Cancer Center moves to Lorry I. Lokey Stem Cell Research Building

‘Designed to be a research thoroughbred’

The Stanford Cancer Center has a new home in the recently completed Lorry I. Lokey Stem Cell Research Building on Campus Drive and Welch Road. The 30,000 net square foot-space on the second floor of the building includes the Cancer Center’s administrative offices and accommodations for 12 investigators carrying out research relevant to cancer and stem cells.

The $200 million Lokey Building was funded in part by a $43.6 million grant from the California Institute of Regenerative Medicine (CIRM) and in part by the generous $75 million gift from Lorry I. Lokey, as well as gifts from other wonderful donors. It was designed to inspire and nurture scientific advances relevant to stem cell and cancer stem cell research that translate quickly from basic research to clinical application.

According to Chris Shay, manager of capital projects at the Stanford University School of Medicine: “This building was designed to be a research thoroughbred.”

The Lokey Building is at the heart of many facets of translational research at Stanford and integrates the resources of the Cancer Center.

The Lokey Building is at the heart of many facets of translational research at Stanford and integrates the resources of the Cancer Center as well as the Stanford Institute for Stem Cell Biology and Regenerative Medicine, and the Stanford Institute for Neuro-Innovation & Translational Neurosciences to promote collaboration, creativity and discovery.

Encompassing 200,000 square feet of floor space and serving about 550 occupants, the Lokey Building is the largest dedicated stem cell research facility in the country. The building includes 60 assigned “hotel benches,” where visiting investigators with interests in stem cell or cancer stem cell research can collaborate with others in the building for periods of one to three years. Other features include the highest ratio of laboratory support space to working space — with housing for large centrifuges, freezers, tissue culture rooms and more — compared with that of older research buildings in the School of Medicine.

The building also houses a dedicated tissue bank to store animal and human tissues, sophisticated flow cytometry and...
Clinical trials are essential to our ability to advance cancer treatments, yet they continue to be regarded with some skepticism by many patients who fear being the “guinea pigs.” In fact, clinical trials are subject to intense scrutiny, not only to ensure that they are safe, but also to ensure that they will identify the best treatments for the diseases in question.

An important role of the Cancer Center is to provide the resources, both structural and financial, that guarantee the best trials. Each proposed clinical trial is carefully evaluated by a committee that includes biostatisticians and basic and clinical scientists. Trials that do not meet the criteria of excellence are either not opened or subjected to revision. Our clinical trials team is an outstanding one, and we owe considerable thanks to Miriam Bischoff and her colleagues for their work.

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CANCER CENTER MOVES TO LOKEY STEM CELL BUILDING

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cell sorting capabilities to capture and analyze individual cells, a microfluidics core, an in vivo imaging core and a state-of-the-art animal research facility.

Each of the building’s 33 research laboratories is situated on the outside of the building, with ceilings that slope upward toward large windows to capture natural light. Lab benches are designed for flexibility, and electrical, gas and vacuum lines descend from above to allow researchers freedom to arrange their workspace. Interior linear equipment halls offer ample support space for freezers, centrifuges and other equipment.

The aesthetics of the building include a wide, open central staircase leading to large landings on the second and third floor, with comfortable seating areas overlooking the elegant hanging sculpture, Tre Stelle di Lapisazzuli by Dale Chihuly (see p 6). This space, as well as additional space at the ends of each laboratory group area, provides an opportunity for communication among scientists and trainees that will enhance collaborations.

The building’s location and exterior appearance were also carefully planned. The facility rests at one end of the Medical Promenade, which leads between the Center for Clinical Sciences Research and the Beckman Center toward the Clinical Cancer Center and the adult and pediatric hospitals. In addition, it brings the School of Medicine in closer proximity to the main Stanford campus, encouraging interactions among clinical investigators, scientists, engineers and others at Stanford.

