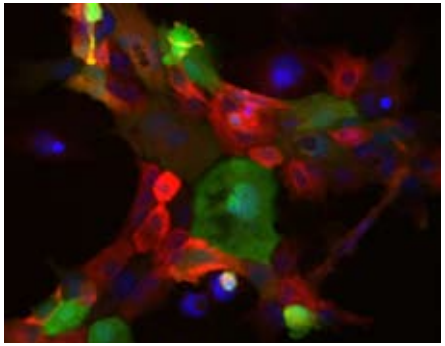
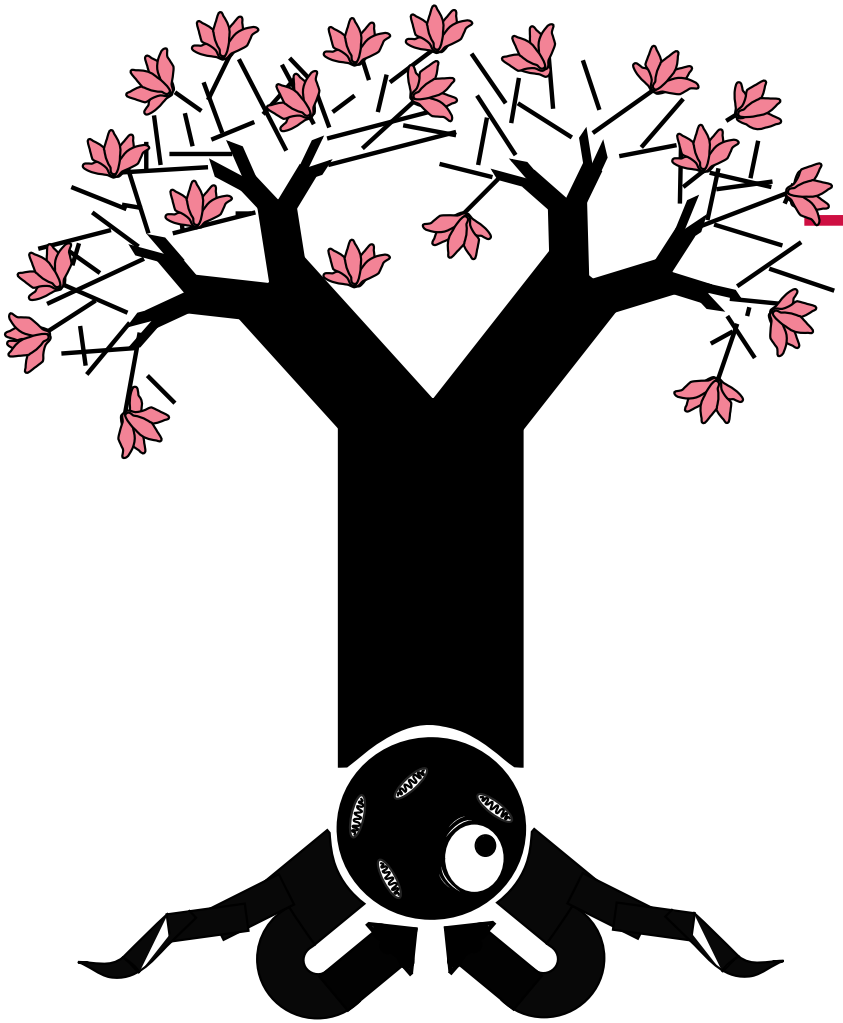



STANFORD MEDICINE | Institute for Stem Cell Biology & Regenerative Medicine

2009 Annual Report



Efflorescence

ef·flo·res·cence (noun) A state or time of flowering

Seven years ago, the Stanford Institute for Stem Cell Biology and Regenerative medicine was founded with a view toward understanding how stem cells function and using that information to repair and renew organs and tissues. We are now beginning to see that vision begin to blossom. Through the farsighted generosity of Lorry Lokey, as well as support from the California Institute for Regenerative Medicine, the new Lorry I. Lokey Stem Cell Research Building is now racing toward completion. Very shortly, researchers will be taking advantage of the building's advanced facilities.

We were also fortunate and gratified to have added three new faculty members to the institute: Marius Wernig, MD; Ravindra Majeti, MD, PhD, and Maximilian Diehn, MD, PhD. These young, distinguished researchers continue an impressive, ongoing expansion of the stem cell research program.

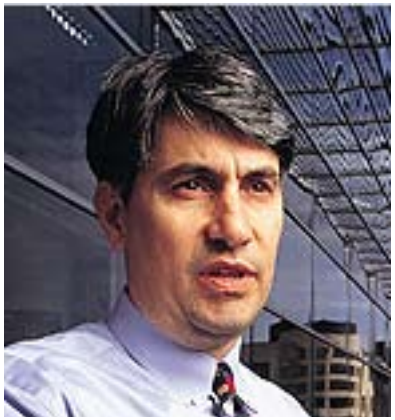
In the last year, institute faculty have been spearheading the creation of a doctoral program in stem cell biology. If ultimately approved by the university, this PhD program will be a significant recognition that stem cell biology is categorically different than developmental biology. Students from around the world have already exressed interest in such a program.

As the Stanford stem cell research effort grows and blossoms, we look forward to the fruits of our labors—clinical trials of therapies that are based on the knowledge we have cultivated in institute laboratories. The year 2009 has been a landmark in that regard: the California Insitute for Regenerative Medicine (CIRM) has awarded major disease team research grants to Stanford stem cell researchers who intend to guide research out of the laboratory and into clinical trials within the next few years.

People at the Institute

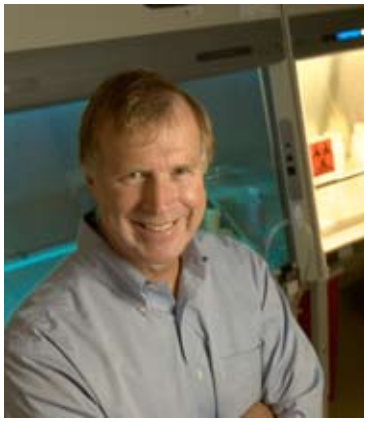
Irving Weissman, MD
Director
Director of the Ludwig Center for Cancer Stem Cell Research
Virginia and D.K. Ludwig Professor for Clinical Investigation and Cancer Research

Irving Weissman has directed the institute since its founding, providing vision and leadership to build one of the nation's top stem cell programs. In 1988, Dr. Weissman became the researcher first to isolate in pure form any stem cell in any species when he isolated hematopoietic or blood-forming stems cell in mice. He subsequently found the human hematopoietic stem cell, the human neuronal stem cell, and the human leukemia stem cell. His work has opened up an entirely new area of scientific research with enormous potential for life-saving therapies.



Michael T. Longaker, MD, MBA., FACS
Deputy Director
Director, Program in Regenerative Medicine
Deane P. and Louise Mitchell Professor

Michael Longaker has broad experience in pediatric plastic surgery, developmental biology, epithelial biology, tissue repair, and tissue engineering. He has extensive research experience in the cellular and molecular biology of extracellular matrix, with specific applications to the differences between fetal and post-natal wound healing, the biology of keloids and hypertrophic scars, and the cellular and molecular events that surround distraction osteogenesis with respect to craniofacial development. Most recently, his research has focused on multipotent mesenchymal cells derived from adipose tissue and their applications for tissue repair, replacement, and regeneration.



