and relay this information to other immune cells of the body and in the process, have the remarkable ability to decide on the appropriate response to mount. This function is pivotal for directing the overall immune response towards either reactivity or tolerance. Overreaction to internal signals can result in autoimmune disease such as rheumatoid arthritis, while under reaction to external signals such as microbes, risks serious infections. Maggie studies an endogenous protein, Galectin-1, that plays a critical role in how these critical decisions are made. She has found that if dendritic cells encounter Galectin-1 during their development, they adapt to function to suppress inflammatory immune responses, whereas if they encounter it in peripheral tissues at sites of inflammation, they become activated and signal the immune system to respond to the particular stimulus. Maggie is in the combined MD/PhD training program at UCLA and as a future physician/scientist, is particularly interested in understanding how these fundamental processes may be used for the development of patient specific dendritic cell-based therapies for the suppression of autoimmune disease or transplant rejection.

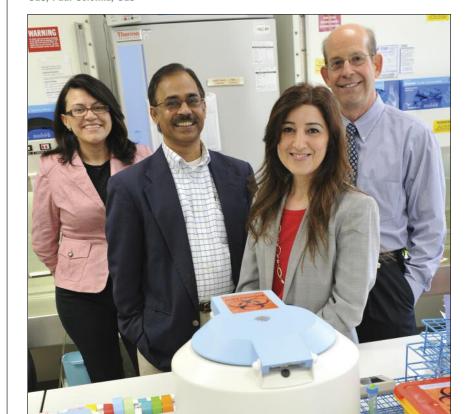
Investigating Genetic Disease using High-Tech Chromosome Analysis

he UCIA Clinical and Molecular Cytogenetics Laboratories operate in service to the larger UCIA patient population, community based physicians and independent laboratories, providing indispensable genetic information from their state-of-the-art facility. Headed by board-certified medical geneticists, Fabiola Quintero-Rivera, MD, and Nagesh Rao, PhD, the facility is one of the largest of its kind, investigating and exploring all aspects of translational genetics research.

Offering a vast array of clinical services including, prenatal diagnosis of chromosomal syndromes, neonatal and pediatric diagnosis and parental chromosome analysis for identification of carrier status and counseling for multiple miscarriages. The laboratory also performs analysis and diagnosis of acquired chromosome abnormalities related to leukemia, lymphoma, solid tumors and other malignant conditions. In addition, molecular cytogenetics techniques are employed for the precise diagnosis of genetic syndromes associated with mental retardation/autism, diagnosis of specific hematological cancers, solid tumors, gene amplification in breast cancer, brain tumors, gene rearrangements in lung cancer, follow-up of patients' post-chemotherapy, or post-sex mismatch bone marrow transplantation and genetic markers in urine for recurrent bladder cancer.

Coming off a successful year that saw the confirmation of ten new gene markers to provide more accurate diagnostic testing for a variety of malignancies, the lab also acquired a state-of-the-art high-throughput automated image analysis system for the scanning and quantification of fluorescent signals in the cell nucleus. Intimately involved in the establishing and promoting the use of high-resolution genomic microarray technologies for identifying small genetic aberrations, the lab's results are not only useful for diagnosis, but help provide crucial information that assists clinicians in determining appropriate treatments.

Below: (left to right) Fabiola Quintero-Rivera, MD, Nagesh Rao, PhD, Lori Noravian, CLS, Paul Colonna, CLS





Genetic Signature Differentiates Benign and Malignant Moles

iagnosis of benign moles and tumors of the melanin synthesizing cells that determine skin color and protect us from the sun's damaging rays, are an important component of the work of the UCLA Dermatopathology Section. The department, under the direction of Scott Binder, MD, routinely differentiates benign nevi from malignant melanomas via expert examination of standard stained sections and immunohistochemical preparations. The process is not without its problems as can be the case when comparing nevi that contain atypical cells and melanomas comprised of tumor cells that resemble nevus cells. To resolve such dilemmas, the department seeks to develop techniques to supplement microscopy and consideration is being made to use several molecular genetic approaches including, Fluorescent in Situ Hybridization and Comparative Genomic Hybridization.

In addition the department is considering the adjunctive potential of gene expression profiling with the assistance of the UCIA Department of Pathology Clinical Microarray Core Laboratory under the direction of Xinmin Li, PhD. RNA extracted from study tissues is reverse transcribed, amplified, then hybridized with the Affymetrix GeneChip U133 plus 2.0 Array which carries DNA from more than 47000 transcripts, to determine the extent that particular expressed genes are present in the study material.