An east-west pedestrian and bike path known as Discovery Walk connects the Lokey Building on one side and the sciences and biology quad on the other side of Campus Drive. The walk features historical highlights in medicine at Stanford. Stone benches in the gardens next to the walk carry images and quotes that amplify history with the human perspective. Taken together, these architectural and garden elements will connect past to present, highlight history and contemporary stories of Stanford students and faculty and provide a context for the histories of medical research at Stanford.

The location and design of the Lokey Building both contribute to the major mission of the Stanford Cancer Center, enhancing discovery and translation to improve the lives of cancer patients. ☝

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The new Nuclear Medicine and Molecular Imaging Clinic at Stanford that opened on Oct. 28, 2010, will help advance a new generation of diagnostic techniques for earlier detection and improved management of cancer and other major disorders.

The $25 million clinic combines state-of-the-art scanning technology with newly engineered imaging agents — sort of ‘molecular spies’ — that target diseased tissues. These scanners are based on single-photon emission computed tomography (SPECT) and positron emission tomography (PET), which measure bodily functions, such as blood flow, molecular receptors and sugar metabolism.

‘As newer technologies continue to evolve, some of the scanners will be replaced by technologies that are more sensitive and don’t involve ionizing radiation.’

In the hands of the imaging experts at Stanford, the scans can be used to detect miniscule evidence of cancer or other diseases.

“As newer technologies continue to evolve, some of the scanners will be replaced by technologies that are more sensitive and don’t involve ionizing radiation. This will include technologies such as fluorescence optical imaging and photoacoustic imaging,” said Sanjiv “Sam” Gambhir, MD, PhD, who heads the division of nuclear medicine at Stanford Hospital & Clinics and the Molecular Imaging Program at Stanford University School of Medicine.

“With these newer technologies, the imaging agents are not labeled with a radioactive atom. This will allow lower-cost solutions and, we hope, more accurate diagnostics for the earlier detection of cancer and management of cancer,” said Gambhir, who is also Virginia and D.K. Ludwig Professor for Clinical Investigation in Cancer Research, a professor of radiology at the School of Medicine and a leader of the Program in Cancer Early Detection and Molecular Imaging in the Stanford Cancer Center.

The clinic occupies 16,000 square feet on the second floor of Stanford Hospital. With several scanning rooms, laboratories, doctors’ offices and a central control room for technologists, it brings together important imaging and lab functions that were previously dispersed across the Stanford University

New clinic will help identify cancer at the molecular level
Medical Center. This consolidation means patients can have molecular imaging work done at one time and in one place, Gambhir said, and will likely speed up how quickly they learn about their diagnoses.

“The clinic is designed to serve patients as well as support clinical trials,” Gambhir said.

**NEW OPTICAL SCANNING TECHNOLOGY**

One of the planned clinical studies involves the use of optical scanners that can detect breast tumors using only light — not X-rays. Light has none of the side effects of radiation. Optical scanners use lasers to look for tumors by measuring how much light emerges from the other side of scanned tissue. The lasers also can be used to illuminate imaging agents that have been injected into a patient and designed to lock on to tumors.

Gambhir said he believes optical scanners will likely replace X-rays in the future as the preferred technique for mammograms. In addition, Gambhir and his team hope to use photoacoustic tomography to look for cancer in patients. This technique involves targeting tumors with lasers that lead to light absorption in the body and the production of sound waves.

**One of the planned clinical studies involves the use of optical scanners that can detect breast tumors using only light — not X-rays.**

“This method can give you excellent depth penetration,” Gambhir said. “The light can be very precisely targeted, but sound penetrates through tissue much better and gives you a better spatial resolution.”

**VALUE OF IN VITRO DIAGNOSTICS**

The scientists at the Canary Center at Stanford for Cancer Early Detection, which Gambhir also directs, will take advantage of the new clinic as they work on new methods to identify cancers and then translate their research into clinical trials and, ultimately, into general practice.

“The Canary Center and this new clinic will go hand-in-hand,” Gambhir said.