Michael F. Clarke, MD
Associate Director
Karel H. and Avice N. Beekhuis Professor in Cancer Biology

In addition to his clinical duties in the division of oncology, Michael Clarke maintains a laboratory focused on stem cells and the role they play in cancer. Dr. Clarke's research is aimed at the identification and characterization of cancer stem cells, and at increasing our knowledge of the factors that control self-renewal in normal stem cells and their malignant counterparts. Dr. Clarke was the first researcher to find cancer stem cells in a solid tumor (breast cancer) and discovered that the inhibition of programmed cell death is essential for the growth of breast cancers.

Renee Reijo Pera, PhD
Director, the Center for Human Embryonic Stem Cell Research and Education

Renee Reijo Pera focuses on understanding human embryo growth and development, and on characterizing the basic properties of human embryonic stem cells, especially their ability to generate pluripotent stem cells, somatic cells, and germ cells. Her early work resulted in identification of one of the first genes specifically implicated in human germ cell development. Subsequently, her laboratory has established techniques for differentiation of human embryonic stem cells to germ cells and genetic manipulation of the pathways.

Phillip A. Beachy, PhD

Phillip Beachy studies the function of Hedgehog proteins and other extracellular signals in morphogenesis (pattern formation) and in injury repair and regeneration (pattern maintenance). The Beachy lab studies how the distribution of such signals is regulated in tissues, how cells perceive and respond to distinct concentrations of signals, and how such signaling pathways arose in evolution. He also studies the normal roles of such signals in stem-cell physiology and their abnormal roles in the formation and expansion of cancer stem cells.

Marius Wernig, MD

Marius Wernig is interested in two major areas of stem cell biology. One focus is the epigenetic reprogramming of somatic cells into pluripotent stem cells, and this technique's translational applications for regenerative medicine. Another area of interest is the study of self-renewal mechanisms of mammalian neural progenitor cells, with the hope of identifying novel approaches to better understand brain cancer. Recently, he has published notable research on the direct transformation of skin cells into nerve cells.

Theo Palmer, PhD

The research of the Palmer lab examines how neural stem cells respond to cues in order to add and integrate new neurons into a functional circuit. Their studies of neurogenesis in the developing brain focus on the influence of maternal health or illness on fetal brain development. Studies of stem cells in the adult focus on the hippocampus, one of the few areas where neurogenesis naturally continues throughout life. The Palmer lab is now able to use human embryonic stem cells and non-embryonic induced pluripotent stem cells to generate several types of human neurons.

Ravindra Majeti, MD, PhD

Ravindra Majeti focuses on the molecular characterization and therapeutic targeting of leukemia stem cells in human hematologic disorders, particularly acute myeloid leukemia (AML). The Majeti lab is also interested in developing a similar characterization of normal human hematopoiesis and hematopoietic stem cells. A major focus of the lab is the identification of cell surface molecules preferentially expressed on leukemia stem cells and the development of therapeutic monoclonal antibodies targeting these proteins. Toward this goal, together with Irv Weissman, the lab is actively developing an anti-CD47 antibody for clinical trials in human AML.

Maximillian Diehn, MD, PhD

Max Diehn's research focuses on cancer stem cell biology and its implications for cancer therapy. He is interested in developing a deeper molecular understanding of cancer stem cells, including identifying pathways and genes important for their survival and self renewal. Additionally, work in the Diehn lab is aimed at overcoming resistance mechanisms to radiotherapy and chemotherapy in cancer stem cells. Dr. Diehn is a radiation oncologist and specializes in the treatment of lung cancer and stereotactic body radiation therapy.

Institute Membership

Members:

Beachy, Phil
Developmental Biology

Clarke, Michael
Medicine/Oncology

Diehn, Maximillian
Radiation Oncology

Longaker, Michael
Surgery/Plastic & Reconstructive

Majeti, Ravindra
Medicine/Hematology

Palmer, Theo
Neurosurgery

Reijo Pera, Renee
Obstetrics and Gynecology

Weissman, Irving
Pathology

Wernig, Marius
Pathology

Associate Members:

Altman, Russ
Bioengineering

Andreasson, Katrin
Neurology

Artandi, Steve
Medicine/Hematology

Attardi, Laura
Radiation Oncology

Axelrod, Jeffrey
Pathology

Baker, Bruce
Biology/Emeritus

Baker, Julie
Genetics

Barres, Ben
Neurobiology

Barron, Annelise
Bioengineering

Behr, Barry
Obstetrics and Gynecology

Berg, Paul
Biochemistry

Bergmann, Dominique
Biology

Blau, Helen
Microbiology & Immunology

Bogyo, Matthew
Pathology

Brunet, Anne
Genetics

Institute Membership

Butte, Atul
Medicine/Pediatrics

Calos, Michele
Genetics

Chang, Ching-Pin
Medicine/Cardiovascular Medicine

Chang, Howard
Dermatology

Chen, Chang-Zhen
Microbiology & Immunology

Chen, James
Chemical & Systems Biology

Cheng, Ivan
Orthopaedic Surgery

Clandinin, Thomas
Neurobiology

Cleary, Michael
Pathology

Cochran, Jennifer
Bioengineering

Cooke, John P.
Medicine/Cardiovascular Medicine

Deisseroth, Karl
Bioengineering

Elias, Joshua
Chemical & Systems Biology

Engleman, Edgar
Pathology

Feldman, Brian
Pediatrics

Ferrell, James
Chemical & Systems Biology

Fontaine, Magali
Pathology

Fuller, Margaret
Developmental Biology

Giaccia, Amato
Radiation Biology

Gonzalgo, Mark
Urology

Gozani, Or
Biology

Graef, Isabella
Pathology

Gurtner, Geoff
Surgery/Plastic & Reconstructive

Hanawalt, Philip
Biology

Heilshorn, Sarah
Materials Science & Eng.