Stephen Koh, MD, Alistair Cochran, MD, Dr. Binder and Richard Scolyer, MD, continue to address questions that concern the sentinel node technique, a technique that has revolutionized management of patients with melanoma and breast carcinoma and was developed at UCIA by Dr. Cochran and Donald Morton, MD. Their studies have shown genetic

differences between the primary melanomas of patients with and without sentinel node metastases and between primary melanomas and their sentinel node metastases. The information gathered continues to enhance the department's ability to personalize medical management, help determine the extent of nodal surgery as well as for chemotherapy and biotherapy, based on each patient's genetic profile.

The entire Dermatopathology research team continues to make great strides in the field with Peter Sarantopoulos, MD, Bob Bernaba, MD, and Jiaoti Huang, MD, PhD, evaluating the genetic differences between atypical nevi and nevocytically differentiated melanomas and Joseph Hillman, MD, and Drs. Koh, Scolyer and Huang working to identify genetic signatures to precisely identify morphologically similar, but behaviorally different tumors. Stan Nelson, MD, is collaborating with Columbia's Basil Horst, MD, to sequence the genes of melanoma tissues to identify the order of base pairs that make up individual genes in an innovative study that will allow the identification of subtle genetic alterations undetectable by previously available techniques. The results of this study, in particular the mechanisms that underlie the development of melanoma, will further incredible precision in patient management.

This exciting and groundbreaking work is made possible by financial support from the NIH and the research funds of the Department of Pathology and Laboratory Medicine as well generous and much appreciated gifts from Mrs. Lya Cordova-Latta and the Pritzker family.

Above: (left to right) Duan-Ren Wen, Alistair J. Cochran, MD, and Rong-Rong Huang

Training Tomorrow's Medical Heroes

he Department of Pathology and Laboratory Medicine, David Geffen School of Medicine at UCLA has offered a 2-year postgraduate fellowship in Medical and Public Health Laboratory Microbiology since 1976. Training microbiologists to direct clinical and public health microbiology, the program is accredited by the American College of Microbiology's Committee on Postdoctoral Educational Programs (CPEP) and graduates are eligible for professional certification by the American Board of Medical Microbiology.

This is a comprehensive, academically oriented training program in diagnostic bacteriology, mycology, parasitology, virology, immunoserology, antimicrobial testing as well as molecular diagnosis of infectious diseases. Fellows receive training at Ronald Reagan–UCLA Medical Center, VA Greater Los Angeles Medical Center and the LA County Public Health clinical laboratories, with an emphasis on clinical and translational research. Fellows participate in laboratory management and infection control garnering clinical problem solving and consultative skills by actively participating in infectious disease rounds.

The program has trained more than 42 doctoral level scientists and physicians from the United States and many parts of the world, including Albania, Canada, Chile, China, England, Greece, Mexico, Saudi Arabia, Taiwan and Thailand. Many of these graduates have gone on to distinguished careers and are working in large managed care settings, reference and public health laboratories, academic institutions, the CDC, the WHO, the USDA and biotechnology. Two examples of distinguished graduates include David Bruckner, ScD. (class of 1978), one of the first graduates from the program, and Ellen Jo Baron, PhD (class of 1983). Shortly after completing his training, Dr. Bruckner became only the second Chief of



Microbiology at UCLA and later the Director of Laboratory Operations for the UCLA Health System. Although retired, he has remained involved in the program as a Professor Emeritus. He is most known for his expertise in parasitology and as the co-editor and co-author of the first three editions of Diagnostic Medical Parasitology—considered to be the seminal reference in the field. Dr. Baron is an internationally renowned microbiologist who has published over 90 peer review papers, numerous guidance documents, reference manuals and clinical microbiology textbooks, including several editions of the Manual of Clinical Microbiology. Their accomplishments and those of all our graduates ensure that our program attracts the brightest candidates from around the world.