One promising area of research is in vitro diagnostics, in which samples of blood and tissue are scanned or otherwise tested at the molecular level and then compared with in vivo imaging — that is, real-time images of patients.

The big advantage of test-tube samples, Gambhir said, is that they can be obtained more frequently than a patient can be imaged.

“You can’t subject someone to PET or CT every couple of days, but a person can provide a blood sample every few days that we can analyze with new diagnostic tests,” Gambhir said.

This way, the progress of a disease can be closely followed, and physicians can better determine whether a particular treatment is working, he said.

“We think the future of early detection monitoring and patient disease management in general is a combination of in vitro and in vivo diagnostics,” he added. “It’s like a merger of pathology and radiology.” ◊

Based on an article by John Sanford, a writer at Stanford Hospital & Clinics.
'Art, in a variety of media and on all floors, reminds us all of the importance of interaction across disciplines, and that such creative interactions are going on in this place.'

— Irving Weissman, MD, Director, Stanford Institute for Stem Cell Biology and Regenerative Medicine

Building’s giant glass sculpture fitting symbol of creativity

When people walk into the Lorry I. Lokey Stem Cell Research Building for the first time, they cannot help but stop and stare, their eyes drawn upward to the imposing 2-ton, blue-glass sculpture by Dale Chihuly that hangs in the atrium. Spanning more than two stories, the chandelier, of Lapis Lazuli”).

The Chihuly sculpture was donated by My Blue Dots (http://www.mybluedots.org/), a nonprofit organization established by local philanthropist Sue McCollum. My Blue Dots supports both research in the areas of stem cell and cancer and artwork that

McCollum launched My Blue Dots after her own struggle with breast cancer. She was treated at Stanford by radiation oncologist Albert Koong, MD, who is one of the cancer researchers whose work has been supported by the foundation.

which glistens with gold when lit up at night, is called the Tre Stelle di Lapislazzuli (Italian for “Three Stars of Lapis Lazuli”).

“serve as inspiration for healing, hope and health for cancer patients and their families,” McCollum said.

(Pictured above) Detail of the Chihuly sculpture, which weighs 2 tons and is composed of 2,071 pieces of blue glass that glisten with gold when lit up at night.
McCollum launched My Blue Dots after her own struggle with breast cancer. She was treated at Stanford by radiation oncologist Albert Koong, MD, who is one of the cancer researchers whose work has been supported by the foundation. The genesis of the name My Blue Dots comes from the blue tattoos that serve as permanent guide marks for repeated radiation treatments.

Now that the Chihuly chandelier is in place, a search has begun for other works of art. A committee, which includes Irving Weissman, MD, director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine, will evaluate possible candidate pieces and reach out to those who wish to assist in their purchase, or to donate pieces to the building.

Such art will be symbolic of the creative process that the building is designed to foster, Weissman said.

“Art, in a variety of media and on all floors, reminds us all of the importance of interaction across disciplines, and that such creative interactions are going on in this place,” he said.

The concept for the chandelier was developed during the groundbreaking for the Lokey Building in 2008, when Weissman and McCollum had a conversation about Chihuly. They decided to ask Chihuly, whose multi-colored glass artworks are featured in permanent and temporary exhibits all over the world, to create a work of art, large or small, for one of a number of possible spots in the building. Ultimately, he agreed to create a central identifying sculpture for the atrium at the building’s main entrance.

My Blue Dots supports both research in the areas of stem cell and cancer and artwork that ‘serve as inspiration for healing, hope and health for cancer patients and their families.’

The 2,071 pieces of glass for the chandelier were blown earlier this year and carefully arranged on metal armatures in Chihuly’s studio in Seattle. The work was so large that it had to be hung in separate pieces. It was then taken apart, packed in 161 boxes and shipped to Stanford for final assembly. The finished work is 33.5 feet long and the lower tip dangles 13 feet above the floor of the atrium. Weighing 4,300 pounds, or roughly the same as a Hummer H3, the chandelier required a few structural modifications in the ceiling during the building’s construction to support its weight.