Heller, H Craig
Biology

Heller, Stefan
Otolaryngology

Helms, Jill
Surgery/Plastic & Reconstructive

Hsu, Teddy
Obstetrics and Gynecology

Kennedy, Donald
Honorary Member

Khavari, Paul
Dermatology

Kim, Seung K.
Developmental Biology

Kovacs, Gregory
Electrical Engineering

Krasnow, Mark
Biochemistry

Kuo, Calvin
Medicine/Hematology

Levenston, Marc
Mechanical/BioMech Engineering

Liao, Yaping
Ophthalmology

Lipsick, Joseph
Pathology

Lowe, Anson
Medicine/Gastroenterology

Institute Membership

Lu, Bingwei
Pathology

Luo, Liqun
Biology

Malenka, Robert
Psychiatry & Behavioral Sciences

McConnell, Susan
Biology

Mitchell, Beverly
Medicine/Oncology

Nusse, Roel
Developmental Biology

Oro, Anthony
Dermatology

Pasricha, Pankaj Jay
Gastroenterology & Hepatology

Peehl, Donna
Urology

Penn, Anna
Pediatrics /Neonatology

Quake, Stephen
Bioengineering

Rando, Thomas
Neurology

Recht, Lawrence
Neurology

Reiss, Allan
Interdisciplinary Brain Science Research

Rosen, Glenn
Medicine/Pulmonary & Critical Care Medicine

Rutt, Brian
Radiology - Diagnostic

Sage, Julien
Pediatrics/Cancer Biology

Schnitzer, Mark
Biology & Applied Physics

Scott, Matt
Developmental Biology

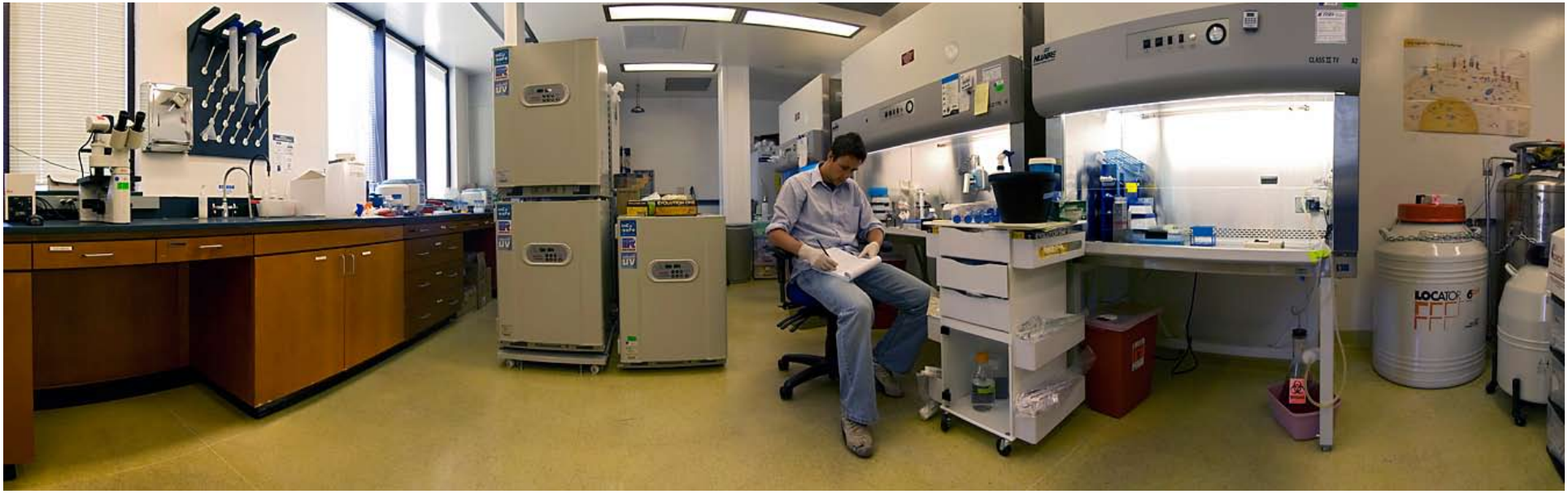
Shizuru, Judith
Medicine/ Blood and Bone Marrow Transplantation

Shortliffe, Linda
Medicine/Urology

Simon, Michael
Biology

So, Samuel
General Surgery

Institute Membership



Stearns, Tim
Biology

Steinberg, Gary
Neurosurgery

Sudhöf, Thomas
Molecular and Cellular Physiology

Sunwoo, John
Otolaryngology

Sweet-Cordero, Alejandro
Pediatrics/Cancer Biology

Talbot, William
Developmental Biology

Wandless, Thomas
Chemical & Systems Biology

Weinberg, Kenneth
Pediatrics

Wong, Albert
Neurosurgery

Wu, Joseph
Medicine/Cardiovascular Medicine

Wysocka, Joanna
Chemical & Systems Biology

Yang, Phillip
Medicine/Cardiovascular Medicine

Yock, Paul
Medicine/Cardiovascular Medicine

Siebel Scholars:

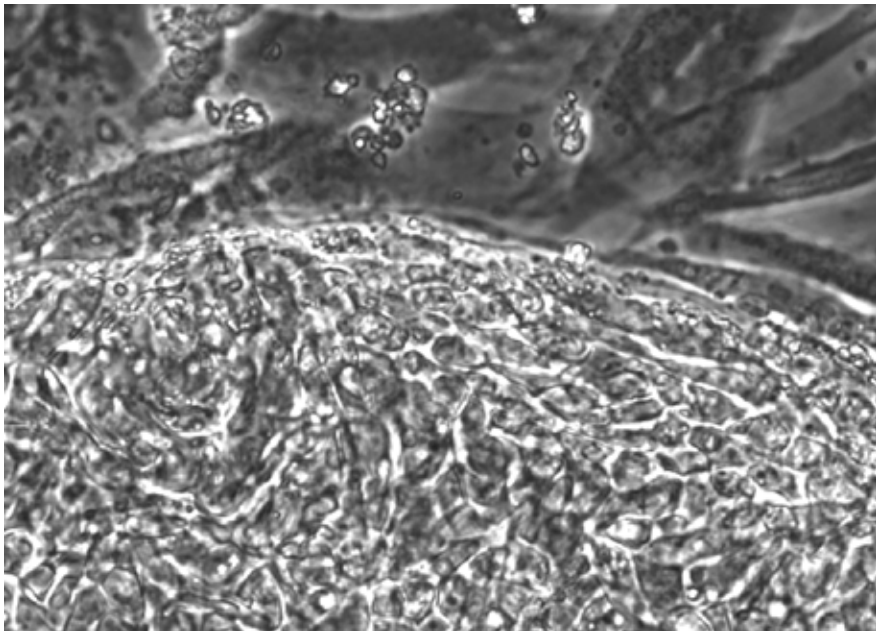
Luke Lee
Debashis Sahoo
Hiroo Ueno

Embryonic and Pluripotent Stem Cells

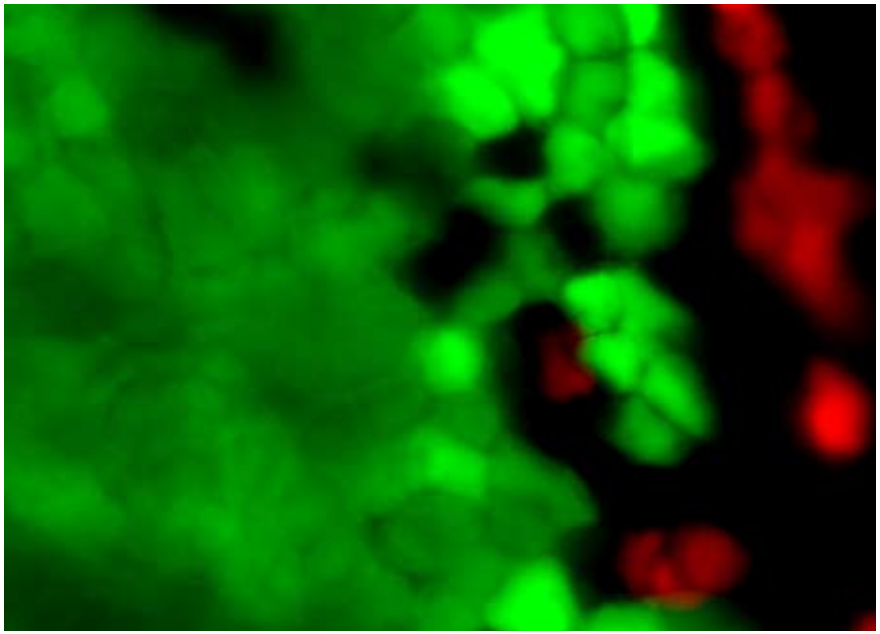
Understanding the Building Blocks of Life