RON EVANS, PhD

A 1974 UCLA graduate with a PhD in microbiology, Dr. Ronald M. Evans, has co-authored more than 300 research papers and received numerous awards. Currently serving as both a Professor and March of Dimes Chair in Developmental and Molecular Biology at the Salk Institute of Biological Studies, Dr. Evans is an authority on hormones, both their normal activities and their roles in disease. UCLA is proud of Dr. Evans' accomplishments and honored to call him one of our own. The Cell and Molecular Pathology (CMP) graduate program at the University of California Los Angeles provides training to graduate students interested in the

cellular and molecular basis of human diseases. The scope of students' research topics ranges from cancer biology to transplantation immunology, but are all connected by the common goal of identifying molecular mechanisms involved in the pathology of human diseases. In addition to working in research labs, students take coursework that exposes them to primary literature surrounding relevant topics. Additionally, students act as teaching assistants to two undergraduate courses during their graduate careers, giving them experience in presenting and explaining scientific information and concepts.

Improving the Outcome of Bone Marrow Transplant Patients

s. Lisa Kohn, in the lab of Gay Crooks, MB, BS, FRACP, is studying how the body makes T-lymphocytes, an important subtype of white blood cells. A healthy person produces billions of blood cells each day that are essential for life through a process that occurs in bone marrow termed hematopoiesis. Red blood cells carry oxygen to our tissues, platelets prevent bleeding and white blood cells provide defense against infection. However, this process can be impaired in diseases such as certain cancers or when there is injury to the bone marrow, often necessitating bone marrow transplantation. Tlymphocytes and other blood cells originate from common progenitor cells called hematopoietic stem cells (HSC). Ms. Kohn's research addresses a critical gap in our knowledge of adult human blood cell development that focuses on the identification and characterization of the immature immune stem cells in the human bone marrow that are particularly able to generate T-lymphocytes, of which little is known. This project incorporates several of her areas of interest, from answering basic biological questions about immune cell development to being able to translate these to finding new ways to improve the outcomes of patients who undergo bone marrow transplantation to treat a life threatening disease.

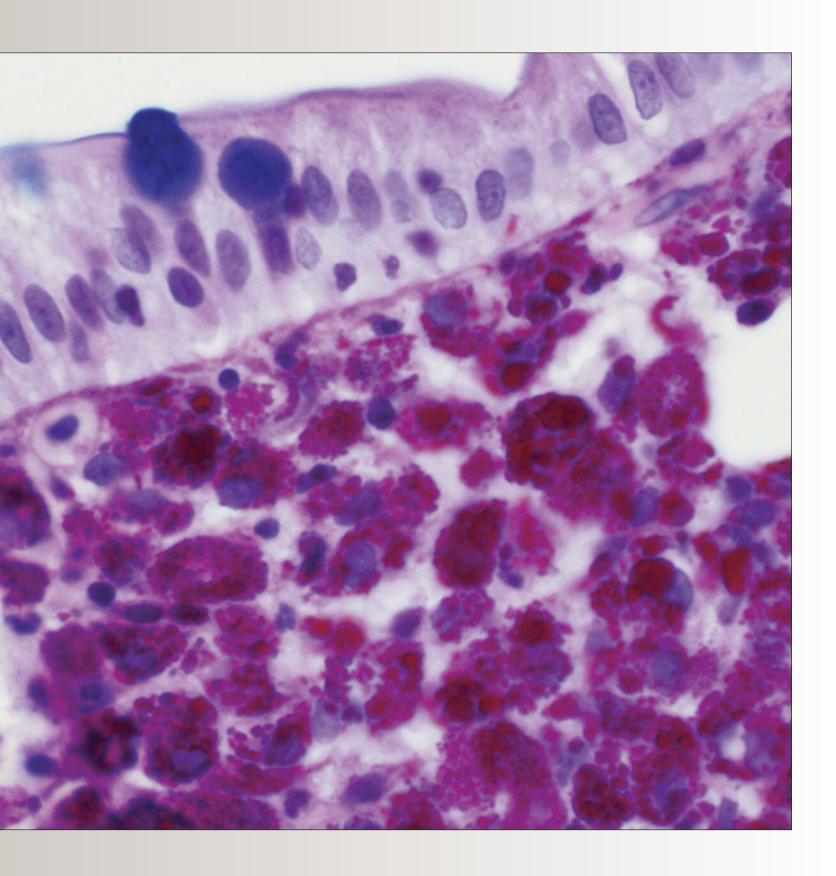


Funding is Vital to Scientist Training Program

The Department of Pathology and Laboratory Medicine at UCLA has been awarded over a combined three million dollars in training support from the National Institutes of Health (NIH), the National Cancer Institute and the National Institute of Environmental Health Sciences, to train voung scientists to conduct research in the areas of tumor immunology and molecular toxicology. However, these awards fall short of the total funding needed for the program, representing only one-third of the required funds. The balance is drawn from research monies or investments to annual allocations by the department, including donor and fellowship funding.