Chihuly said he was pleased to have been asked to create a work of art for the Lokey Building.

“Art, architecture and science all seem to work interchangeably with one another,” he said.

Based on an article by Christopher Vaughan, a writer for the Institute for Stem Cell Biology and Regenerative Medicine.
Dermatologist Jean Tang has forged a distinctive career path. As a physician and clinical researcher, she investigates novel treatments of non-melanoma skin cancers, particularly basal cell carcinoma (BCC), the most common cancer in the nation. Basal cell carcinoma rarely metastasizes (spreads), but it is still considered dangerous because it can cause significant local disease and disfigurement.

The multi-tasking Tang, who has MD and PhD degrees, is also a skilled basic researcher focused on translating laboratory discoveries, such as the identification of certain tumor signaling pathways important in cancer cell growth, into new therapies to treat skin cancer. In addition, she is a population-based researcher currently conducting groundbreaking studies to determine if vitamin D can prevent and/or treat melanomas and BCC in the United States, both of which are markedly increasing in incidence.

“I’m passionate about learning more about the effects of nutrition and a healthy lifestyle on cancer prevention,” Tang said.

The potential of Tang’s research on vitamin D as a chemopreventive for skin cancer recently was recognized by the Stanford Cancer Center with a Developmental Cancer Research Award of $50,000.

Through the Seed Grant Program, now in its fourth year, the Stanford Cancer Center stimulates the development of high-quality, multidisciplinary cancer research with direct application to cancer diagnosis, treatment or care. The Seed Grant program funds innovative research that does not fit neatly into established programs.

**Tang’s research was recognized by Stanford with a Developmental Research Award of $50,000.**

“Young, unconventional and innovative researchers may not receive adequate funding until they are able to publish preliminary study results,” said Beverly S. Mitchell, MD, director of the Stanford Cancer Center. “Even if these individuals have the potential to publish and receive funding, the system favors researchers working in an established area of study. The Seed Grant Program thus provides critical support to enable budding scientists and clinical investigators to launch their careers.”

**VITAMIN D AND SKIN CANCER**

Skin cancer affects over 1 million Americans a year. BCC occurs most frequently while melanoma is the deadliest type of skin cancer, carrying a poor prognosis in advanced stages. Over the past 40 years the incidence of both BCC and melanoma has increased dramatically, especially among young women.

Forty to 50 percent of Caucasian-Americans who live to age 65 years will develop a non-melanoma skin cancer, the majority of which will be BCCs. At present, there is no treatment other than surgery to prevent the growth of BCC lesions.

For some time, researchers have become increasingly interested in the cancer-preventing effects of vitamin D. Some studies have shown that vitamin D may reduce the risk of prostate, colon and breast cancer. In one preclinical study, Tang and her mentor, Erwin Epstein, Jr., MD, of the Children’s Hospital Oakland Research Institute, showed that vitamin D prevented growth of BCC tumors in mice. In another study Tang and Epstein found...
that men with higher levels of serum vitamin D have decreased odds of developing non-melanoma skin cancer. However, evidence from large, randomized-controlled trials of the effect of supplemental vitamin D on skin cancer risk has been lacking until now.

Tang’s Developmental Research proposal, titled “Vitamin D Plus Calcium for Prevention of Skin Cancer in Women,” will examine whether 36,282 women enrolled in the Women’s Health Initiative (WHI) who received vitamin D and calcium for seven years have a reduced risk for BCC and melanoma. Her collaborators are Marcia Stefanick, PhD, professor of medicine and co-director of the Cancer Prevention and Control Program at the Stanford Cancer Center, and David Feldman, MD, professor of medicine-endocrinology.

Stefanick noted that the “strengths of Tang’s proposal include its randomized study design [in the WHI, participants received vitamin D and calcium, or a placebo], a large number of incident BCC (900) and melanoma (170) outcomes that have been prospectively collected and detailed information on baseline demographic factors such as sun exposure and diet history.”

