Discoveries

UCLA CANCER

Basic Science:
Driven by Inquisitive Minds

2010 – 2011

UCLA’s Jonsson Comprehensive Cancer Center
Designated a Comprehensive Cancer Center by the National Cancer Institute
As a basic scientist myself, I have always emphasized the importance it plays in providing the strong foundation on which much of cancer research is built. A series of laboratory observations leads to the formulation of an idea (a hypothesis). Experiments are designed to test the validity of the hypothesis. Results are analyzed and the hypothesis is supported or, as is often the case, not supported and a new hypothesis is generated. This is the way basic science cancer research has been conducted for decades. I always enjoyed the excitement that came with seeing results for the very first time. It gives one the sense of knowing something for a brief moment that no one before has ever known.

As you’ll read in the accompanying issue of UCLA Cancer Discoveries, basic science research is changing. With the sequencing of the entire human genome, availability of powerful technological platforms and enhanced computational abilities, we are all moving toward a more collaborative, team-based approach. No single investigator will have the requisite knowledge and skills to attack a problem as complex as a cancer cell without joining forces with colleagues.

We have an advantage at the Jonsson Comprehensive Cancer Center (JCCC), because the necessary colleagues are already part of our organization. We are fortunate to be on one campus where the JCCC has members from the David Geffen School of Medicine, the colleges of Life Sciences and Physical Sciences and the schools of Engineering, Dentistry, Nursing and Public Health. We have a long history of collaboration, in part funded by the Jonsson Cancer Center Foundation’s Interdisciplinary grant program dating back to the mid-90s. Our 12 scientific program areas integrate faculty from diverse backgrounds into groups addressing critical themes in cancer research. Seven of our shared resources strive to meet the ever changing technological challenges associated with generating more and more data, at faster and faster rates.

Everything we do at JCCC is focused on one goal - improving the way cancer is prevented, detected, treated and the quality of life of the survivors. We have tremendous depth and breadth in all of these areas.

So, it’s back to the basics…….
Science Driven by Inquisitive Minds
Despite an enormous explosion of technology, basic science is still
driven by the need to answer a burning biological question.

Profile: Scientist James Wohlschlegel
He was at the right place at just the right time, the intersection of
biological chemistry and mass spectrometry.

Playing the Lottery in Cancer Research
Molecular screening is a bit like playing the cancer lottery, you
just need a little bit of luck.

Melanoma Survivor Celebrates Two Birthdays
Melanoma survivor Bill Bushnell now celebrates two birthdays, the
day he was born and the day he was reborn.

Award-Winning Faculty and Science Update
Meet our award-winning faculty and read about the leading-edge science
being conducted at the Jonsson Cancer Center.

News of the Center
The latest grants, the launch of new programs and other good news
coming out of the Jonsson Cancer Center.

Shared Resources
A remarkable array of tools aid in speeding discovery of newer
and more effective ways to treat cancer.

The Jonsson Cancer Center Foundation
Highlights of giving, ways to advance cancer research and links to
honor roll of donors making advances in research possible.
Science Driven by Inquisitive Minds

Science has seen an enormous explosion in technology in the past three decades, advances that have changed the way experiments are conducted in laboratories and how discoveries that can save lives are made.

In a monumental project that spanned 10 years, the human genome was revealed as scientists identified and mapped the 20,000 to 25,000 genes that make up each individual. Although work on interpreting the data is still in its scientific infancy, it is anticipated that detailed knowledge of the human genome will open up new, unimagined avenues for advances in medicine. The mapping also has led to easier methods for genetic testing, which can now tell a woman if she is at higher risk for breast or ovarian cancer.

Advances in imaging technology – Positron Emission Tomography (PET) and the development of new imaging probes to be used with it - allow scientists to watch the immune system as it recognizes and responds to cancer in the body. Using PET, researchers are testing a method that would track cancer treatments inside a patient’s body in real time as the therapy finds and kills the diseased tissue. In another project, a non-invasive approach is being developed that may one day allow doctors to evaluate a tumor’s response to a drug before therapy is even prescribed, allowing a treatment to be personalized to the patient’s unique biochemistry.

Automated, computerized molecular screening technology allows up to 100,000 small molecules to be screened in one day to gauge their ability to fight cancer, a task that used to take years when done by hand in a laboratory. (See story on page 10.)

In addition to looking for new, more effective and less toxic cancer treatments, the technology also allows scientists to find out what’s going on inside a cancer cell, which signaling pathways are activated and interacting in a way that may be promoting disease.

Gene expression microarrays are a powerful technology that allow millions of different probes to be designed throughout the human genome so that every gene can be simultaneously assessed. That data can be quickly assessed to determine whether individuals genes are on or off in cancers and other cell types. This information, unavailable a decade ago, gives biologists critical information about which genes within the genome are active in the development of cancer.

The identification of cancer stem cells in several types of cancer may result in the development of new treatments to target and kill these cells, which are the very root of the disease. It is thought that without the cancer stem cells, these cancers could not come back, a stage when they’re much more deadly and harder to treat.

Lab-on-a-chip technology is on the cusp of changing the way cancer is diagnosed. The room-sized laboratory needed to process such a cancer diagnostic test in the past is being reduced to a computer chip the size of a stamp due to the emerging fields of nanotechnology and fluidics. One day, a single drop of saliva placed on a cell phone-sized machine in a dentist’s office may be able to determine whether a patient has head and neck cancer, well before it is obvious on a physical exam.

But as much as those advances and others are changing the face of basic science, what really drives discovery has remained constant – a driven, curious person with a burning biological question that must be answered.

"The fundamental unit of scientific discovery is still and will always be the inquisitive mind," said Dr. Owen Witte, who has been conducting basic research at UCLA for more than 40 years and whose science has led to the development of new drugs to treat leukemia. “What really drives scientific advances is the people who have to, must, know the answer to a question and that should never change.”

And that one question then leads to another and another, taking the basic scientist on a journey down a road often times with no specific destination but whose twists and turns could result in a discovery that may lead to new and better ways to treat cancer.
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TRANSLATION
It used to be that basic scientists labored with their teams in a lab, seldom crossing paths with the physicians who one day might be working with the treatments that sprang from their research.

Today, in another transition that is altering the face of science, basic researchers often collaborate with physician scientists on translational projects that move discovery from the lab bench to the patient bedside.

"Basic scientists were so far removed from the clinical context that those intellectual bridges could not be crossed," said Dr. Harvey Herschman, director of basic research for UCLA's Jonsson Comprehensive Cancer Center, who also has been a scientist for more than 40 years. "The gulf between the two was so great, there was no way to translate the work."

But as knowledge of some of the fundamental aspects of cell biology has expanded, and clinics have started more and more to measure biochemistry and metabolic processes to monitor the efficacy of treatment, the unbridgeable gulf is narrowing, Herschman said.

"Opportunities to reach across the gulf and join hands are much more prevalent today," he said. "Basic research discoveries in the lab are continuing to accelerate and amaze, and as an added bonus we are more and more able to exploit this new knowledge and collaborate with clinicians to change the standard of care."

And all those advances, which today are saving lives, began with an idea, a question that a scientist wanted to answer, had to answer.

UTPAL BANERJEE
Utpal Banerjee knew from the time he was five that he wanted to be a scientist. Later, simple experiments performed in high school chemistry labs held him enraptured. Chemistry kits featuring bottles filled with dangerous fluids like mercury were like a siren song.

"There was no question," he recalls. "I knew that I would become a scientist."

Banerjee attended St. Stephen's College in New Delhi, India, for his undergraduate work and there earned both a bachelor's and master's degree in physical chemistry. He then came to Pasadena as a student and obtained his doctorate degree in chemistry at Caltech. In his post doctoral work, also at Caltech, Banerjee made a big change in his focus and started working in genetics.

"I always wanted to work on live systems," said Banerjee, now chairman of the department of molecular, cell and developmental biology at UCLA. "And I hadn't had an opportunity earlier to do that."

In his quest to explore genetics, Banerjee studied with the renowned Seymour Benzer at Caltech, and it was there that he first began his work with Drosophila, the common fruit fly. He focused on a particular gene called sevenless, which functions in the fruit fly's eye and shares a similarity to many genes that have implications in cancer development. In his own laboratory at UCLA, Banerjee then studied another member of this oncogenic pathway, which he named Son of sevenless, or Sos.

Banerjee studied the basic normal development of the eye, what cellular pathways were at work in that development and what happened when that development went awry.
“If you want to understand cancer, and have a chance to actually cure cancer, you have to first understand how the gene works,” Banerjee said. “Then you can understand what happens when it doesn’t work the way it should.”

And Banerjee has studied that extensively over the years, in fruit flies, zebrafish, and now in stem cells.

In the zebrafish blood, Banerjee found a new gene that may have implications in transforming normal blood cells into leukemic cells, a pilot study funded by the Jonsson Cancer Center.

“These small molecules can act as an internal communicator, signaling certain blood precursor cells, or blood stem cells, to differentiate into immune-bolstering cells in reaction to a threat. After the progenitor cells differentiate, the ROS levels return to normal, ensuring the safety and survival of the mature blood cells.

Banerjee discovered that when ROS was taken away in the blood stem cells, they failed to differentiate into the immune-bolstering cells, called macrophages. On the other hand, when levels of ROS were further increased by genetic means, the blood stem cells “differentiated like gang busters,” Banerjee said, making a large number of macrophages.

The ROS, Banerjee said, acted as a signaling mechanism that kept the blood stem cells in a certain “sensitized” state – when levels rose, it was a message to the cell to differentiate.

The implications from the finding are several fold, Banerjee said. The blood stem cells are stress sensing cells, their function is to sense conditions that increase oxidative stress and react with an immune response. Keeping their ROS levels slightly elevated puts the cells on alert, sensitive and ready to respond to any threat quickly.

LUISA IRUELA-ARISPE
Scientist Luisa Iruela-Arispe sees endless opportunities for basic scientists in the future. Technology will continue to advance and in her laboratory and throughout the Jonsson Cancer Center, she encounters young researchers with a “true enthusiasm for moving science forward in a way that makes an impact on health.”