Steven M. Dubinett, MD, and Michael Teitell, MD, PhD, co-direct the Tumor Immunology Training Program, which encourages trainees to develop and/or apply new molecular immunological technologies to prevent, diagnose and treat human cancers. Oliver Hankinson. PhD, heads the Molecular Toxicology Program. Areas of focus for this program include study of the mechanisms by which chemicals, especially those in the environment, cause cancer and other diseases such as Parkinson's disease, as well as study of air pollution toxicology, and the potential toxicities of nanoparticles. Faculty in both programs are leaders in biomedical sciences and cancer research who are drawn from multiple departments at UCLA.

These programs have been highly successful in developing trainees to become academic investigators. Because the program's awards represent only one-third of funds required, the department must find donor and fellowship funding for the remainder of support. Donor and fellowship funding provide vital and sustainable sources of support. Both are important investments toward the successful development of these gifted researchers.



Whipple's disease, a rare condition that prevents the small intestines from properly absorbing nutrients, is caused by infection by bacteria called *Tropheryma whippelii*.



"Because medical science is progressive, so then, must also be our school, curriculum and standards for the skill levels obtained."

— ELENA STARK, MD, PhD

rogress has been made on our efforts to apply telemedicine and state-of-the-art broadcasting technology to anatomy instruction as our plans to remodel the Department's Gross Anatomy Lab are proceeding timely and successfully. This summer the laboratory will be transformed into a fully equipped "telemedicine lab" with capabilities to broadcast live teaching and training events to other areas of the medical school and hospital, as well as other UC and non-UC campuses. David Geffen School of Medicine (DGSOM) students and dental students will undoubtedly benefit from the advanced technology to learn and integrate anatomy with radiology, surgical skill and clinical instruction. Furthermore the innovation the lab remodeling offers will open the possibilities of expanding the use of the lab to residency training and to research for applied anatomy specialties, specifically for surgical-skills training and surgical procedure research.

The DGSOM Gross Anatomy Laboratory houses 30 cadaver stations and comfortably allows for the use of both embalmed cadavers and unembalmed cadavers for the study of basic, clinical, applied, radiological and surgical anatomy.

In compliance with UCLA, Environmental Health and Science and OSHA, the Gross Anatomy laboratory will soon offer a technologically advanced environment that will incorporate high-heat instrument-cleaning equipment, aspirators, surgical lighting, surgical and dissection tools as well as first-rate audiovisual equipment capable of broadcasting to the highest resolution plasma screens throughout the lab and to individual monitors adjacent to each cadaver table. Live and recorded activities and events will also be easily broadcasted to adjacent classrooms, other areas in the hospital and even other campuses. The sound system is being updated to allow for guided instruction from the teaching tables to all student tables.

The use of human cadaveric materials is vital for no risk anatomy learning and training, most relevantly in the area of



surgical anatomy—to resemble live patients. The Anatomy Laboratory will widen the scope of education and competency-level to include training and practicing of advanced surgical procedures and will encourage the innovation of prospective surgical techniques. In the past decade, a number of episodes involving surgical inaccuracies have been noted. In a study from 2003, the findings from the cases analyzed, were that roughly two thirds of the incidents involved "intra-operative" issues. Namely, 53 percent of the circumstances were due to "inexperience or lack of competence of the surgical task."

Other recent surveys confirm this conclusion with the prominent problem being "damage to underlying structures" which could very well reflect the fact that anatomical knowledge on the part of residents could be improved.

Today, to combat this predicament, surgical training is being extended to encompass intense periods of practice in safe 'rehearsals' regulated procedures on continued →



embalmed and un-embalmed cadavers and on computer animation in simulation centers. This advancement in medical education mirrors the already established requirements for other professions with commitments to the protection of lives. Dedicated hand-eye coordination and focused thinking are reinforced with abundant hours of training and continual practical application scenarios. Repeated exposure also confirms the commitment to acquiring, developing and maintaining accurate anatomical-structure knowledge that is crucial when performing any surgical procedure.

The Gross Anatomy Laboratory will expand its capabilities and functions to "hands-on" surgical training that includes the experience of identifying, handling and manipulating the varying textures of actual human tissue by using prosection and dissection of cadaver specimens, and audiovisual capability to review the materials (sophisticated computerized 3-D models and animations, text, case-study discussions, and radiological imaging for cross-referencing anatomical knowledge).