Stefanick, a renowned epidemiologist, was chair of the Steering and Executive committees for the Women’s Health Initiative from 1998 to 2005. The 15-year, multimillion-dollar WHI was established in 1991 to address the most common causes of death, disability and impaired quality of life in 161,808 postmenopausal women aged 50 to 79 years. Stefanick is currently the principal investigator of Stanford’s Women’s Health Initiative Center, which is following about 3,900 women, now between 60 and 90 years of age, who participated in the WHI diet, hormone or calcium/vitamin trials. Feldman is one of the world’s foremost authorities on using vitamin D as a treatment for cancer, especially prostate and breast cancer.

Funds from the grant will enable Tang to collect medical records from WHI participants who reported the development of a new skin cancer over the course of the seven-year trial. She will then review the medical and pathology records to ascertain diagnoses, prepare the data and perform basic statistical analyses. Thus, the Seed Grant Award will help Tang create a unique database containing extensive information on key environmental, dietary and hormonal factors important to skin cancer development.

“If higher vitamin D levels are shown to reduce BCC or melanoma risk, we will have found the first practical chemopreventive agent for BCC or melanoma, as it is safe and well tolerated at most doses,” Tang said.

REPURPOSING DRUGS TO TREAT SKIN CANCER

Another of Tang’s research interests is finding ways to block molecular signaling pathways in order to develop treatments for BCC. She is currently working with Philip Beachy, PhD, Ernest and Amelia Gallo Professor, to determine whether FDA-approved drugs that block a molecular signaling pathway called Hedgehog can be repurposed to stem the growth of BCC tumors. The Hedgehog signaling cascade plays a major role in fetal development and also in driving the development of BCCs in adults.

In the 1990s Stanford researcher Matthew Scott, PhD, professor of developmental biology and of genetics, discovered that a mutation in a gene called Patched, which is involved in the Hedgehog signaling pathway, causes Gorlin syndrome.

“I’m passionate about learning more about the effects of nutrition and a healthy lifestyle on cancer prevention.”
— Jean Tang MD, PhD

(Pictured above) Histology of basal cell carcinoma tumor from mice, stained with hematoxylin and eosin (courtesy of Jean Tang, MD, PhD).
Translating science into
treatment and prevention
of cancer

Miriam Bischoff, MS, MBA, was hired by the Stanford Cancer Center in 2003 to create an operational Cancer Clinical Trials Office (CCTO), as well as to help launch two important committees, the Scientific Review Committee and the Data and Safety Monitoring Committee. These committees are designed to ensure that the quality and safety of Stanford’s clinical trials are of the highest order. In the seven years since, Bischoff, now the Cancer Center’s Executive Administrative Director of Clinical Research, has spearheaded the creation of a highly effective system for developing and implementing cancer clinical trials.

The CCTO was originally headed by Branimir I. Sikic, MD, professor of medicine-oncology, to bring greater efficiency and speed to the process of initiating clinical trials for cancer patients. In 2004 George A. Fisher, MD, PhD, associate professor of medicine-oncology, became the faculty director and currently co-leads the CCTO with Bischoff, while Dr. Sikic has taken the position of Associate Director of Clinical Research within the Cancer Center.

Since taking on this challenge, Bischoff has developed a strong organizational structure, and initiated a strategy for growth and improved management of ongoing CCTO operations. As a result, despite being continually challenged by a growing burden of regulatory oversight, the CCTO has significantly reduced the time to implement new trials and expanded its services to investigators. In 2009, the CCTO staff oversaw budgeting and contracting for more than $11 million in sponsored studies and was responsible for more than 300 regulatory submissions. Of the 330 clinical trials currently open to accrual, 70 percent are conducted at the Stanford Cancer Center; 25 percent at the Lucile Packard Children’s Hospital; and 5 percent at the affiliated Cancer Prevention Institute of California (CPIC). More than one third of these studies have been developed from ideas by a Stanford or CPIC investigator.