“Before, we would analyze data in the context of what others have done and interpret results in a far more speculative manner,” she said. “Now we can be more definitive and move ahead more quickly, which is important because every question leads to 50 other questions.”

These tools hadn’t yet been conceived when science first piqued Iruela-Arispe’s interest. Since she can remember, she’s had questions she wanted answered, what she calls the “why, why, why of things.” Even as a young girl, she was more likely to dissect a dead insect she found on the sidewalk than scale a jungle gym.

Those questions led Iruela-Arispe to science, where she now studies the normal and abnormal development of blood vessels and how that plays a role in cancer. She came to UCLA from Harvard more than a dozen years...
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ago, and has since made important discoveries about angiogenesis, the physiological process involving the growth of new blood vessels from pre-existing vessels.

Solid tumors cannot grow larger than a pinhead without creating an independent blood supply to provide the oxygen and nutrients they need to grow and spread. Researchers had posited that interrupting the development of that blood supply could result in starving, and hopefully killing, the tumors.

Iruela-Arispe’s lab was among the first to develop the concept of naturally occurring angiogenesis inhibitors. She explored the idea that natural inhibitors of this process were responsible for regulating the ability of blood vessel to expand and might be useful in fighting cancer. (Click here to watch Iruela-Arispe talk about her work.)

She was the first to clone METH-1 and METH-2, two potent, naturally occurring human proteins that inhibit angiogenesis. They act by inhibiting the growth of endothelial cells, which line the inside of blood vessels and are key to new blood vessel formation.

Her idea, then a novel concept, proved to be prescient. A little more than a decade after her observations, the angiogenesis inhibitor Avastin is approved for use in metastatic colorectal, non-small cell lung cancer and breast and kidney cancers, as well as glioblastoma, a deadly brain cancer.

In the years since - her work funded in part by a seed grant from the Jonsson Cancer Center - Iruela-Arispe has continued to study how normal vasculature develops. Looking at the “normal” system has helped her gain information on how things go awry in cancer. She and her team developed genetic tools to play with the gain and loss of endothelial cell function in the normal system to see what occurred.

That work led her to study blood stem cells, the cells that give rise to all the cells in the bloodstream. Four years later, that work led to another important finding. Iruela-Arispe proved definitively that blood stem cells are made during mid-gestational embryonic development by endothelial cells. Her discovery put to rest a long-standing controversy over whether blood stem cells were created, or born, in the endothelium or originated from another cell type in a nearby location.

The finding ultimately could lead to new therapies for certain blood disorders and cancers, said Iruela-Arispe, a professor of cell, molecular and developmental biology and director of the cancer center’s Cancer Cell Biology Program Area.

Blood stem cells currently cannot be grown outside of the body without losing their “stemness,” their ability to differentiate into the different blood cell types. If blood stem cells can be grown outside the body from endothelial cells and be programmed to only self-renew, or make more of their own kind, researchers may one day be able to produce blood stem cells to replace the bone marrow in transplants or the mutated blood cells that result in diseases like leukemia.

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SIAVASH KURDISTANI

The journey to science for Dr. Siavash Kurdistani was not an easy one. He was born in Tehran, and fled the social and political turmoil sweeping his country after the 1979 revolution and the eight-year war with Iraq that followed.

At 17, and not permitted to emigrate, Kurdistani fled his country with the aid of smugglers. Over 10 days, he traveled by car and hiked over mountains to reach Pakistan, where he was jailed for being in the country illegally.

Designated by the United Nations as a refugee, Kurdistani was able to relocate to Austria and, later, to New York City. Living with a cousin in a basement apartment next to an elevated subway track in Brooklyn, Kurdistani studied diligently and rapidly progressed through his English as a Second Language courses. Soon he was able to graduate from high school. After graduating, he traveled west and attended Santa Monica College for two years, then transferred to UCLA, where he graduated summa cum laude with a bachelor's degree in biochemistry.

Armed with a medical degree from Harvard, where he graduated magna cum laude, Kurdistani returned to UCLA for his residency.
Today, Kurdistani studies epigenetics, a field focused on inherited information other than that encoded on DNA. Specifically, he studies chemical modifications of proteins called histones, which are found in nearly all eukaryotic organisms whose cells contain complex, membrane-bound structures such as a nucleus.

“My research involves the study of processes that are associated with DNA, but don’t involve genetic mutations,” said Kurdistani, an assistant professor of biological chemistry who joined the UCLA faculty five years ago.

DNA, which carries all the instructions for a cell, wraps itself around histones, which serves as a kind of scaffold that allows for the compaction of the long DNA molecules. The complex of the DNA and the histones is called chromatin, the physiologically relevant form of the genome in humans.

The chemical modification of these histones, which is the basis of Kurdistani’s work, is crucial because they regulate such processes as gene transcription, DNA repair and other DNA-related functions.

Kurdistani is studying how histone modifications are exploited by cancer cells to support their unregulated growth, although alterations of histone modifications are involved in many disease processes, he said.

What Kurdistani has found in the lab is that loss of histone modifications is associated with cancers that behave more aggressively. Patients with these types of cancers had poorer prognoses, decreased survival rates and increased chances for recurrence. The finding allowed him to develop a tool, a type of clinical test, to distinguish between cancers that are less aggressive versus those that are more aggressive.

“This is important because it allows an oncologist to tailor therapies to the specific traits of the cancer,” said Kurdistani. “Patients with more aggressive cancer could get more aggressive therapies, while those with more indolent cancers could be spared the most aggressive regimens and the side effects that come with them.”

The assay, which still needs further development, can be used in cancers of the glandular tissues, including breast, lung, kidney, prostate and pancreas.

Like his contemporaries, Kurdistani has benefited from the explosion in technology that has helped to speed the basic research process. The advances are great, he said, but what is most vital to the research process is creativity.

“First, you have to have a good idea,” he said. “Creativity is helped by having the space and time to be able to think, to let ideas develop on their own. It also is helped by interactions and collaborations with other scientists in a multidisciplinary environment. UCLA is a great place for that.”

STEPHEN SMALE
For scientist Stephen Smale, the genomics era has - literally - changed everything in basic research and the study of gene regulation. One of his projects focusing on the inflammatory response in the cancer microenvironment, in fact, could not be done without the advent of the study of the genome.

“The emergence of sequencing, evaluating and studying the genome did not exist prior to 2001,” said Smale, a professor of microbiology, immunology and molecular genetics and director of the cancer center’s Gene Regulation Program Area. “Basic research will be divided into two eras – pre-genomics and post-genomics. There’s a lot more to study now, we can move faster and the value of what we’re learning is greater. We can see the broader relevance of what we’re doing more easily in the post-genomics era.”

Prior to genomics, scientists could only study gene regulation by looking at one gene at a time in great detail with the hope that the results obtained would be relevant to a much broader set of genes. It was informative, but slow and frustrating, Smale said.

Further complicating the science, different researchers focusing on different model genes believed to be similarly regulated often came up with disparate results.

“The question was, is one researcher right and one wrong or is there some underlying logic we’re missing?” Smale said. “Now, with genomics, we can look at a broad set of genes at the same time and immediately gain insight. We can find specific sets of genes regulated by a given strategy, which increases the value of the information and allows us to interpret our findings much more effectively.”

A UCLA professor for 20 years - a period he said has “flown by’ - Smale studies the molecular mechanisms of gene regulation in cells of the immune system.

In addition to gene regulation associated with an inflammatory response, Smale studies the development of the immune system. Blood stem cells give rise to lymphocytes, red blood cells, macrophages, neutrophils and other immune cell types in the bone marrow. Studies of immune development are very important for understanding many types of leukemia and lymphoma, Smale said, because these cancers are derived from immature immune cells undergoing development.
One focus of Smale’s work on immune system development is a transcription factor called Ikaros, which Smale co-discovered in 1991. Ikaros is a protein that binds to specific DNA sequences and Smale has been studying how it regulates genes during immune system development.

It appears to work, he said, through an unusual mechanism and, while his lab and others have gained insights, they still haven’t uncovered how it operates. Ikaros is mutated in more than 85 percent of certain types of acute lymphoblastic leukemia (ALL) and if he could uncover how it works, it would be a giant leap forward in understanding the molecular basis of these ALL subtypes, an understanding that could be translated into new and more effective therapies for the disease.

Smale’s work on inflammatory responses in the cancer microenvironment employs genomics to uncover the selective regulation of different genes involved in inflammation.

“The reason this is important for cancer is that within the tumor microenvironment, some inflammation molecules enhance tumor growth, while others stimulate an immune response to fight the tumor. If we could identify strategies for inhibiting the genes that promote tumor growth without inhibiting those that promote the immune response, we may have a new way to fight cancers.”

In his illustrious career, Witte has answered many questions and some of those answers have led to remarkable discoveries that were translated into clinical uses - new drugs to treat chronic myeloid leukemia (CML), understanding of immune disorders like X-Linked Agammaglobulinemia (XLA), defining a surface antigen in prostate cancer that led to clinical trials of a monoclonal antibody, and the development of a new probe for Positron Emission Tomography scanning that will allow modeling and measuring the immune system in action and monitoring response to new cancer therapies.

Witte discovered the Bcr-Abl oncogene as a tyrosine kinase produced from the Philadelphia chromosome and its mode of action in CML. His work provided a target for a new therapeutic and as a result the drug Gleevec was tested and approved for use in patients with CML. Prior to the discovery and the development of Gleevec, patients were given Interferon, which had serious side effects. In some patients, Gleevec stopped the cancer dead in its tracks. The basic defect in XLA is a failure of B-lymphocyte precursors to mature into B-lymphocytes, and ultimately, into plasma cells. Since they lack the B lymphocytes that are responsible for producing protective antibodies, XLA patients often have severe and chronic infections. In his lab, Witte discovered that in patients with XLA, the BTK gene is missing from the lymphocytes, defining for the first time that a genetic immune deficiency was caused by a loss of function of a specific tyrosine kinase. That finding has led to the development of a class of targeted drugs, which are being tested in clinical trials to control B cell growth in malignancy and autoimmunity.