Pluripotent stem cells--including totipotent embryonic stem cells--are the self-replicating cells that can give rise to all the specialized cells in the body. These cells are extremely versatile and can develop into any kind of organ or tissue, depending on their programming and the signals they receive from their environment. Understanding embryonic and pluripotent stem cells will likely provide the keys to creating therapies for new disease, repairing or replacing damaged organs, or solving problems in human reproduction. Because each cell type in the body can be created from stem cells, developing pluripotent stem cells may also reveal paths for creating tissue and organ-specific stem cells, many of which have yet to be discovered.

A colony of LSJ-1 stem cells



Stem cells labeled with fluorescent genes



The Center for Human Embryonic Stem Cell Research and Education

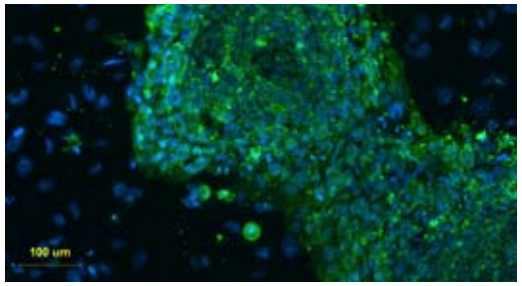
The Center for Human Embryonic Stem Cell Research and Education has become a powerful presence in the world of embryonic research because of its focus on human development. Although researchers around the world study embryonic stem cells from mice or other organisms, human embryonic stem cells can behave quite differently. The emphasis of the Center for Human Embryonic Research and Education is on research with human embryonic stem cells, as opposed to work in animal models, making the research highly relevant to the effort to create medical therapies from stem cell research.

Researchers at the center have had a highly productive year, publishing several notable studies.

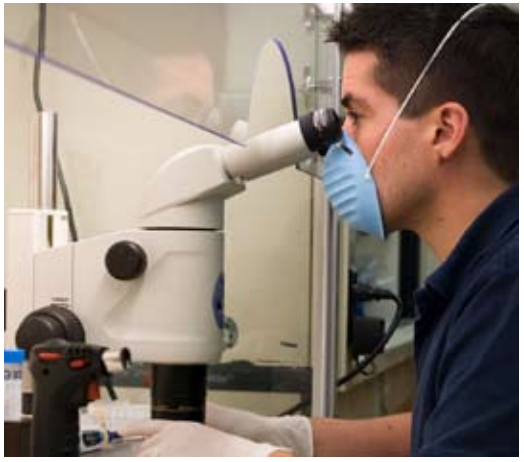
• In collaboration with the Stanford Photonics Center, researchers at the Center for Human Embryonic Stem Cell Research and Education have developed a valuable new method to predict the success or failure of human embryos in culture. Researchers have developed algorithms that predicted survival of the embryo based on light transmission. By using web cams inside an incubator, they measure light transmission through the embryos every five minutes, allowing them to calculate the rate of cell division without having to take the cells out of the incubator and thereby expose them to changes in lighting, temperature and oxygen levels.

• Scientists at the center discovered that cells very similar to embryonic stem cells can be created fairly easily from spermatogonial cells, the cells that normally create sperm. Further research may reveal such cells to be an easily accessible source of pluripotent stem cells.

Renee Reijo Pera, PhD



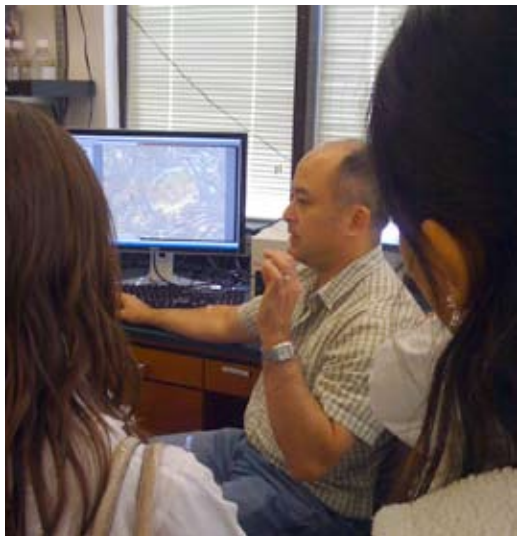
A colony of LSJ-1 stem cells



James Byrne, PhD

• Researchers at the center have devised a way to efficiently coax cells to become human germ cells—the precursors of egg and sperm cells—in the laboratory. Unlike previous research that yielded primarily immature germ cells, the cells in this most recent study functioned sufficiently well to generate sperm cells.

• The center has also taken part in several outreach efforts during the year, providing information about stem cell research to visiting high school science teachers and college students from Mexico.



Eric Chiao, PhD

Induced Pluripotentent Stem Cells

One of the most exciting discoveries in recent years was the finding that fully mature cells could have their genetic machinery reset to a nearly embryonic state through exposure to four specific factors. This technique has the potential to create pluripotent stem cells more easily and with more efficiency that with previous techniques. Furthermore, iPS techniques can be used to create stem cell populations that carry the disease-related genetic profiles of specific individuals, thereby providing a testing platform for understanding and treating those diseases.

Research Highlights:

• Researchers at the Center for Human Embryonic Research and Education received funding to create iPS cells from skin cells of Parkinson's patients, which should speed research on the disorder.

Sarita Panula, MS

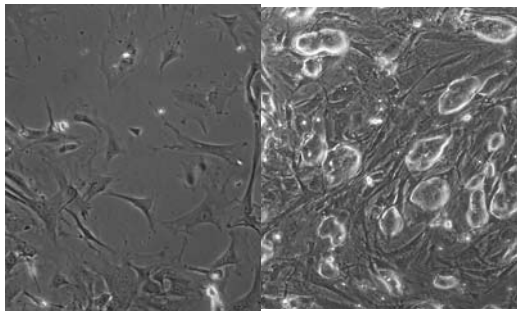
• The institute recruited one of the fast-rising researchers in the iPS field, Marius Wernig, MD, who came from the Jaenisch laboratory at the Whitehead Institute.

• Wernig and Co-PI Alfred Lane, MD were awarded $11.7 million from the California Institute for Regenerative Medicine to use iPS cell technology to research a therapy for epidermolysis bullosa, a painful and life-threatening blistering disease of the skin.