The Gross Anatomy Laboratory can also collaborate with the high-tech UCLA Simulation Center for the interactive practice of such procedures and technical skills. This combination promotes a tri-level comprehension of applied anatomy, simulation and procedural-skills training with cadavers for medical students, residents and researchers. Because medical science is progressive; so then, must also be our school, curriculum and standards for the skill levels

obtained. The innovative design of the Department's Gross Anatomy Laboratory will promote such exploration within the spheres of basic anatomy, clinical, radiological and surgical anatomy. Furthermore, the atmosphere of the Laboratory will unify the recurrent advancements by expanding the experience for students, residents and UCLA faculty to embrace innovations and navigations of practical and technical applications. The goal of the Laboratory is education, research and innovation, specifically:

- Advancing the education of anatomy
- Elevating the levels of what students and residents should be learning and retaining
- Training detailed procedures to the students going into applied anatomy specialties, residents and faculty
- Exercising the technical skills of students going into applied anatomy specialties, residents and faculty
- Evaluating the students' skill-sets
- Encouraging research and innovation of applied anatomy technologies and procedures
- Promoting investigation into improving upon established applied anatomy procedures
- Promoting innovation of creative applied anatomy technologies and procedures

Bench to Bedside: Tailor-made Treatment

uring a routine yearly physical check up in the summer of 2009, my primary care physician detected a nodule on my prostate and recommended that I consult a urological specialist. My urologist suggested a biopsy to check if the nodule was malignant. Being a researcher, I wanted to see if there were any new research techniques. I found there was an ongoing prostate MR Imaging research program at UCLA using noninvasive MRI techniques to detect prostate cancer with potentially greater detection accuracy. I enrolled in the program and to my surprise, the MRI results indicated two suspicious areas, which needed further examination via biopsy.

The radiologist, Dr. Daniel Margolis, and my urologist, Dr. Mark Litwin, worked together on my biopsy plan and the subsequent pathology report indicated the cancer was small, confined in a local region, in its early stage, but moderately aggressive.

There are three well-known treatment approaches for prostate cancer: watchful waiting (periodically monitor the tumor growth via biopsy and PSA score); surgery to remove the prostate; and radiation therapy. Because the many organs surrounding the prostate can also be affected, there are many pros and cons for these treatment approaches. Further, the outcome also depends on the stage of the cancer, the patient's age and health conditions. I was oscillating among the three approaches and unable to decide which was the

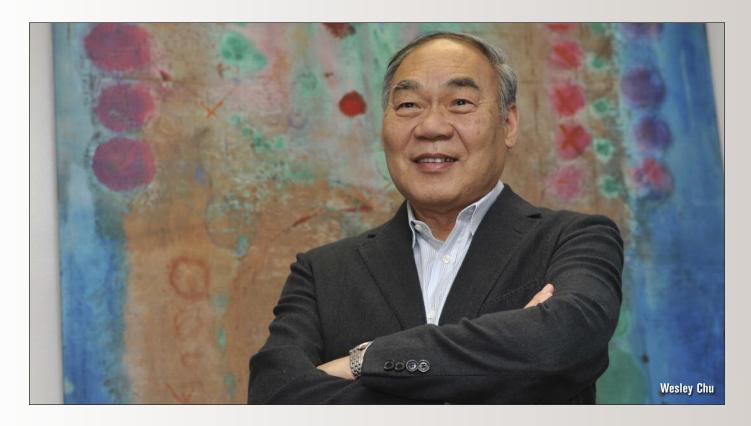
most suitable therapy.

Dr. Huang, who has a joint appointment in the Urology Department and is a specialist in prostate disease, recommended radiation therapy because it is less invasive and less risky than surgery while yielding similar outcomes. I feel very fortunate and very grateful to have received expert advice from someone with combined knowledge of pathology and urology to help me make my final "tailormade" treatment decision.

From my first hand experience, I truly believe that UCLA has a first rate radiation oncology department with well known distinguished faculty and state-of-the-art equipment. I was treated by Dr. Chris King, a well known expert on prostate research and by Dr. Steve Tenn, a young and rising medical-physicist who was able to generate a two-arc treatment plan with far less radiation exposure than the normal guideline.

The team of radiation therapists were very professional and a result, I went through the eight weeks therapy with very little if any lasting side effects.