Witte has also discovered surface antigens in prostate cancer that may be important in the development and treatment of the disease. Among the most important is a surface antigen in prostate cancer called Prostate Stem Cell Antigen, or PSCA, which Witte and several colleagues helped to uncover. That finding led to development of a monoclonal antibody targeting PSCA that is now being tested in clinical trials.

Most recently, Witte and colleagues modified a common chemotherapy drug to create a new probe for Positron Emission Tomography (PET), which enables scientists to monitor the immune system – at the whole body level in 3D – as it tries to fight some cancers or when it goes awry as it does in autoimmune diseases. Called FAC, the small molecule was created by slightly altering the molecular structure of one of the most commonly used chemotherapy drugs, gemcitabine. The team then added a radiolabel so the cells that take in the probe can be seen during PET scanning.

The probe is based on a fundamental cell biochemical pathway called the DNA Salvage Pathway, which acts as a recycling mechanism that helps with DNA replication and repair. All cells use this pathway to different degrees. But in lymphocytes and macrophages, the cells of the immune system that initiate an immune response, the pathway is activated at very high levels. Because of that, the probe accumulates at high levels in those cells.
“None of the projects started began with the sole intention of making therapeutic or diagnostic tools,” he said. “We had a question and asked it. We found an answer and then had a second question to ask. And so it goes.”

HONG WU
When Dr. Hong Wu began her career in basic science more than 20 years ago, discoveries were made slowly by a scientists working alone in a laboratory on a project. Today, basic research is much more multidisciplinary, with researchers from different disciplines collaborating on projects, using leading-edge technologies to shine a new light on science.

And so it is for Wu at UCLA, where her work on the biological function of a tumor suppressor gene in cancer development has led to very fruitful collaborations with a team from UCLA’s soft tissue sarcoma and pancreatic cancer programs, where she shares insights with clinicians who are treating patients in the clinic.

A professor of molecular and medical pharmacology and an expert in cell signaling and animal models, Wu has focused her research on the PTEN gene, the second most frequently deleted human tumor suppressor gene. When it’s missing in a cell, it divides out of control and the result is cancer. She and her team use both a genetic model and a cellular model to study how PTEN functions in humans and the pathways it uses, which may provide future targets for therapeutics.

PTEN was cloned about a decade ago, about the same time that Wu came to UCLA from the Whitehead Institute at MIT. PTEN was the first tumor suppressor gene shown with phosphatase activity, so Wu was able to study how its enzymatic activity controls tumorigenesis.

“We now know PTEN plays an essential role in the PI3 kinase pathway and know the mutation of it will lead to resistance to certain therapies,” she said.

For example, a patient with a PTEN deletion will not respond well to treatment with an inhibitor targeting the epidermal growth factor receptor (EGFR). So that could be used as a prognosis marker for breast cancer patients with that mutation, she said.

In a lung cancer trial, a similar conclusion was reached – patients with PTEN mutations do not respond to EGFR therapies.

PTEN itself does not provide a target for therapy, but the pathways it controls may prove to be targets for therapy, including the pathways mTOR, AKT and PI3 kinase. Wu is also studying what effect PTEN might have in controlling stem cell activity in leukemia, brain and prostate cancers, which also could lead to new and more effective therapies.

By analyzing cells and animal models lacking the PTEN tumor suppressor, Wu and her colleagues have demonstrated that PTEN negatively affects stem cell self-renewal, proliferation and survival. The finding provides a strong link between stem cell biology and cancer biology, and suggests that tumors may originate through the transformation of stem cells. If that transformation could be targeted or interrupted, it might provide yet another new and more effective way to treat these cancers.

“The big challenge and next step is to integrate and work with physician-scientists,” Wu said. “With this collaboration, you realize your basic research can have a real impact on patients.”

Wu also is credited with establishing animal models for various human cancers, including leukemia, brain and prostate cancer models. These animal cancer models offer unique tools for exploring the molecular mechanism underlying human cancers and for the development of new therapies.

“For someone like me, trained in and conducting basic research for the past 20 years, the big challenge and next step is to integrate and work with physician-scientists.”

– Hong Wu
JAMES WOHLSCHELEG came to science at a time when his two interests could intersect – the global analysis of proteins with mass spectrometry and using his biological chemistry training to study cell signaling pathways that are mis-regulated in cancer.

He was definitely at the right place at the right technological time.

Wohlschlegel, an assistant professor of biological chemistry who joined the UCLA faculty in the fall of 2006, always wanted to be a scientist. He liked figuring out how things worked.

Near the end of high school, he entered a project in the science fair and loved the time he spent preparing it in a laboratory.

“Being a scientist is a career where you’re given the freedom and independence to ask questions that are interesting to you, how some fundamental life process works,” said Wohlschlegel, 34, who was born in Taiwan to an American father and a Japanese mother. “You get to ask the questions in a number of ways and be creative about how to get your answers.” (Click here to see Wohlschlegel talk about his desire to be a scientist.)

Wohlschlegel attended Texas A&M University and worked in a laboratory from his first day, studying bacterial genetics. It was his first exposure, he said, to “cutting-edge, mainstream experimental science.”

He was hooked.

Wohlschlegel worked in the bacterial genetics lab for two years before moving to a lab that focused on enzyme reaction mechanisms, providing him with his first exposure to biological chemistry. He promptly made biological chemistry his major.

“This is a very open area of biology.”

– James Wohlschlegel

After graduation, Wohlschlegel attended Harvard Medical School where he pursued a doctorate in biological chemistry. There, he joined a lab that studied cell cycle control and DNA replication in cancer. This exposure to cancer cell biology again altered his scientific path, just as his later experiments would take him down different pathways in his quest to uncover what could be a cause of cancer.

After earning his doctorate from Harvard, Wohlschlegel went to the Scripps Research Institute in La Jolla in 2002 with a very specific goal – to work in the lab of analytical chemist John Yates, who was developing methods for global analysis of proteins using mass spectrometry, an analytical technique that is able to determine the identity of proteins based on their weight. He also worked in the lab of Steve Reed, who specialized in the regulatory mechanisms of cell cycle control.

In the Yates lab Wohlschlegel could develop new methods or techniques to study the biological processes he was focusing on in Reed’s lab. And so his interests – and technology – intersected.

Specifically, Wohlschlegel wanted to study the ubiquitin family of small modifier proteins, which get attached to target proteins in the cell and regulate their activity. For the next four years, Wohlschlegel developed various proteomic methods and techniques that enabled him to study the biological importance of ubiquitin and SUMO, a ubiquitin family member, at a global level to see how these different proteins are organized into large regulatory networks that are
central to their function. (Click here to see Wohlschlegel talk about his work.)

Ready to launch his own lab, Wohlschlegel sought a place to call his scientific home. UCLA was attractive to him because many scientists were doing work that was complementary to his and also because of the highly collaborative atmosphere that is fostered at the university and within UCLA’s Jonsson Comprehensive Cancer Center.

And because UCLA was a large academic institution, he would have his own mass spectrometer and the flexibility to pick and choose his collaborations to best bolster his own research.

Again his interests have merged. He is back where he started, focusing on biological chemistry, but using mass spectrometry to study the proteins at work in cells and how they regulate their growth and development.

He is still focusing on the ubiquitin family of small protein modifiers and hoping, through his work, to characterize the functions of a huge number of enzymes that are responsible for attaching ubiquitin to target proteins, but whose biological purposes have remained a mystery. Between 500 and 700 enzymes remain uncharacterized, Wohlschlegel said, and if their function can be revealed it may answer some fundamental questions about the development of certain cancers.

“This is a very open area of biology,” Wohlschlegel said. “We know these enzymes are important and it’s a great opportunity with the technology we have now to study them and get some quick answers. We know some of these enzymes are de-regulated in cancer.”

Wohlschlegel currently is focusing on a subset of enzymes he thinks may have a role in the development of cancer. He doesn’t know where that road will lead him scientifically, but, for him, that’s really not the point.

“Being a scientist is a career where you’re given the freedom and independence to ask questions that are interesting to you, how some fundamental life process works. You get to ask the questions in a number of ways and be creative about how to get your answers.”

– James Wohlschlegel

“It almost doesn’t matter to me where (the investigation) goes,” he said. “It’s going to be interesting whatever happens. It’s an exciting time in that with the technology we have we can ask really sophisticated questions about a biological system. Our tool set really enables us to approach problems at different levels from the reductionist analysis of individual components to system-level analyses that help us to see how these components fit together.”

“I feel like I’m at the interface of two fields, mass spectrometry and traditional molecular biology and there’s where I’m trying to carve a niche for myself,” he said. “I can integrate the two fields and ask questions that are uniquely mine.”
Playing the Cancer Lottery and Hoping for a Payoff

Molecular screening in cancer research is kind of like playing the lottery. You just have to buy lots and lots of tickets.

And be a little lucky.

In screening tens of thousands of compounds at once, the head of the Molecular Screening Shared Resource (MSSR) at UCLA’s Jonsson Comprehensive Cancer Center is hoping to hit the jackpot - finding one that may be developed into a new, more effective and less toxic therapy to fight cancer.

As scientific director of the MSSR, Robert Damoiseaux plays a vital role in a process that begins in a laboratory with the development of cancer cell lines. Housed in the new California Nanosystems Institute, the state-of-the-art molecular screening facility - one of a handful nationwide - speeds a painstaking, manual process that once took years in laboratories into an automated, computer-run process that can take just days to complete.

The high-throughput technology – once available only to well-heeled pharmaceutical industry companies - is capable of screening as many as 100,000 compounds in a single day. It is available to Jonsson Cancer Center researchers, UCLA scientists and academic collaborators from around the world.

“The idea of high-throughput screening is to do a single experiment over and over and over again with the hope that in all the compounds you’re testing you find something that works,” Damoiseaux said. “The hallmark of cancer is that it grows, and fundamentally we’re interested in compounds that stop cells from proliferating so rapidly or stop them from growing at all.”