• Wernig discovered a new cocktail of genes that can convert mouse skin cells directly into neurons without passing through an intermediate pluripotent stage. This discovery opens the door to deeper study of many neurodegenerative and mental disorders, if the method is successfully applied to human cells.

• Stanford researchers discovered that fat cells left over after liposuction can be converted into pluripotent stem cells much more easily than other types of cells. Not only are researchers able to start with many more cells, but they can reprogram these cells much more efficiently. Fibroblasts (skin cells) must be grown in the lab for three weeks or more before they can be reprogrammed, but the stem cells from fat are ready for transformation without preparation.

• Wernig was awarded the 2009 Cozzarelli Prize for his finding that skin cells can be reprogrammed into neural precursor cells that, when implanted in the brain, would improve the symptoms of mice with Parkinson's disease. The Cozzarelli Prize is awarded each year for the best papers published in the Proceeding of the National Academy of Science during the previous year.



Fibroblasts

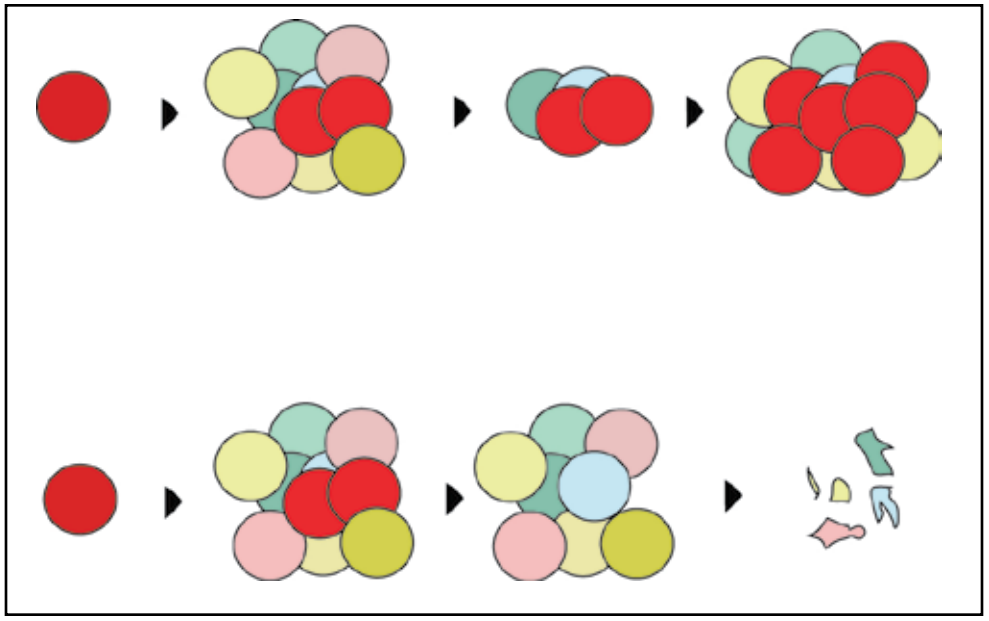
Marius Wernig, MD

Cancer Stem Cells

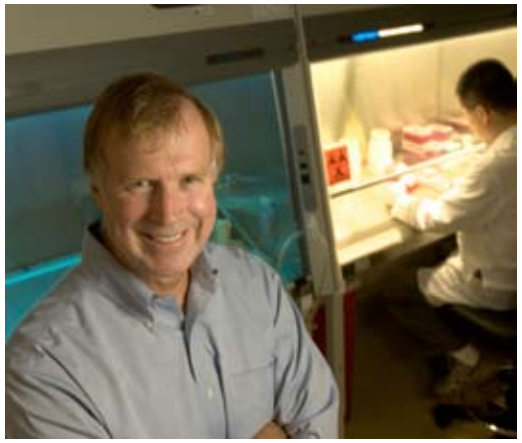
Attacking Cancer at the Root

The application of stem cell biology to cancer research is likely to have profound impact on for the future of cancer treatment. Researchers at the Institute for Stem Cell Biology and Regenerative Medicine are making progress on a number of fronts in understanding how cancer cells arise and spread, and in finding the cells' vulnerabilities that can be exploited in targeted treatments.

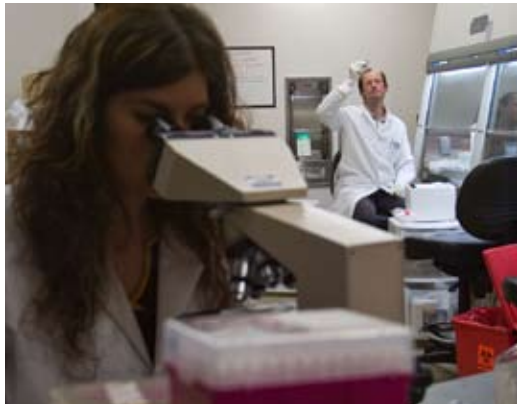
The cancer stem cell theory is that all cancers contain cancer stem cells that acquire or retain the self-replicating capabilities of stem cells, without the controls that usually regulate their growth. Just as stem



Two potential courses of cancer treatments, one (at top) in which cancer stem cells (CSCs, shown in red) are not targetted, and another (bottom) in which CSCs are specifically targetted. In the first case, failure to eliminate CSCs leads to a later resurgence of cancer. In the second case, when cancer stem cells are eliminated, the body's natural defenses may eliminated remaining cancer cells.



Michael Clarke, MD



Maider Zabala Ugalde, PhD
and Piero Dalerba, MD

cells are a minority of the cells in the body the cancer stem cells that initiate and drive malignancy can be a minority of the cells in a tumor or circulating in a myeloid leukemia. Effectively treating cancer requires attacking the cancer stem cells. Shrinking a tumor with drugs or beating back a leukemia will buy time, but curing a cancer likely will only come from destroying the cancer stem cells.

The institute has made significant progress in cancer stem research in 2009, due to the depth of experience in cancer this area and powerful collaborations with other Stanford faculty.

Max Diehn, MD, PhD

Research Highlights:

• Radiation is often used to combat cancer, but cancers frequently return after radiation treatment. Researchers Max Diehn and Robert Cho, in collaboration with Michael Clarke, discovered that cancer stem cells are resistant to irradiation because they have a higher concentration of specialized proteins that knock out the destructive small molecules created by exposure to radiation. Understanding how cancer stem cells resist radiation treatment may ultimately lead to therapeutic approaches that make cancers more vulnerable to the therapy.

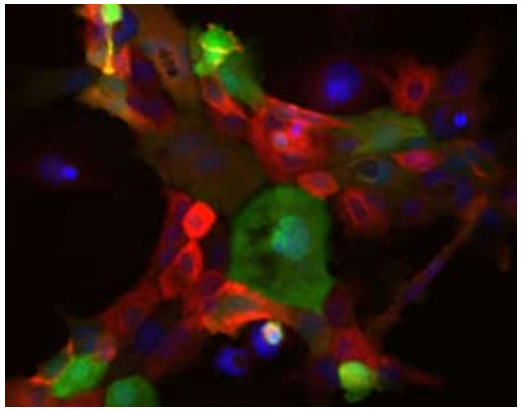
• Working in the Clarke lab, Bolaji Akala showed that three specific genes have a central role in limiting the expansion potential of multipotent progenitors in the hematopoietic pathway. This finding offers further insight into how hematological cancers may develop, and may point to better ways to prevent and treat them.