My PSA score fell to 1.0 three months after treatment then and has further to 0.58. Dr. King told me I am on the right track to recovery. Overall, I feel that I was well taken care of by the excellent and caring medical team here and had a very positive experience from diagnosis, decision of treatment approach, radiation therapy, to post-treatment follow ups.



News of the Department



WORKING TO CURE ATAXIATELANGIECTASIA

Every 2 to 3 years, the international community of scientists and doctors working to cure Ataxiatelangiectasia (A-T) come together, most recently at the A-T Workshop 2010, to present the results of their research.

Degenerative in nature, A-T is a nerve disease that causes severe disability. A rare affliction, it is a recessive genetic condition requiring two mutated versions of the gene, which renders patient exquisitely sensitive to radiation.

The workshop is a melding of basic and applied science. Often parents of A-T children sit in the audience while their children are taken to visit local sights. This year was UCLA's opportunity to host the workshop. Sponsored by the Department of Pathology and organized by Dr. Richard Gatti, MD, the world's foremost expert on the disease, more than 200 biologists and physicians listened to three days of informative lectures. Material presented expanded the understanding of how the A-T protein coordinates the body's response to broken strands of DNA so they can be repaired within minutes of being damaged. Also discussed was a drug, in development at UCLA, that will help replace the missing protein in A-T children which may, in turn, prevent or reduce the leukemias and lymphomas suffered by many of them. ATW2012 will be held in New Delhi in February 2012.

NEW COMMITTEE LINKS GRADUATES BACK TO THE UNIVERSITY

The newly created Research Alumni Committee is designed to facilitate social connections and become a resource for career development through activities such as online alumni networks, invited alumni speakers, career panels and alumni profiles in the departmental newsletter. Seeking to foster the idea of the department as a place that was personally meaningful in our alumni's past and can be professionally beneficial to their future, the focus has been on creating an on-line alumni directory. Available to all former and current residents and fellows, the directory will serve as a way to rekindle old connections as well as form new ones.

Additional plans include an annual alumni day, complete with departmental tours and guest speakers. With funding always a looming issue, redirecting the interest of our graduates back to UCLA will lead to potential fundraising avenues.

DR. WAYNE GRODY NAMED PRESIDENT OF THE AMERICAN COLLEGE OF MEDICAL GENETICS

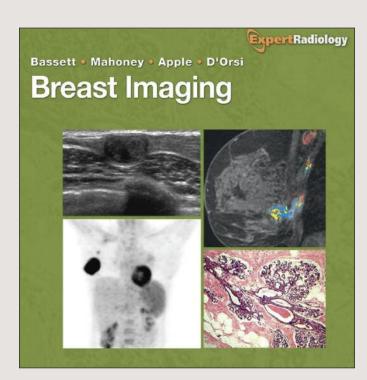
Wayne W. Grody, MD, PhD, of Los Angeles, CA, is the new president of The American College of Medical Genetics (ACMG), the national professional organization for medical genetics professionals.

Dr. Grody takes over from Bruce R. Korf, MD, PhD, FACMG, of Birmingham, AL, who completed his two-year term at the 2011 Annual Clinical Genetics Meeting in Vancouver, BC, Canada in March.

"I have many different mixed emotions about taking over as president," Grody said. "It's made me tremendously proud, also humbled, also nervous. I think the ACMG is so important. It may be the most important of all the Colleges in organized medicine at this moment in history. To be the one at the helm during these critical years is daunting and exciting."

Dr. Grody is a Professor in the Departments of Pathology & Laboratory Medicine, Pediatrics, and Human Genetics at the UCLA School of Medicine. He is the director of the Diagnostic Molecular Pathology Laboratory within the UCLA Medical Center, one of the first such facilities in the country to offer DNA-based tests for diagnosis of a wide variety of genetic, infectious, and neoplastic diseases, as well as bone marrow engraftment, patient specimen identification and paternity testing by DNA fingerprinting.

He is also an attending physician in the Department of Pediatrics, specializing in the care of patients with or at risk for genetic disorders.



DR. SOPHIA APPLE CO-AUTHORS TEXTBOOK

Imaging of the Breast, by Drs. Lawrence Bassett, Mary Mahoney, Sophia Apple, and Carl D'Orsi, is a comprehensive look at breast imaging. It correlates radiologic images with pathology slides to strengthen the accuracy of your diagnosis. This entry in the Expert Radiology Series also addresses topics such as appropriateness criteria for various imaging approaches, the BI-RAD quality assessment and reporting tool, and image-guided interventional procedures.