The compounds - small molecule drugs already approved by the U.S. Food & Drug Administration as well as purified natural products and fully synthetic molecules - are brought to UCLA from all over the world. Other compounds were developed at UCLA by chemists. The MSSR compound collection is constantly updated, Damoiseaux said. And although there is much thought and reasoning that goes into a screen, the process can be a lot like looking for the proverbial needle in the haystack.

“Typically, under one percent of the compounds tested are active on a first pass screen,” Damoiseaux said. Fortunately, the first pass screen is not the last.

The process starts in a lab, with a Jonsson Cancer Center researcher developing cells lines for various types of cancer in Petri dishes, seeking to hit a known or unknown target on the cancer cell - a protein that is over-expressed and causing uncontrollable growth, a cell signaling pathway that is not operating correctly.

Targeting therapies to what is broken in a cancer cell, what causes it to grow or keeps it from dying, results in less toxic therapies. Unlike chemotherapy, which operates like a non-specific bomb hitting all fast growing cells in the body, targeted therapies generally leave the healthy cells alone and patients experience far fewer debilitating side effects.

A handful of successful targeted therapies have been approved to fight cancer - Herceptin for breast cancer, Gleevec and Sprycel for chronic myeloid leukemia and Avastin for metastatic colorectal, breast, brain and kidney cancers, to name a few. Herceptin, Gleevec and Sprycel were all developed based on basic and clinical research done in Jonsson Cancer Center labs, while early pre-clinical testing on Avastin also was done at UCLA. That research was conducted without the benefit of high-throughput screening.

“Think of what we may be able to accomplish now,” Damoiseaux said, “using our automated equipment that is integrated into a single robotics system, technology that can work around-the-clock, 24 hours a day, seven days a week.”

Once a cancer cell line is developed, the researcher develops an assay, a procedure in molecular biology to test or measure the activity of a drug or biochemical compound in an organic sample, in this case cancer cells.

Damoiseaux’s services are part of what the shared resources fees pay for. He consults extensively with the researchers to assure the cell lines are optimal for testing and the assays are designed for the best outcome. Then the compounds to be screened must be carefully selected.

“Since you don’t really know which compounds will work, you have to have a collection of all sorts of small molecules with different properties, ideally with low toxicities - a compound may be effective but highly dangerous to humans - the right size and polarities,” said Damoiseaux, who compiles the shared resource small molecule library. “Then we have to strategize about how to pick which compounds to screen first.”

He also has developed sub-libraries, kinases for example, to test against cancer cells. Kinases are unregulated in cancer and inhibitors to them have been successful at treating the disease.
Molecular Screening

Once the first collection of compounds has been selected, the cell line and assay system can be tested in a small trial run of about 1,500 compounds. The cells are loaded into plates with 384 wells each and the drugs are added. The plates are about the size of the palm of an adult hand. After the assay test is performed and success with a small library is achieved, up to 90,000 compounds are screened against the cell lines.

The robotic screening system is as big as a small walk-in closet and the air in the facility is HEPA filtered to protect the cell lines and compounds. The computerized, robotic system executes the screening process from start to finish, adding the compounds sitting in the tiny wells in the plates to the cancer cells, located in corresponding assay plates. A robotic arm with an automated liquid transfer system places a miniscule amount (about 4/10,000,000 of a quart) of the compound onto a plate containing the cancer cells and moves on to the next plate, cleaning and drying liquid transfer system components at regular intervals to insure purity. (Click here to see the robotic screening system at work.)

In 90 seconds the transfer of compounds onto cancer cells is completed and the cells go into an incubator, where they remain for about 48 hours. After 48 hours, a reagent is added that prompts a luminescent reaction, making the living cells light up. A plate reader then looks into each well and records how much signal or light is coming out – in other words, which cancer cells are alive and which have been killed.

Text files or spread sheets can be generated to analyze the data to determine which compounds are active. The automated system can retrieve all the compounds that appear to be active and put them into one 384-well plate for further screening.

The screen of the potentially active compounds is done again, with three different plates containing the same compounds.

“By repeating the screen three times, we know which compounds are really active,” Damoiseaux said. “There is a certain rate of false positives, so we do the screen multiple times to be sure.”

Once they have their “hits,” or active compounds, they study their chemical structure to see if they share similar properties. If a pattern emerges among the active compounds, other similar compounds can be purchased from libraries and added to the screen.

Armed with this new information, a sub-library of the hits is assembled and screened on different kinds of cells, cancerous, non-cancerous, metastatic cancer cells, to analyze what effect the compound has on different cell types. What may work on one type of breast cancer cell, for example, may not work on another. Like many other cancers, breast cancer is not one disease, but six or seven sub-types, each of which may react differently to small molecule compounds. The treatment, Damoiseaux explained, must be personalized to the patient for the most effective results.

Once the compounds that are the most active against the cancer cells and the least toxic to non-cancerous cells are identified, they can then be tested in animal models, and perhaps later in humans in clinical trials.

Fuyu Tamanoi, a professor of microbiology, immunology and molecular genetics and director of the cancer center’s Signal Transduction and Therapeutics Program Area, has used the high-throughput screening resource to search for small molecule inhibitors. An assay developed in his lab could test for inhibitors, but was not designed for high-throughput screening, he said. Damoiseaux and his team helped in adapting the assay for screening.

His assay was targeted against a gene product activated in pancreatic cancer and Damoiseaux was able to quickly screen 10,000 compounds using the resource. Tamanoi then screened for a different target in pancreatic cancer. While finding a compound to test as a drug to fight pancreatic cancer would have been optimal, the process revealed much to Tamanoi about what was going on within the cancer cells.

“It would not have been easy for us to develop a high-throughput assay without help from the shared resource,” Tamanoi said. “The hits we got through the screening have proven to be useful for further research and experimentation. It helped us validate hypotheses and has been very useful in figuring out where we want to go next. It helped us to know what pathways are talking to each other in this cancer and has aided us in writing grants for new funding.”

The Molecular Screening Shared Resource was developed five years ago and has been able to service more than 100 users.

As the technology advances, new capabilities are added to the screening resource. A newer technology employs automatic microscopy rather than a plate reader. Instead of adding a reagent and looking for a chemical reaction, individual cells are examined to determine how they are reacting to a compound.

“That gives you more information on the cellular level,” Damoiseaux said.

But with all the awe-inspiring technology at play, it’s the human factor that drives discovery.

“At the end of the day, what really makes this tick and tick fast is the scientists who come through the door and invest their time, energy and intellect into this,” Damoiseaux said. “They come to the MSSR with a system they know well. In contrast to many other screening facilities, we involve them as much as possible in the research process to get them the best results possible, which they can use to further their research.”
BILL BUSHNELL now has two birthdays – the day he was born and the day he was reborn.

Bushnell never expected to be reborn. Diagnosed in May 2005 with stage IV metastatic melanoma, his prognosis was not good. The cancer had spread to his lungs by the time doctors found it. Surgery at first appeared to be an option, but there were two many nodules, three in one lung and two in the other.

Left with few other choices, Bushnell underwent chemotherapy but did not respond. More conventional treatment wasn’t an attractive option for the 55-year-old Cardiff-by-the-Sea resident and didn’t offer much hope for a cure, so he decided to consult with UCLA oncologist Dr. John Glaspy and then join a leading-edge clinical trial at UCLA’s Jonsson Comprehensive Cancer Center. He hoped it would help him, but if it didn’t, at least he was doing his part to move cancer research forward.

“When faced with the type of odds I was facing... it caused me to go back and reflect on my life,” said Bushnell, who is general manager for a Toyota dealership in Carlsbad. “If I could do anything for someone else through this process and we could get closer to a cure for this hideous disease, I felt that whatever the outcome was for me, it would be in some way positive.”

Although he held out little hope, Bushnell enrolled in a study led by Dr. Antoni Ribas that paired two experimental approaches to beat his disease. As always, his wife, Maxine, was at his side.

“Luckily, Bill was able to get into the clinical trial. They told us about it and it all was kind of a blur then because we didn’t really know anything,” said Maxine, who married her husband just one year before his diagnosis. “The percentages they gave us for success were not good.”

In fact, Ribas told them the experimental treatment probably wouldn’t work.

The trial required the Bushnells to be at UCLA at least twice a week for three months. The long drive from San Diego County was taxing, but they wanted the best care.

The clinical trial was testing two experimental drugs, a dendritic cell vaccine and an antibody. The goal was to teach the immune system to recognize and kill Bushnell’s melanoma cells, which carried a specific marker or protein called MART-1.

Dendritic cells are a type of blood cell that specializes in stimulating the immune system. They don’t directly fight cancer. Instead, they teach other cells in the body to seek out cancer cells with the MART-1 protein and destroy them. In effect, the vaccine functions as an “on” switch for the immune system. For the study, dendritic cells were grown in the laboratory from Bushnell’s blood and loaded with the MART-1 protein.

The second component of the protocol was an antibody called tremelimumab, which binds and blocks to a protein called CTLA-4. CTLA-4 is found on the surface of certain white blood cells and acts as an “off” switch or brake for the immune system, so the antibody would release this brake.

“When faced with the type of odds I was facing... it caused me to go back and reflect on my life.”

– Bill Bushnell
The rationale for combining the drugs is to turn on the immune system with the dendritic cell vaccine and then block the off switch, the CTLA-4, with the antibody tremelimumab. Hopefully, Ribas said, the combination of the two therapies would result in a greater activation of the immune system against the melanoma cells.

“What I liked about the study was that instead of the treatment killing the immune system, it hyper-stimulated the immune system,” Bushnell said. “It seemed like a smart and logical approach.”

Bushnell got his first treatment in September 2005.

On a follow-up appointment, a cancerous mole on Bushnell’s arm looked different. Ribas, intrigued, took photographs of the mole. Another follow-up appointment was scheduled.

“When I came up the next time, the mole was gone,” Bushnell said. “Dr. Ribas said the treatment was really working.”

A series of scans was scheduled to monitor the lesions in Bushnell’s lungs. Over time, they could see the lesions were shrinking.

Bushnell was told to come back in February 2006 for further follow-up. What the Bushnells walked into that day was more like a party than an appointment with an oncologist.