Bolaji Akula, PhD

• While in the Weissman lab, Ravindra Majeti (with students Mark Chao and Sidd Jaiswal) discovered that the cell marker CD47 is associated with more severe malignancy and worse outcomes in leukemia. The CD47 molecule is normally carried at low levels on normal blood cells and acts as a "don't eat me" signal to circulating macrophages. The theory is that immune mechanisms that would normally fight cancer cells are held in check by the presence of this molecular signal. When the CD47 molecule is blocked in mice that have human cancers, the cancer cells were more easily destroyed by the body's natural defenses. Weissman and Majeti are co-leaders of a CIRM-supported effort to bring CD47 antibodies to clinical trial, initially targeting acute leukemias.

Ravindra Majeti, MD, PhD

• Collaborations between the Weissman lab (including Jens-Peter Volkmer, Stephen Willingham, and Robert Chin) and other researchers has revealed the presence of high levels of CD47 in many other cancers. Work with Michael Clarke and Nelson Teng (OB/Gyn) showed a high expression of CD47 in ovarian cancer. High CD47 levels were found in breast and colon cancer through work with the laboratory of Michael Clarke. Work with Linda Shortliffe (Medicine) revealed the molecule's presence in bladder cancer. A collaboration between the Weissman lab (involving Tal Raveh and Siddhartha Mitra), and Griffith Harsh and Albert Wong in neurosurgery, showed that the molecule is present in glioblastoma. The presence of CD47 at high levels in medulloblastoma was revealed by research between the Weisman lab and Michael Edwards (Neurosurgery), Collaboration with Alejandro Sweet-Cordero revealed the presence of CD47 in Ewing's sarcoma. Collaboration between Alexander Boiko in the Weissman lab and Michael Longaker (Surgery), Susan Swetter (Dermatology), and Jan Matthijs van de Rijn (Pathology) revealed CD47 on melanoma cells. Research with Glen Rosen (Medicine) showed the presence of high levels of CD47 in lung cancer.

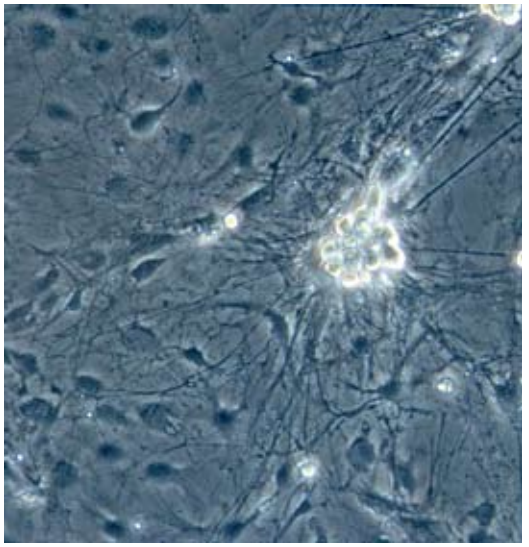


Breast cancer stem cells

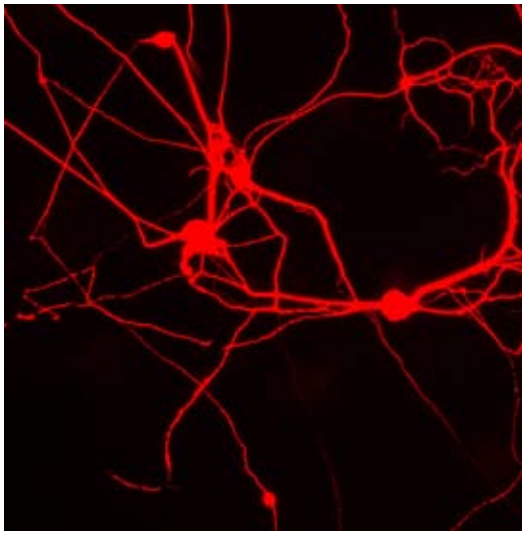
• In collaboration with the Weissman and Majeti labs, stem cell researchers have demonstrated that anti-CD47 antibodies can be effective in fighting leukemia. Ash Alizadeh and Ronald Levy in Oncology, working with Chao, Majeti and Weissman found that, in a mouse model infused with human Non-Hodgkins lymphoma cells, anti-CD47 antibodies and another drug led to complete remission in a large percentage of the mice.

• The Beachy lab, working with other researchers, showed that the growth and maintenance of myeloid leukemias require the activity of the Hedgehog gene pathway. The drug resistance and disease recurrence associated with imatinib (Gleevec) therapy might be avoided if a drug is developed to target this essential stem cell pathway.

• Researchers in the Clarke and Diehn labs discovered a common molecular pathway that is used by both normal stem cells and cancer stem cells when they reproduce. Clarke and his colleagues showed that breast cancer stem cells and normal breast stem cells lower the level of a specific group of cell signals when they are reproducing. Increasing the amount of a molecule called miR-200c strongly suppressed the ability of both cancer stem cells and normal stem cells to divide and reproduce.



Skin cells that have been converted to neurons



Neural cells from fibroblasts

Adult Stem Cells

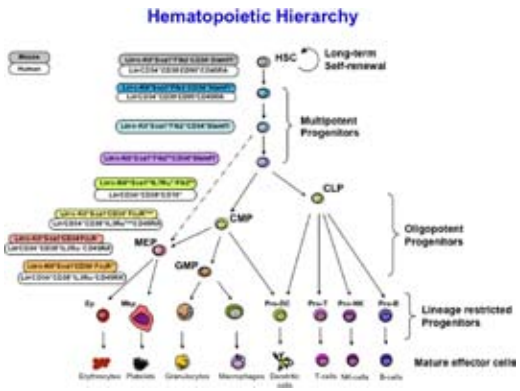
Studying the Framework of Future Therapies

Following their initial genetic programming, adult stem cells self-replicate to renew specific organs and tissues. When injury or illness occurs, these cells are key to restoring lost or damaged tissue. However, in some cases, adult stem cells cannot reproduce adequately, and many disease and disorders outpace the body's natural healing ability.