TRANSLATIONAL RESEARCH FUND

Advances in medicine have become increasingly dependent on translational medical research, namely the integration and application of ideas and discoveries between basic science and clinical practice. Recognizing the evolving national mandate to focus on translational science, the Department Practice Plan Executive Committee created the Translational Research Fund (TRF) in 2006. The TRF provides funding of up to \$10,000 for 10-15 Department of Pathology faculty initiated translational research projects each year. "As part of it mission the TRF also places emphasis on projects that involve residents and fellows," states David Dawson, MD, PhD, who presently heads the review committee for TRF grant applications. TRF-funded projects have routinely led to publications in peer-reviewed journals or have been leveraged to secure greater extramural funding. "The TRF is an outstanding example of the Department's efforts to promote improved clinical care through academic research and education," adds Dr. Dawson.



DR. PAUL MISCHEL
ENDS TERM AS
PRESIDENT
OF THE AMERICAN
SOCIETY FOR
CLINICAL
INVESTIGATION
(ASCI)
Paul Mischel, MD,
served as the 101st
president of The

American Society for

Clinical Investigation

(ASCI) The ASCI,

established in 1908, is one of the nation's oldest and most respected medical honor societies. The ASCI comprises more than 2,800 physician-scientists from all medical specialties elected to the Society for their outstanding records of scholarly achievement in biomedical research. The ASCI is dedicated to the advancement of research that extends our understanding and improves the treatment of human diseases, and members are committed to mentoring future generations of physician-scientists. The ASCI represents active physician-scientists who are at the bedside, at the research bench, and at the blackboard. Many of its senior members are widely recognized leaders in academic medicine. http://www.the-asci.org

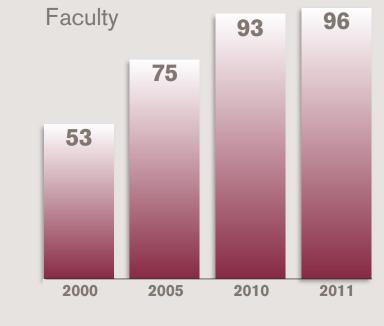
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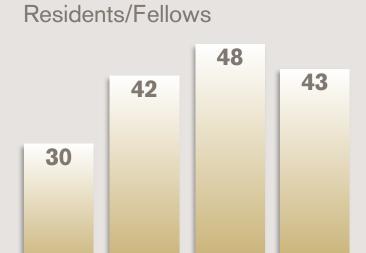
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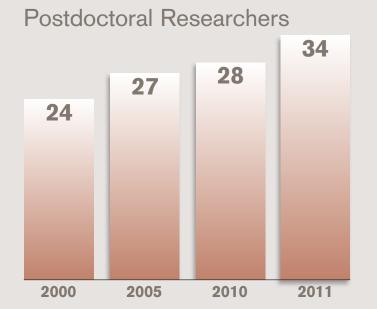


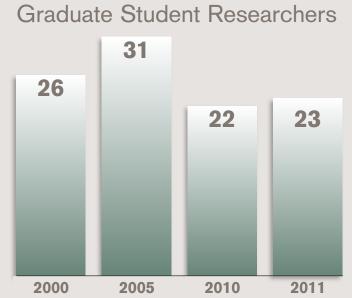
Total number of faculty, staff, residents/fellows, post doctoral researchers and graduate student researchers = 1,212