“I remember we walked in and there were a bunch of people in the room, Dr. Ribas, Dr. Glaspy, nurses and study coordinators,” Bushnell recalled “Then they shared with me in that room that it appeared there was no sign of cancer other than a little bit of scar tissue in my lungs.”

The immune system-boosting therapy, it seemed, had worked. Better than anyone had thought it would. Better than anyone had hoped it would.

“The day in the clinic, when we learned that his lung metastases were regressing, it was like a party,” Ribas said. “Everyone was very happy.”

It’s been more than three years since that day and Bushnell remains cancer free. These days, he celebrates two birthdays.

“My real birthday is Feb. 9, and my appointment on that day was Feb. 6. Now I call Feb. 6 my new birthday. I really started my new life that day,” Bushnell said.

“I can’t share enough what that emotion was like, when they told me the cancer appeared to be gone. We were planning a funeral, and now we are figuring out what we’re going to do with our lives. Every meal is a banquet and every day is a holiday. I used to say those words, but I didn’t mean them. Now I really am experiencing that. I can’t tell you how great that is.”
# Award-Winning Faculty

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<tr>
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<th>Name</th>
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<td><strong>September 2007</strong></td>
<td><strong>Kathrin Plath</strong></td>
<td>New Innovator Award National Institutes of Health</td>
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<td><strong>October 2007</strong></td>
<td><strong>Dr. Patricia Ganz</strong></td>
<td>American Cancer Society Distinguished Service Award</td>
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<td><strong>Anne Coscarelli</strong></td>
<td>Los Angeles County Psychological Association Distinguished Service to the Profession of Psychology Award</td>
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<td><strong>Dr. Patricia Ganz</strong></td>
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<td>Member</td>
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<td><strong>Kathrin Plath</strong></td>
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<td>V Scholar</td>
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<td><strong>November 2007</strong></td>
<td><strong>Helene Brown</strong></td>
<td>American Cancer Society Woman of Courage Award</td>
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<td><strong>Michael Phelps</strong></td>
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<td><strong>Rita Effros</strong></td>
<td><strong>Gerontological Society of America</strong></td>
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<td><strong>Dr. Lawrence Bassett</strong></td>
<td><strong>Radiological Society of North America</strong></td>
<td>Award of Honor for the Annual Oration in Diagnostic Radiology</td>
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<td><strong>April 2008</strong></td>
<td><strong>Utpal Banerjee</strong></td>
<td>American Academy of Arts and Sciences Member</td>
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<td><strong>Dr. David Dawson</strong></td>
<td>AACR/Pancreatic Cancer Action Network Career Development Award</td>
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<td><strong>May 2008</strong></td>
<td><strong>Michael Grunstein</strong></td>
<td>National Academy of the Sciences Member</td>
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<td><strong>Dr. Steven Dubinett</strong></td>
<td>American Thoracic Society Scientific Achievement Award</td>
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<td><strong>June 2008</strong></td>
<td><strong>Dr. Patricia Ganz</strong></td>
<td>American Society of Clinical Oncology American Cancer Society Award</td>
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<td><strong>Dr. Fritz Eilber</strong></td>
<td>Sarcoma Foundation of America Shelby Richter Memorial Research Award</td>
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<td><strong>Dr. Michael Teitell</strong></td>
<td>Luekemia &amp; Lymphoma Society Stohlman Scholar</td>
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<td><strong>Dr. Dennis Slamon</strong></td>
<td>Van Andel Research Institute The Daniel Nathans’ Memorial Award</td>
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<td><strong>January 2009</strong></td>
<td><strong>Christopher Saigal</strong></td>
<td>American Urological Association Gallagher Health Policy Scholar</td>
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<td><strong>Simin Liu</strong></td>
<td>Burroughs Wellcome Fund Institutional Program Unifying Population and Laboratory Based Sciences Award</td>
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<td><strong>February 2009</strong></td>
<td><strong>Dr. Dennis Slamon</strong></td>
<td>UCLA Medical Alumni and Aesculapians Association Medical Science Award</td>
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<td><strong>March 2009</strong></td>
<td><strong>David Eisenberg</strong></td>
<td>Harvey Foundation Harvey International Prize in Human Health</td>
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<td><strong>Dr. Patricia Ganz</strong></td>
<td>UCLA School of Public Health Dean’s Distinguished Scholar</td>
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<td><strong>James Heath</strong></td>
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<td><strong>North American Vascular Biology Organization Judah Folkman Award for Excellence in Vascular Biology</strong></td>
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<td><strong>May 2009</strong></td>
<td><strong>Linda Sarna</strong></td>
<td>UCSF School of Nursing 29th Helen Nahm Award</td>
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<td><strong>Annette Stanton</strong></td>
<td><strong>Cancer Council Queensland, Australia William Rudder Fellowship</strong></td>
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<td><strong>Linda Sarna</strong></td>
<td>Oncology Nursing Society Oncology Nursing Distinguished Researcher Award</td>
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<td><strong>June 2009</strong></td>
<td><strong>Dr. Noah Federman</strong></td>
<td>St. Baldrick’s Foundation St. Baldrick’s Scholar Award</td>
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<td><strong>Kathrin Plath</strong></td>
<td><strong>David Geffen School of Medicine at UCLA John H. Walsh Young Investigator Research Prize</strong></td>
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### Award-Winning Faculty

**June 2009**

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<td>Dr. Kathleen Sakamoto</td>
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<td>Dr. Owen Witte</td>
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<td>Dr. Noah Federman</td>
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<td>UCLA Academic Senate Undergraduate Mentorship Award</td>
<td>Luisa Iruela-Arispe</td>
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**August 2009**

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<td>Dr. Mark Litwin</td>
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**September 2009**

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<td>National Institutes of Health New Innovator Award</td>
<td>Dr. Siavash Kurdistani</td>
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<td>Doris Duke Foundation Innovations in Clinical Research Award</td>
<td>Dr. Donald Kohn</td>
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<td>Pope Benedict XVI Pontifical Academy of Sciences</td>
<td>Dr. Edward De Robertis</td>
<td>UCLA CAnCer DisCoveries Award-Winning Faculty</td>
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### Science Update

**Decreased Expression of Tumor Suppressor Gene Turns Benign Tumors into Sarcomas**

Researchers at UCLA’s Jonsson Comprehensive Cancer Center showed for the first time that the loss or decreased expression of the tumor suppressor gene PTEN plays a central role in the malignant transformation of benign nerve tumors called neurofibromas into a malignant and extremely deadly form of sarcoma. The work, a collaboration between the Institute for Molecular Medicine, the Department of Molecular and Medical Pharmacology and the cancer center’s Sarcoma Program, could lead to the development of new therapies that target the cell signaling pathway regulated by PTEN. A novel mouse model of neurofibromatosis type 1 (NF1) developed at UCLA first illustrated the importance of PTEN tumor suppressor in malignant transformation and this finding was validated in human malignant peripheral nerve sheath tumors, the deadly sarcomas. The study, conducted by Drs. Hong Wu and Fritz Eilber, was published Oct. 12, 2009 in the early online edition of the peer-reviewed journal Proceedings of the National Academy of Sciences.

**Is Excessive Use of Antioxidants Depleting our Immune Systems?**

For years, health conscious people have been taking antioxidants to reduce the levels of reactive oxygen in their blood and prevent the DNA damage done by free radicals, which are the result of oxidative stress. But could excessive use of antioxidants deplete our immune systems? Research at UCLA’s Jonsson Comprehensive Cancer Center has raised that question. It has been known for decades that reactive oxygen species (ROS) — ions or very small molecules that include free radicals — damage cells. But much to their surprise, Jonsson Cancer Center researchers found that in Drosophila, the common fruit fly, moderately elevated levels of ROS are a good thing. These small molecules act as an internal communicator, signaling certain blood precursor cells, or blood stem cells, to differentiate into immune-bolstering cells in reaction to a threat. After the progenitor cells differentiate, the ROS levels return to normal, ensuring the safety and survival of the mature blood cells, said Utpal Banerjee, a Jonsson Cancer Center researcher and senior author of the study. The study is published in the Sept. 24, 2009 issue of the peer-reviewed journal Nature.
Use of the Targeted Therapy Avastin Increases Response Rates and Survival in Brain Cancer

The targeted therapy Avastin, alone and in combination with the chemotherapy drug CPT-11, significantly increased response rates, progression-free survival times and survival rates in patients with a deadly form of brain cancer that had recurred. Patients with recurrent glioblastoma have grim prognoses, and conventional treatments were typically limited to largely ineffective and highly toxic chemotherapies. Only about 5 percent of patients respond to further treatment – meaning their tumors shrink by 50 percent or more. And only 15 to 20 percent of patients make it to the six month mark before their disease progresses again. Survival is limited to six to seven months.

But a randomized Phase II study of Avastin alone and Avastin given with CPT-11 have improved those statistics, dramatically increasing response rates, progression-free survival times and overall survival, said Dr. Timothy Cloughesy, director of the Neuro-Oncology Program at UCLA’s Jonsson Comprehensive Cancer Center and senior author of the study. The study was published Sept. 3 in the early online version of the Journal of Clinical Oncology.

Common Treatments for Prostate Cancer Significantly Impact Quality of Life

A long-term study by researchers at UCLA’s Jonsson Comprehensive Cancer Center found that the three most common treatments for localized prostate cancer had significant impacts on patients’ quality of life, a finding that could help guide doctors and patients in making treatment decisions. The four-year study, which followed 475 men treated for early stage prostate cancer, also resulted in the development of “probability plots,” gauges which can be used to predict when treatment side effects such as urinary incontinence, sexual dysfunction or bowel problems might return to normal, or whether the patient will ever fully recover.

Such predictions could be used to determine whether further treatments or surgeries are needed to deal with adverse side effects, said Dr. Mark Litwin, a professor of urology and the study’s senior author. The study appeared in the June 9, 2009 issue of PLoS One, a peer-reviewed journal of the Public Library of Science.