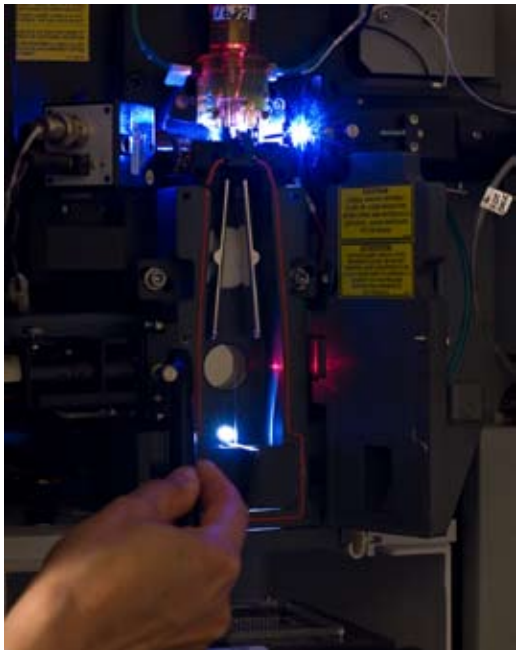
Learning how these cells operate will help us bolster our natural regenerative abilities. For example, Judy Shizuru, MD is working with the Weissman lab to develop clinical trials for the transplantation of pure, blood-forming stem cells. Such stem cell transplants may be used to repair the immune system in patients with Severe Compromised Immune Deficiency (such as the "Bubble Boy") and to stop an autoimmune attack in disorders such as childhood diabetes, mulitiple sclerosis, and lupus. Such transplants may also be used to end the need for lifelong immune supression among patients given kidney, heart, lung or pancreas transplants.

Judy Shizuru, MD

Sorting cells with the FACS machine



Blood cell differentiation



Inside the FACS machine

Research highlights:

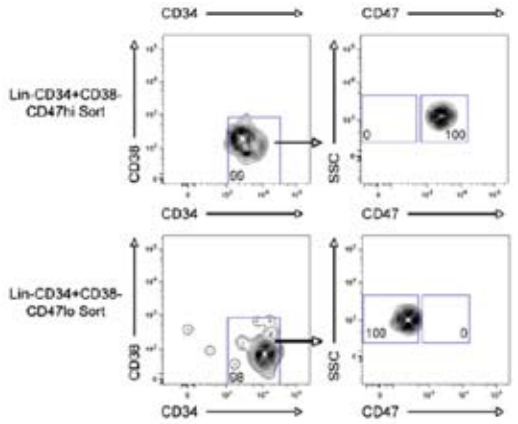
• Researcher Charles Chan in the Weissman lab created an artificial “niche” that attracted and nurtured stem cells in an adult animal. The research marked the first time that scientists have successfully recreated a functional stem-cell niche for further study. Weissman and his colleagues plan to use the model system to determine how the niche environment interacts with the blood forming stem cells to affect their development and fate, and how leukemias respond to these niches. They will also investigate the bone and cartilage healing capacity of these cells.

• Researchers in the Weissman lab are creating a detailed map of the path that blood stem cells take to become mature cells. The old diagram of blood development showed a simple fork between two cell types. The new research shows the complex paths along which blood stem cells develop as they grow to maturity.

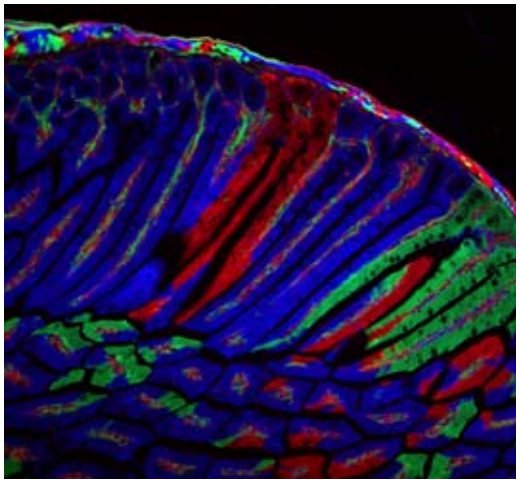
Interdisciplinary Collaborations

• Computer scientist and Siebel Scholar Debashis Sahoo, working with David Dill (Computer Science), Sylvia Plevritis (Radiology), and Jun Seita, Deepta Bhattacharya and Matt Inlay in the Weissman laboratory, has shown that Boolean search strategies can reveal the presence of completely new and unknown stem cell control molecules. Sahoo asks researchers to supply the names of two marker genes, one of which is expressed by a stem cell and one of which is expressed by a more differentiated or adult cell. Sahoo then uses Boolean searches of existing databases to find the genes that are transiently expressed in the same developmental pathway. Using this method, Sahoo has identified many new molecules and genes that are associated with stem cell development.

• Siebel Scholar and visiting scientist Hiroo Ueno, working with the Weissman lab, has developed two new technologies that trace developing stem cells from embryo to adult organism. By incorporating into embryonic stem cells the genes for proteins that encode red, green or blue fluorescent proteins and then implanting those cells in an early embryo, Ueno has shown how germ cells migrate and develop into adult reproductive organs. He also showed how various layers of the intestinal wall are produced from the earliest endodermic stem cells. Biochemistry deparment Chair Mark Krasnow and Kristy Red-Horse have used the method to define the embryonic origins of coronary arteries in mice.



Boolean searches of proteins



Intestinal wall, showing cell origins

Stephen Quake Introduces Technologies that Shake Up Cell Science

Technological innovation plays a large part in any scientific revolution. Part of the reason that Stanford has historically been at the forefront of stem cell science is that some of the technology that is critical to research efforts has been developed here at the university. For instance, the fluorescence-activated cell sorter, which allows researchers to isolate a relatively few cells of a certain type from millions of other cells, was invented at Stanford.

Now cancer stem cell research is benefiting from another technological innovation: microfluidics. Bioengineering Professor Stephen Quake, working with researchers Norma Neff and Luke Lee, has invented a system for doing complex biochemical experiments with single cells in microscopic channels inside rubber silicone wafers. The technology allows researchers to do chemical, genomic, proteomic and other analyses on hundreds or thousands of single cells at a time. Since understanding cancer means understanding cancer stem cells, it is important to be able to analyze the properties of those cells in isolation, so their particular characteristics are not lost in noise from cancer cells that are not cancer stem cells. Microfluidics technology allows researchers to do that sort of analysis on a very large scale.

Quake also developed a single-molecule sequencer that allows researchers to quickly and cheaply sequence large DNA molecules. Using the technology, Quake successfully sequenced his own complete genome with only $50,000 and a team of three people. Previously, sequencing a complete genome required over 200 people and at least $250,000. Recently, Quake and Neff teamed up with Weissman and Majeti to get the genomic sequences of acute myelogenous leukemia stem cells as well as genomic sequences of normals cells from the same patient.

Microfluidics chamber

Stephen Quake, PhD

Finances

The fragile economy made 2009 a difficult year financially for most organizations, both operationally and financially. Although the Institute for Stem Cell Biology and Regenerative Medicine was not immune to these difficulties, it has remained financially strong throughout the year. The promise of stem cell research is undimmed. It is generally recognized that the opportunities for dramatic medical advances are upon us, and donors have continued to make contributions to fund capital improvements. In addition, researchers have been awarded a number of large research grants that will broaden the institute's scientific program. Two key examples of this expansion are the three large CIRM grants aimed at moving stem cell therapies toward clinical trials.