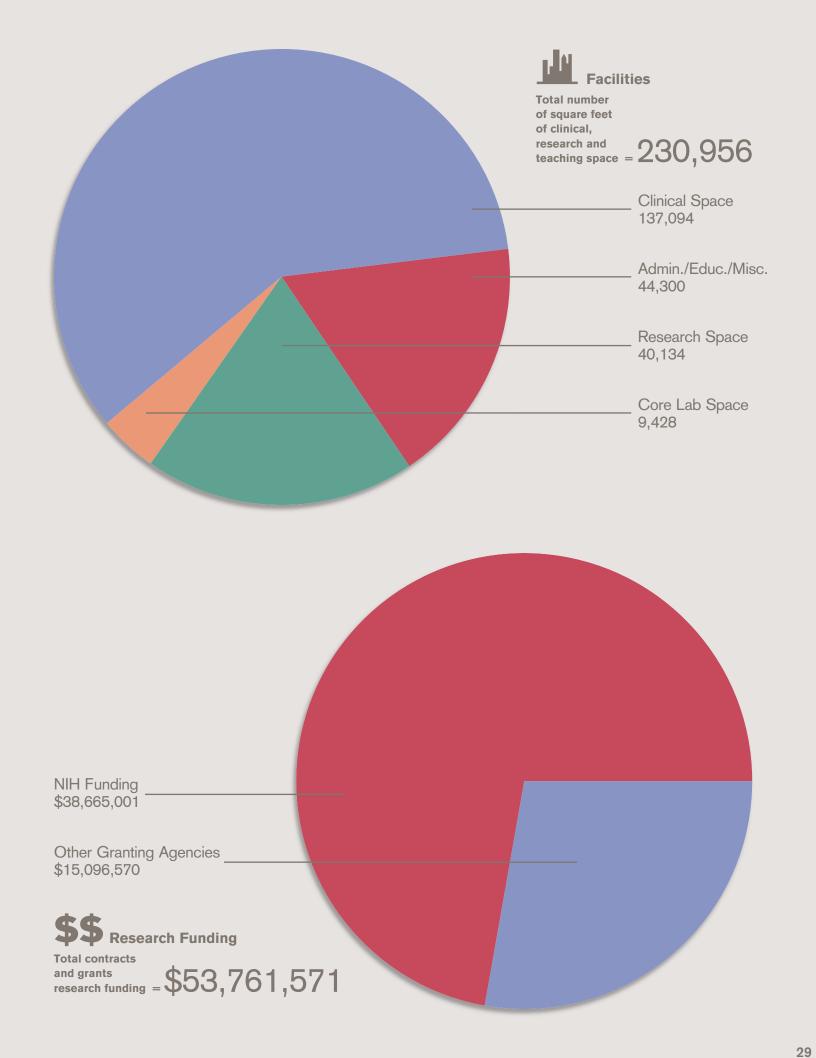












Department in Depth: Listinas

FACULTY

Sophia K. Apple, MD Tamar Baruch-Oren, MD

Linda G. Baum, MD, Ph.D

Steven J. Bensinger, PhD Assistant Professor

Sunita M. Bhuta, MD Professor

Scott W. Binder, MD

Marjorie Bonhomme, PhD Assistant Professor

Jonathan Braun, MD, Ph.D Professor Anthony W. Butch, PhD

Professor

Lily C. Chao, MD Clinical Professor

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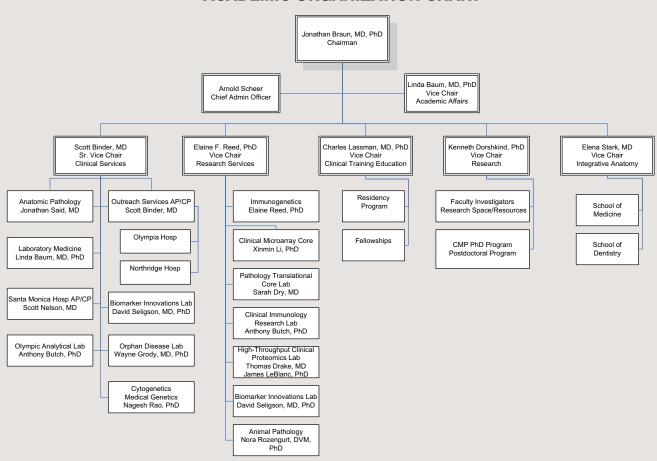
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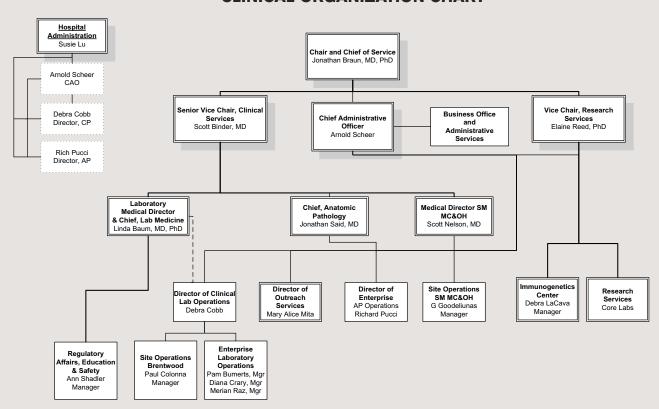
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