Intestinal Inflammation Linked For the First Time Wit Systemic Chromosome Damage in Mice

Scientists for the first time have linked intestinal inflammation with systemic chromosome damage in mice, a finding that may lead to the early identification and treatment of human inflammatory disorders, some of which increase cancer risk. Jonsson Cancer Center researchers found that local intestinal inflammation induced DNA damage to lymphocytes of the peripheral blood circulating through the body – meaning the chromosome damage was not limited to the intestine but involved distant body tissues. The team found single- and double-strand DNA breaks in the blood, indicating systemic genetic damage. Inflammatory diseases have been linked to some lymphomas and abdominal, liver and colorectal cancers, said Robert Schiestl, a professor of pathology, radiation oncology and environmental health sciences and senior author of the study. If inflammation can be found early – before any symptoms arise - and the diseases treated immediately, it may prevent the damage that eventually leads to these cancers. The study appeared in the June 1, 2009, edition of CANCER RESEARCH.
about a week after the first dose of chemotherapy. Typically, patients are scanned at about three months into treatment to determine whether it’s working. The question was, how early could response be picked up? If a patient is not responding, there's no point in administering toxic therapies that make them sick, said Dr. Fritz Eilber, an assistant professor of surgical oncology and the study's senior author. The study appeared in the April 15, 2009 issue of the journal Clinical Cancer Research.

Low-income Men More Likely to Present with Advanced Prostate Cancers

Low-income men are more likely to present with advanced prostate cancers, most likely because they don't receive screening services shown to reduce the diagnosis of later-stage cancers, Jonsson Cancer Center researchers found. The study focused on 570 disadvantaged men enrolled in the state's IMPACT (Improving Access, Counseling and Treatment for Californians with Prostate Cancer) program, which provides high-quality care to poor, underserved and uninsured men. Of the men studied, 19 percent had metastatic cancer at diagnosis, compared to 4 percent of men from the general population. Previous studies showed that widespread adoption of PSA screening for prostate cancer has resulted in more men being diagnosed with organ-confined, low-risk disease. This trend has not been mirrored among the disadvantaged IMPACT patients, who don’t have access to or don’t take advantage of screening. Published in the February 2009 issue of the Journal of Urology, the study sheds light on the challenges that public assistance programs face in reducing cancer-related socioeconomic disparities.

Cell Pathway Linked to Breast Cancer Drives a Highly Lethal Sub-type of the Disease

An intracellular pathway not previously linked to breast cancer is driving a sub-type of the disease that is highly lethal and disproportionately over-represented in African American women. The pathway regulates how cells identify and destroy proteins and represents a class of genes called proteasome targeting complexes. The work by Jonsson Cancer Center researchers shows that basal cancer cells degrade the tumor suppressor gene p27 by making a new type of proteasome targeting complex. The gene p27 is one of a handful of proteins that are expressed in normal cells and act to prevent the rapid cell growth indicative of cancer. Beyond chemotherapy, no therapeutic target has been identified for this sub-type of cancer, found in between 12 to 15 percent of breast cancers in the general population and up to 25 percent of cases in African American women, where mortality rates are very high, said Tim Lane, an associate professor of obstetrics and gynecology and senior author of the paper. The research, done in animal models and human breast cancer cell lines, was published in the Nov. 15, 2008 issue of the journal Genes and Development.

HPV Allows Infected Cervical and Head and Neck Cancer Cells to Become Therapy Resistant

The human papillomavirus (HPV) allows infected cervical and head and neck cancer cells to maintain internal molecular conditions that make the cancers resistant to therapy and more likely to grow and spread, resulting in a poor prognosis for patients, Jonsson Cancer Center researchers found. Virtually all human cancers experience a state called intratumoral hypoxia, or low oxygen within the tumor. In the study, researchers showed that the HPV-positive cancer cells adapted to and took advantage of the hypoxic environment by expressing a protein that activates a cell signaling pathway that helps the cancers survive, grow and spread. The study was published in the Nov. 4, 2008 issue of the journal Cancer Cell. The research, done on cells in culture and in animal models, may lead to the development of new therapies that target the cell signaling pathway, thereby interrupting ability of the cancer cells to thrive, said Dr. Matthew Rettig, an associate professor of urology and medicine and the study's senior author.

Non-invasive Imaging Approach Developed to Evaluate Tumor Response Before Therapy

For many cancer patients, chemotherapy can be worse than cancer itself. A patient may respond to one drug but not another - or the tumor may mutate and stop responding to the drug - resulting in months of wasted time, ineffective treatment and toxic side effects. Now, scientists at UCLA's Jonsson Comprehensive Cancer Center have tested a non-invasive imaging approach that may one day allow doctors to evaluate a tumor's response to a drug before prescribing therapy, enabling physicians to quickly pinpoint the most effective treatment and personalize it to the patient's unique biochemistry. The Proceedings of the National Academy of Sciences published the findings in its Feb. 2, 2009 advance online edition. This will represent the first time researchers will be able to watch a chemotherapy drug working inside the living body in real time, said Dr. Caius Radu, an assistant professor of molecular and medical pharmacology and lead author of the study. Previous studies were done in mice. Radu’s method will be tested in healthy volunteers to determine whether the results can be replicated in humans.
Entertainment Industry Executives Elected to Foundation Board

Entertainment industry executives Randall M. Katz and Jay Sures have been named chairman and vice chairman, respectively, of the board of directors for the Jonsson Cancer Center Foundation, the fundraising arm of UCLA’s Jonsson Comprehensive Cancer Center.

On the JCCF board since 2007, Katz is a generous supporter of the Jonsson Cancer Center through the Ron and Maddie Katz Family Foundation, where he serves as a director. The president of Milestone Entertainment, Katz earned his undergraduate degree from Yale University. Sures is a board member and partner at United Talent Agency and the 2007 recipient of JCCF’s Gil Nickel Humanitarian Award. A JCCF board member since 2008, Sures also co-chaired the 2008 and 2009 dinner committees for Taste for a Cure, the foundation’s signature fund-raising event. Sures also serves as treasurer of the Entertainment Industry Foundation, a charitable organization. Sures holds a bachelor’s degree in economics from UCLA.

Other board officers include treasurer Jonathan Davidson. A partner at Westridge Capital LLC, Davidson has served as the organization’s treasurer since 2007. He earned two degrees from UCLA, a bachelor’s degree in economics in 1987 and a master’s degree in business administration. The foundation also welcomed David Kramer, a partner at United Talent Agency, as a new member of its board. Kramer earned his bachelor’s degree from the University of Georgia and master’s degree from University of Southern California School of Cinematic Arts.

New Integrative Oncology Center Opened

A new center providing leading-edge integrated care to cancer patients and their families has been launched at UCLA’s Jonsson Comprehensive Cancer Center. The center offers such services as art therapy and QiGong, one-on-one and group counseling and advice on nutritional, spiritual and complementary approaches to healing.

The Simms/Mann-UCLA Center for Integrative Oncology is designed to help patients and family members optimize wellness and assist them in dealing with challenges during and after their cancer treatment.

"Cancer affects the mind, the body, the soul and the emotions. At our center, we are committed to treating the whole person, not just the disease,” said Anne Coscarelli, a psychologist and the center’s founding director. "A cancer diagnosis should not be faced alone. Everyone needs information, guidance and support during treatment and recovery.”

Most patients, Coscarelli said, want to feel as well as they can despite the challenges that come with a cancer diagnosis. Patients also often want to combine modalities and need the most accurate information available about nutrition, supplements, mind/body approaches and psychological concerns.

Dr. Mary Hardy, the center’s medical director, advises patients on nutrition and dietary supplements and can suggest complementary therapies such as massage and acupuncture. She evaluates each patient individually and tailors her advice based on their lifestyle, treatment regimen and emotional and physical condition.

Leading-edge Research Management System Launched

In an effort to improve and streamline clinical trials management, UCLA’s Jonsson Comprehensive Cancer Center has acquired and launched Velos eResearch, software that allows for better use of information systems and clinical databases in medical research. UCLA officials chose Velos eResearch because the system offered the best functionality for managing clinical trials.

"We have a very complex structure here on campus and in our affiliated research network,” said Nancy Ryba, a registered nurse and administrative director of the cancer center’s Clinical Research Unit. “Velos allows us to accurately track the patients and studies with the level of detail that we require. Equally important, Velos is the most user-friendly for those who work with the system. It also is the most flexible and adaptable for addressing all of our on-campus and off-campus needs.”

The system supports patient recruitment, patient scheduling, Internal Review Board and study monitoring, project planning, study design, protocol compliance, budget, invoicing, data safety monitoring, adverse event reporting, system integration and study execution. The cancer center tracks everything from simple studies to very complex, multi-arm clinical trials that require very detailed patient information, Ryba said. Velos will also be used to track studies within the Translational Oncology Research International (TORI) network, a large network of participating research sites and medical practices located throughout the country.
New Tool Delivers Higher Doses of Radiation in Less Time

UCLA has added a new tool to its cancer-fighting arsenal, a state-of-the-art, image-guided device that provides more accurate, concentrated doses of radiation, allowing patients to be treated in fewer visits and suffer from fewer side effects.

UCLA’s Department of Radiation Oncology was the first center in the Los Angeles area to install Novalis Tx, a non-invasive stereotactic radiosurgery machine that includes three imaging modalities. The modalities track the location of tumors during respiration and other movement and allow physicians to pinpoint the tumor and position the patient so the radiation is delivered with the highest precision to the cancerous tissue while protecting the healthy surrounding tissues.

The Novalis Tx has an advanced system that continuously re-shapes the radiation beam to mirror the tumor’s size and dimensions as it rotates around the patient delivering treatment from different angles.

Physicians using the machine likened it to a high-performance sports car with all the bells and whistles that make such a vehicle desirable.

“This is like having a really nice BMW. With Novalis Tx, you get all the basic features of stereotactic radiosurgery, but you also get all these amazing, high-tech accessories,” said Dr. Percy Lee, an assistant professor of radiation oncology and director of the stereotactic body radiation therapy program. “This machine has state-of-the-art features to cover every clinical circumstance and make it more precise and accurate.”