We gratefully acknowledge the generous support of the following individual donors to the Lorry I. Lokey Stem Cell Research Building:

Anonymous
Joe Lacob
Laurie Lacob
Lorry I. Lokey
Regina and John Scully
Kat Taylor and Tom Steyer

Donor Profile: Lorry I. Lokey

Lorry Lokey, a native of Portland, Oregon, is a 1949 Stanford graduate. His degree in journalism and experience as editor of *The Stanford Daily* led to a job at United Press (later United Press International), one of the country's major wire services, and to other jobs in newspapers and public relations. He founded, and later sold, Business Wire, a highly successful wire service. In recent years, Lokey has focused on giving away the fortune he earned, and he has generously supported Stanford. Knowing how important philanthropy is for the institute has made Lokey an unwavering supporter since 2001. His generosity has led to the construction of the Lorry I. Lokey Stem Cell Research Building.

"The most important thing to me is that stem cells might not only extend life, but also improve the quality of life. I think stem cells will have applications across the entire lifespan."

—Lorry Lokey

• Three research teams at the Stanford University School of Medicine received $51.7 million from the California Institute for Regenerative Medicine (CIRM) to develop FDA-approved therapies within the next four years. The Disease Team Research Awards are designed to bring promising therapies more quickly to patients through the work of teams that include basic scientists, clinicians and industry.

--Institute Director Irving Weissman, co-principal investigators Ravindra Majeti, and Director of the Stanford Cancer Center Beverly Mitchell, along with partners in the United Kingdom, will receive $20 million to conduct coordinated basic research, clinical studies, and the development of pre-clinical therapeutics leading to a Phase II clinical trial of a leukemia stem cell-targeted antibody therapy for the disease. Weissman and Majeti are also members of the Stanford Cancer Center.

--Marius Wernig, Anthony Oro and Alfred Lane lead an international team that will receive $11.7 million to use stem cell therapy to treat a devastating genetic skin condition called epidermolysis bullosa, or EB. The team includes Howard Chang, Paul Khavari, Peter Marinkovich (all from Dermatology) and Seung Kim (from Developmental Biology). People with a version of the condition called dominant dystrophic EB suffer severe blistering and sloughing of the skin that is usually lethal by young adulthood. The team will use patient-specific induced pluripotent stem cells to correct the genetic defect that causes the disease.

--Gary Steinberg, professor and chair of the Department of Neurosurgery, heads a team focused on ischemic stroke. His team will collaborate with researchers from the University of California-Los Angeles. They will receive $20 million to investigate ways to use neural stem cells derived from human embryonic stem cells to ameliorate motor deficits that arise due to ischemic stroke.

• Renee Reijo Pera, Theo Palmer, and researchers at the Parkinson's Institute in Sunnyvale, California, have been given a $1.8 million grant to conduct research that may overcome a major bottleneck in Parkinson's disease research and drug discovery. The researchers were awarded the grant to develop induced pluripotent stem cells from patients who have Parkinson's disease. The iPS cells will be useful as a model system to allow researchers to study how Parkinson's disease develops in the first place and to test potential medications for the disorder.

Grants

• CIRM has granted Renee Reijo Pera and her colleauges a $5.7 million to share stem cell lab techniques and technologies. Anyone from a CIRM-funded institution can, without charge, sign up and learn basic techniques for creating and cultivating stem cells and induced pluripotent cells in the laboratory.

• The National Cancer Institute has awarded Michael Clarke, Irving Weissman, and Stephen Quake a $9.4 million grant to use innovative new technologies to identify cancer stem cell therapeutic targets.

• The National Heart, Lung and Blood Institute has granted Irving Weissman, Stephen Quake, and Ravindra Majeti $8 million to precisely map hematopoietic development in humans and mice and to share technologies with the team of Mark Krasnow and Pat Brown in Biochemistry in order to study the stem cells and progenitor cells of the lung.

• CIRM has awarded Michael Longaker a 3 year grant to train 16 young researchers in stem cell techniques and technologies.

• The federal government has provided a $1 million American Recovery and Reinvestment Act of 2009 Challenge Grant grant to Michael Longaker and Joseph Wu to study the derivation of porcine iPS cells and iPS-derived cardiomyocytes.

• The federal government has provided a $2 million American Recovery and Reinvestment Act of 2009 Challenge Grant grant to Michael Longaker, Irving Weissman, and Annelise Barron to study skull regeneration using biomatrix-encapsulated skeletal progenitors.

• Michael Longaker, Jill Helms, Roel Nusse, Joseph Wu, Theo Palmer, Howard Chang, and Anthony Oro were awarded a 3-year Early Translational Research Award to investigate Wnt to promote tissue regeneration.

• Renee Reijo Pera was awarded a CIRM Bridges to Stem Cell Research Grant to train students from San Jose State University, San Francisco State University and Humboldt State University in stem cell techniques.

The Lorry I. Lokey Stem Cell Research Building

A California Institute of Regenerative Medicine Facility

The Lorry I. Lokey Stem Cell Research Building rose from its foundations in 2009 and is now speeding toward completion. Construction is running on time and on budget, with building slated to be finished by summer 2010.

Providing 200,000 gross square feet of new space on four floors, the Lokey Stem Cell Research Building will be the largest stem cell research building in the world. It will house 33 laboratories and more than 500 scientists, students and fellows, along with core technologies and services to support their work. A conference center, which will include three meeting rooms and is centrally located on the first floor, will provide space for seminars, training, and other meetings.

The interior space promotes the concept of integrated neighborhoods of collaborative research. A notable innovation will be the creation of 60 collaborative guest benches where physicians and scientists from other programs at Stanford, or from other universities, can work side-by-side, further accelerating the process of discovery. Major efforts in every aspect of stem cell research will be headquartered in the building, including programs that aim to improve the understanding and treatment of genetic diseases like diabetes and birth defects, as well as cancer, neurological disorders, and cardiovascular diseases.

Atrium in the northeast corner of the building

The last piece of steel lifted into place

The building process has been given a boost by an advanced, three-dimensional system by which many pieces of the building are planned, designed and built off-site, and then brought to campus for installation. “We are building this like Boeing builds the 777,” according to Chris Shay, the Manager of Capital Projects for the building. “The system has dramatically cut down on the number of corrections we have to make at the job site.” Detailed, computer-based design also prevents costly construction conflicts. On most building projects, conflicts such as different pipes or ducts passing through the same space are only caught as the pieces are installed in the actual building, which requires a halt in construction while the builders, supervisors, and architects work out a solution. Problems like this can add tens of thousands of dollars to construction costs. With the Lokey Building, however, a computer spots conflicts long before construction occurs, and a small group of architects and builders is able to work out a solution quickly and easily.

North side of the building

Entrance to the northeast corner of the building

Arts at the Stem Cell Institute

Artwork will be an important part of the Lorry I. Lokey Stem Cell Research Building. From the beginning of the architectural design process, certain areas in the building were designated for the display of permanent or loaned artworks.

One highlight of the building will be a specially commissioned glass installation by Dale Chihuly. This dramatic piece, the creation of which was made possible through a generous gift from My Blue Dots, a non-profit founded by Sue McCollum to support cancer stem cell research, will hang in the atrium at the northeast corner of the building. The institute has established a group of "Friends of the Institute" to purchase and/or loan significant sculptures, paintings and photography, to be placed throughout the building.

Orange shading indicates areas designated for major pieces of art.

Artist's rendering of the Dale Chihuly sculpture

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