Bischoff was the primary author of Stanford’s Data and Safety Monitoring Plan, displayed by the National Cancer Institute on its website as a model of how such plans should be developed. She was instrumental in founding and currently co-leads a coalition of eight California NCI-designated Cancer Centers addressing delays in insurance authorization for clinical trials participants. Bischoff is also a founding member of the Association of American Cancer Institutes (AACI) Clinical Research Initiative Steering Committee, which was created to provide a forum for sharing information and examining best practices that promote the efficient operation of cancer center clinical research facilities. The initiative was also formed to leverage the influence of the AACI cancer center network to advocate for improvement in the national clinical trials enterprise.

Bischoff considers one of her major contributions to be co-authoring the development of a plan that incorporates the CCTO into the new Freidenrich Center for Translational Research (FCTR). This state-of-the-art building, scheduled to open in 2012, will house up to 152 cancer clinical research personnel in addition to the clinical and translational research facility that will enable patients to get the most advanced treatments on clinical trials.

Among the CCTO’s other major accomplishments was the launch in September 2010 of a new, user-friendly search engine (http://med.stanford.edu/clinicaltrials/cancer-search.do) that significantly improves the ability of both physicians and patients to find appropriate cancer trials at the Stanford Cancer Center. Studies can be identified using one or more of the following terminologies: Keyword, Age
Group, Disease Type (incorporates “patient-friendly” terminology), Drug, Doctor, Trial Number, Study Phase and Recruitment Status.

Another CCTO website improvement is the availability to the public of flowcharts that demonstrate the number and priority of clinical trials open within any disease group. The charts are organized by Clinical Research Groups. Those trials that are open to accrual of new patients are clearly indicated within this chart: (http://med.stanford.edu/clinicaltrials/cancer-search.do).

Bischoff attributes the CCTO’s success to the support of the Cancer Center leadership and the 31 members of the CCTO staff and its leadership, including the senior leaders: Monique Bertrand, Business and Financial Manager; Deb Bouvier, OnCore Project Manager; Lee Doherty, EdM, Regulatory Manager; Nancy Mori, Cooperative Group Regulatory Specialist; and Cathy Kahn Recht, RN, MS, Research Nurse Coordinator. Bischoff and her team continue to work on initiatives to decrease the time it takes to open research studies and to implement improvements in clinical trial conduct that will further support the translational research mission of the Stanford Cancer Center.

Tang is now heading a clinical study using itraconazole in patients with BCC. Beachy, Kim and Epstein are her co-researchers on the project. The good news is that because oral itraconazole is already FDA approved, Tang has been able to treat 10 patients with the drug to try to shrink their BCC tumors. (A separate clinical study is under way in the Stanford Cancer Center to assess the benefits of itraconazole in prostate cancer.)

Normally, drugs that are new chemical entities first must undergo many years of safety and toxicity studies before they can be tested for efficacy in cancer patients. This is why “drug development is time-consuming and costly, on average taking close to 10 years and $800 million for a new drug to come to market,” Tang said.

“We can circumvent this delay and expense by repurposing FDA-approved drugs for new indications. We already have information about dosage and possible side effects, which should enable us to start clinical trials earlier,” she said.

These research findings may be a boon to patients and perhaps have positive implications for health care costs. Skin cancer imposes a huge burden on national health services, estimated at greater than $800 million per year in the United States.

Tang suggests that itraconazole could be used to treat or prevent BCCs in two clinical populations, patients with Gorlin syndrome and individuals with sporadic BCC tumors. She and her colleagues are also investigating other molecules that can be combined with itraconazole or applied topically to the skin to block the Hedgehog pathway.
(Pictured above) The 22nd Annual Bone Marrow Transplant Patient Reunion was held on the Dean’s Lawn on July 31, 2010. Of the nearly 1,100 people who attended the reunion, 330 had received blood and marrow transplantations at Stanford Hospital & Clinics (photo: Stuart Brinin Photography).