In some cases, Novalis Tx can reduce needed radiation from daily treatments for six weeks to just three to five days because of the high doses that can be delivered. This results in less radiation dose to the neighboring normal tissues, sparing side effects while also improving tumor control rates. The device will be used to treat cancers of the brain, spine, lung, liver, pancreas, prostate and kidney. Because the radiation is so precisely aimed, Novalis Tx also will allow patients that may have inoperable, untreatable tumors to receive therapy they might not otherwise have been given.

New Urologic Oncology Institute Will Develop Leading-Edge Therapies

UCLA has launched a first-of-its-kind, patient-centered institute dedicated to developing leading-edge therapies for the treatment of kidney, bladder, testicular and prostate cancers.

The Institute of Urologic Oncology at UCLA challenges the traditional model of academic departments operating independently of each other, bringing a multi-disciplinary team of scientists and physicians together as part of one cohesive organization. Their goal is to expedite the development of new therapies for patients with genitourinary cancers.

The disciplines represented in the institute include urologic oncology, medical oncology, diagnostic and interventional radiology, pathology, nursing, basic sciences and clinical trials. The new institute will allow experts from these areas to collaborate more efficiently and effectively, bringing to patients the most promising advances in medical and surgical treatments, including targeted therapies, chemotherapy, immunotherapy, radiation therapy and minimally invasive and ablative surgery.

“This is a one-stop shop. All the experts will be involved in their care, all working together,” said Dr. Arie Belldegrun, a researcher at UCLA’s Jonsson Comprehensive Cancer Center and director of the new institute. “Our goal is to bring all our resources to the patient, rather than the patient going from office to office to see everyone they need to see.”

That multi-disciplinary, translational approach to care and targeted therapies was pioneered at UCLA. The molecularly targeted drugs Herceptin for breast cancer and Gleevec for chronic myeloid leukemia, among others, were developed based on research conducted in Jonsson Cancer Center laboratories. Such leading-edge work will be done within the institute to develop new, more effective, less toxic therapies for urologic cancers.

Avon Walk Raises $1.35 Million for UCLA Breast Cancer Program

The sixth annual Avon Walk Los Angeles, held in September 2008, raised $1.35 million for a program at Olive View-UCLA Medical Center that helps poor and uninsured women navigate their way through breast cancer detection, diagnosis, treatment and survivorship.
The UCLA-Avon Care for Life program, offered through UCLA’s Jonsson Comprehensive Cancer Center, has proven invaluable to low-income women, many of them minorities, who are treated for breast cancer at the county hospital. The women are guided by bilingual care coordinators from diagnosis through chemotherapy and beyond. Services offered include on-site patient navigation, survivorship programs, access to screening and genetic counseling for high-risk women, clinical trials infrastructure and support for breast imaging fellowships at the Iris Cancer Center for Breast Imaging and UCLA Santa Monica Women’s Imaging Centers.

“The Avon Care for Life program ensures that patients understand their diagnosis and are seen by the appropriate doctors in a timely manner,” said Lori Viveros, program manager. “The coordinators help our patients overcome language barriers, receive follow-up care, as well as facilitate their access to vital community resources. Each patient receives literature and educational materials to help them understand what’s ahead. It really helps to have the big picture and to have someone who they can turn to if they have any questions.”

The UCLA-Avon Care for Life Program received one of seven grants given by Avon to local organizations.

**Cancer Center Joins Statewide Effort to Revolutionize Breast Cancer Care**

UCLA’s Jonsson Comprehensive Cancer Center is taking part in an unprecedented statewide University of California collaboration to revolutionize care for breast cancer patients by designing and testing, system-wide, new approaches to research, technology and health care delivery.

Called the ATHENA Breast Health Network, the groundbreaking project will initially involve 150,000 California women, who will be screened for breast cancer and followed for decades through the five UC cancer centers. The ATHENA project is supported by a $5.3-million University of California grant and by a $4.8-million grant from the Safeway Foundation.

The project is expected to generate a rich collection of data and knowledge that will shape breast cancer care the way the renowned Framingham heart study changed the care of patients with heart disease.

Dr. Arash Naeim, principal investigator for the Jonsson Cancer Center’s part in the project, said the primary goal of ATHENA is to accelerate research, “effectively translating it into innovative clinical care and demonstrating the value that can be leveraged when institutions share knowledge and technology.”

“Breast cancer is the most common cancer in women, and innovative efforts aimed at preventing and treating breast cancer require significant financial, intellectual and organizational resources to improve survival and reduce suffering from the disease,” Naeim said. “If the University of California cancer centers, their researchers and healthcare providers work together in an organized and cohesive way as equal partners, there will be a tremendous opportunity to leverage research to improve prevention, diagnosis, treatment and survivorship for all women developing breast cancer.”

**UCLA Scientists Receive nearly $50 Million in Grants to Fund Research**

Three UCLA scientists have been awarded grants totaling $49.2 million to take leading-edge stem cell science from the laboratory and translate it into new therapies for such devastating diseases as brain, ovarian and colorectal cancers, sickle cell and HIV/AIDS.

In all, 14 disease team grants totaling more than $250 million were awarded in October by the California Institute for Regenerative Medicine (CIRM), the state’s stem cell agency. To date, scientists with the UCLA stem cell center have been awarded 32 grants totaling nearly $122 million in state funding since 2005.

The UCLA grants include one awarded to a top researcher at UCLA’s Jonsson Comprehensive Cancer Center, Dr. Dennis Slamon. That grant focuses on developing novel drugs that kill cancer stem cells, which are believed to be the root cause of several different types of cancer. The two other scientists who received grants also are Jonsson Cancer Center members, but their grants focus on other diseases.

The four-year grants are part of CIRM’s Disease Team Initiative, which seeks to explore new ways of integrating and organizing the highest quality basic, translational and clinical research with the aim of developing new therapies and diagnostic tools. As part of the approval process, disease teams must submit an investigational new drug application to the Food & Drug Administration within four years, fast-tracking stem cell-related drug development.
Shared Resources Provide Leading-Edge Research Tools
Researchers at UCLA’s Jonsson Comprehensive Cancer Center have access to a remarkable array of tools that can aid in speeding discovery of newer and more effective ways to treat cancer.

Through the 10 shared resources provided by the cancer center, scientists can screen 100,000 compounds in a day, conduct clinical trials of promising, novel experimental therapies and conduct whole genome analyses using DNA microarrays.

“The cancer center leadership strongly believes it is important to provide access to technology that might not otherwise be available to our scientists,” said Harvey Herschman, director of basic research programs at the cancer center. “The idea of these shared resources is to supply a sort of one-stop-shopping for cancer center members, making it easier for them to do their science and making them more productive. That way, everyone doesn’t have to reinvent the wheel.”

Shared Resources include:
Biostatistics, Analytical Support & Evaluation (BASE) Unit
Director – Gang Li
Co-director – Robert Elashoff
This shared resource was established in 1994 to provide the highest quality biostatistical support to cancer-related research, including basic science, clinical and translational research and cancer prevention and control research at UCLA. BASE offers a group of highly regarded statistics faculty and staff with expertise in a variety of areas, including biostatistical methods for the design and analysis of clinical trials, survival analysis, longitudinal data analysis, imaging analysis, missing data and high-throughput data such as microarray data. Biostatisticians of BASE participate and help in all phases of cancer research, from study design in the planning stage, monitoring and implementing the study, to the analysis, interpretation and reporting of study results. BASE also develops novel statistical methodology when needed in cancer center studies. BASE Unit members develop various educational programs including courses, seminars and short presentations for investigators. BASE also provides and maintains the necessary computer equipment and software for computerized data analysis and management, for general biostatistical methodology and specialty areas such as pharmacokinetics, tissue array, microarray gene expression, clinical trials, imaging, repeated measures and survey methods.

Clinical Research Unit
Director – Dr. Sara Hurvitz
The Clinical Research Unit (CRU) Shared Resource provides administrative oversight of cancer center studies conducted both on campus and in the Translational Oncology Research International (TORI) network. Services to investigators include providing trained research nurses, coordinators, data managers and regulatory coordinators to conduct the clinical trials, with priority given to translational/institutional studies, followed by cooperative group, then industry-sponsored but under-funded innovative research. In addition, consultation services are available for new and/or junior investigators to develop clinical research protocols, review sponsored research and provide guidance in budgets and study logistics. Monitoring and auditing of investigator-initiated and sponsored studies is provided to ensure uniform scientific merit, patient safety, quality assurance and compliance. UCLA investigators collaborate with research institutions and health care providers across the United States in order to offer translational oncology research studies to patients in their own communities through the TORI network. Under the supervision of the CRU leadership, patients at TORI community locations can participate in the same high quality, leading-edge research studies that are available in our campus-based clinical trials program.
ES Cell/Transgenic Mice
Director – Dr. Hong Wu
Co-Director - Dr. Xin Liu
Co-Director - Meisheng Jiang
The mouse is the most useful animal model for most cancers, because it recapitulates the major features of human malignancies. Recent technological breakthroughs allow for mouse genome manipulation, such as removing, adding or changing a specific gene or installing a gene “on and off” switch in the genome, providing powerful tools for studying the causes and development of cancers in a living organism. This shared resource provides access to the latest technology for generating a variety of genetically modified animal models for research. One service provided is a transgenic service that generates animal models by introducing genetic information directly into the genome. The other service allows germ line manipulation via embryonic stem cells. The use of transgenic animals and of germ line manipulation for the creation of mutations has resulted in many mouse models for cancer research. The generation of mouse models that lack genes that encode proteins of oncological interest or tumor suppressor ability has proven to be a useful way of elucidating gene function in vivo. Transgenic mouse models, which have extra copies of either functional or dysfunctional genes, have provided important insight into the complex events contributing to cellular de-regulation and the loss of growth control that can lead to cancer. Animal model studies contribute greatly to the identification and characterization of proteins that contribute to the development of cancer.

Flow Cytometry
Director – Beth Jamieson
Manager – Ingrid Schmid
The flow cytometry shared resource allows researchers to count and examine cells and other particles suspended in fluid. Laser light is aimed at cells suspended in a focused liquid stream. Each cell scatters the laser light and fluorescent probes that are either directly bound to cellular components or are conjugated to reagents bound to cell structures excited by the laser light to emit fluorescence at a longer wavelength specific for the fluorochrome. The combination of scattered and fluorescent light signals is recorded by detectors and converted into images on computer screens. A special flow cytometer called a cell sorter not only analyzes cells, but also can physically separate cells which differ in scatter and fluorescent properties, allowing further study of the isolated sub-populations. Flow cytometry permits rapid analysis and separation of complex cell mixtures into cell populations with differing properties. The shared resource houses five analytical flow cytometers and three high-speed cell sorters with different color lasers to assist UCLA cancer researchers with their experimental needs. Equally as important as the state-of-the-art instrumentation are the consultation and training available. Staff members provide help with designing experiments and develop or adapt new flow cytometry methods. Classes in basic flow cytometry principles and hands-on training in running samples on the analyzers offer an opportunity for researchers to discover the potential of flow cytometry and acquire skills that serve them throughout their careers.

Gene Expression
Director – Dr. Stanley Nelson
Co-director – Dr. Christopher Denny
The Gene Expression Shared Resource offers whole genome analyses using DNA microarrays. Services include the ability to assess whether individual genes are on or off in cancers and other cell types. This data gives biologists critical information about which genes within the genome are active in a given process such as cancer. Microarrays are a powerful technology that allow millions of different probes to be designed throughout the entire genome so that every gene can be simultaneously assessed at a modest cost. The shared resource offers the ability to process these complex experiments with materials provided by scientists, expanding their arsenal of tools available to study cancer. The resource also offers microarray services that permit the entire genome to be assessed for DNA mutations critical in cancer formation, created by the mutation of an unknown number of genes that change a normal cell into a cancerous clone that grows, divides and spreads uncontrollably. Understanding the exact mutations that occur within the cancers provides key insights into how they develop and thus provides insight as to how to create novel therapies. The resource has recently implemented massively parallel sequencing that can simultaneously sequence every gene in individual cancers. The first cancer cell line completely sequenced was completed using the resource. These studies are revealing the fundamental basis of various cancers.
Informatics
Director – Dr. Arash Naeim
Associate director – Courtney Martin
Informatics is focused on supporting the cancer center in its effort to collect, process, share and use data electronically. Currently, a clinical trials management system, Velos eResearch, is being implemented. This electronic system allows for the central management of clinical trials study and patient information, providing real time tracking, auditing and resource management. The study and patient information managed are critical for required National Cancer Institute (NCI) annual reports. As the system expands, additional functionality will be incorporated to allow the cancer center to share clinical data collaboratively with the NCI and other cancer centers. This effort is part of a larger initiative to determine the best ways to electronically capture patient, treatment and specimen data. Other ongoing projects with some Informatics office involvement include deploying a new electronic medical record system, Varian, and implementing a tissue bank, Daedalus. In addition to developing collaborative relationships with industry-leading software companies, the Informatics group is working with the cancer center community and NCI to test new open source tools and share data in a national grid. Additionally, the Informatics group is supporting the development of electronic repositories of data for the Avon Cares for Life project, the UCLA Sarcoma Group and has just started on a University of California effort called ATHENA to advance treatment and research in breast cancer.

Molecular Screening
Director – Kenneth Bradley
Co-director – Robert Damoiseaux
The state-of-the-art molecular screening shared resource can screen as many as 100,000 compounds in a day, a manual process that used to take years. The compounds - small molecule drugs already approved by the FDA as well as purified natural products and fully synthetic molecules - come to UCLA from all over the world or are developed by UCLA chemists. Researchers can use the resource to test cancer cell lines developed in their laboratories. The researcher with the assistance of shared resource staff develops an assay, a procedure in molecular biology to test or measure the activity of a drug or biochemical compound in an organic sample, in this case the cancer cell lines. The cells are loaded into plates with 384 wells each and the drugs are added. After the assay is performed and success with a small library of compounds is achieved, up to 90,000 compounds can be screened against the cell lines in an effort to find one that may be developed into a cancer therapy. A computerized, robotic system executes the screening process, adding the compounds to the cancer cells. A robotic arm with an automated liquid transfer system places a miniscule amount of the compound onto plate containing the cancer cells. The cells are checked after 48 hours to see if any of the compounds showed activity. For more information on the shared resource, see this LINK.

Small Animal Imaging
Director – Harvey Herschman
Co-director – David Stout
A highly used shared resource on campus for cancer researchers is the small animal imaging center, which supports in vivo molecular imaging, primarily of metabolic function, using PET, CT, bioluminescent and fluorescent optical methods and autoradiography. Investigators have access to the equipment and protocols, as well as the expertise of the imaging center staff, who have worked together for more than 19 years. The ability to measure metabolism in mice and rats has been made possible through development of small animal imaging systems such as the microPET system, created at UCLA in the mid-1990’s. Optical imaging was also introduced very early after its development and has become a proven low cost, high-throughput way to observe tumor growth and treatment effect in living animals. The center also has pioneered ways to create a safe, pathogen free environment using gas anesthesia and temperature control to ensure animals are kept at near normal physiological conditions. The creation of reproducible ways to conduct imaging with minimal impact on the animals means that fewer experiments are needed and better data can be obtained through use of the same subject multiple times in the same experiment. Findings from research in the imaging center often are directly put into use in clinical settings to better measure and understand the mechanism of disease and treatment.
Shared Resources

Translational Pathology

Director – Dr. Sarah Dry  
Co-director – Dr. Jonathan Said

The translational pathology shared resource facilitates research using human cancer tissues with the aim of performing translational research. Most of this tissue, collected with a patient’s consent, is derived from leftover tissues after surgery and would otherwise be discarded. Researchers can then perform a wide variety of experimental modalities, including genetic testing, an essential part of cancer research. The tissues also are essential for research on specific tumor markers, which can be used to diagnose cancer, follow tumor progression and predict response to specific therapies. In addition to collecting tissues, the shared resource offers services related to the handling and processing of tissues. The pathologists and technologists providing services are specially trained and experienced with all aspects of tissue processing. It also offers state-of-the-art technology, including new methods to convert microscope slides into computerized images for sophisticated image analysis. Additionally, laser-capture micro-dissection enables researchers to extract small numbers of cancer cells from the specimen, which can be submitted for analysis. In addition, shared resource staffers are available for consultation regarding tissue procurement and processing. The shared resource also provides immunohistochemistry, a tool for studying cancer tissues to determine expression of markers that aid in understanding cancer biology, assist with cancer diagnosis and predict tumor outcome or response to treatment.

Vector Core

Director – Dr. Nori Kasahara  
Co-director – Christopher Logg

The mission of this shared resource is to facilitate basic and translational research by providing investigators with access to viral vectors, which are used to deliver genes into cells. The resource provides, at minimal cost, various retrovirus, lentivirus and adenovirus-based vector stocks expressing standard reporter genes for use in “gene-marking” experiments to trace the fate of specific cells, as well as a library of available pre-made vectors that already express various mammalian genes and corresponding inhibitory sequences. It also constructs and produces custom viral vectors that contain a specific sequence of interest for individual researchers and provides an educational and advisory resource to assist with safe use and handling of viral vectors, and with regulatory compliance and grant proposal submissions. Easy access to these technologies can facilitate and expand the scope of research activities, and provide ways for investigators to rapidly generate preliminary data. The shared resource also helps increase research productivity and assists in their efforts to understand the functional significance of specific genes during normal growth and development, to determine the contribution of specific genes to the pathogenesis or amelioration of malignant diseases, and to identify and validate novel therapeutic targets for conventional and genetic therapies.
UCLA’s Jonsson Comprehensive Cancer Center (JCCC) relies on philanthropic support to fuel its life-saving research. Donors contribute through the Jonsson Cancer Center Foundation (JCCF), the Cancer Center’s fund-raising arm and the single-most important vehicle for raising private funds for cancer research at UCLA. Gifts to the JCCF fund research to rapidly translate laboratory discoveries into improved cancer screening, treatment and prevention.

The JCCF is grateful to the thousands of individuals, foundations and organizations that make contributions to advance the JCCC’s research agenda. The JCCF recognizes donors who contribute $25,000 or more in one year in Gifts of Note.

**Spotlight: Events**
The Jonsson Cancer Center Foundation’s signature fundraising event, *Taste for a Cure*, brings together great chefs, wineries and entertainment in support of a great cause.

*(from left)*  
Gary Newman, JCCC Director Judith Gasson, Ph.D., Dana Walden, and Seth MacFarlane

Learn more at [www.tasteforacure.com](http://www.tasteforacure.com)

Since its inception in 2005, the annual Par for the Cure Charity Golf Classic has raised more than $450,000 for breast cancer research.

*(from left)* Dr. Dennis Slamon with JoAnn Esposito, Lanna Venturino and Brian Esposito.

**PerseVerance by Equinox**
A three-hour outdoor stationary cycle ride took place at Equinox Palos Verdes raising more than $23,000 to support highest priority cancer research.

Learn more about organizing your own event to benefit the JCCF.
Spotlight: Lifeline Connection
With annual contributions of $1,000 or more, Lifeline Connection members fund the Cancer Center’s most pressing needs, including early-stage research through seed grants. Individuals who join Lifeline Connection receive a members-only e-newsletter, invitations to the JCCF Board of Directors meetings, and recognition in the annual Honor Roll.

To make your own gift in support of research at the JCCC, visit www.cancer.ucla.edu/givenow or contact the Jonsson Cancer Center Foundation.

Other Ways to Support Life-Saving Cancer Research
Because 90 cents of every dollar the Jonsson Cancer Center Foundation raises supports cancer research at UCLA, you can be confident that your gift will make a difference in the fight against cancer. Here are a few other ways you can lend your support:

Become a fan of UCLA Fights Cancer on Facebook or connect with us on Twitter or YouTube.

Make a tribute gift: Honor a family member, favorite teacher or boss with a gift that is truly meaningful. Show your appreciation while demonstrating your commitment to an important cause.

Consider a planned gift, such as a bequest, that will benefit cancer research in the future.

Learn more at Ways to Give.

The End of Cancer Begins with Research