

Impact Report

THE ELI AND EDYTHE BROAD CENTER FOR REGENERATIVE MEDICINE AND STEM CELL RESEARCH AT USC



MARCH 2015



TABLE OF CONTENTS

Letter from the Director	5
Research	IO
Faculty	2 I
Core Facilities	26
Education	32
Communication and Outreach	38
Philanthropy	45

These mouse sensory hair cells (red) of the inner ear are showing symptoms similar to the human genetic disorder Cockayne syndrome, in which patients experience rapid aging and hearing loss. (*Image courtesy of the Segil Lab*)

LETTER FROM THE DIRECTOR

At the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC, discovery and translation underpin our research mission. In 2014, we have continued to accelerate our progress from laboratory bench to patient bedside.

Discovering the future of medicine

USC has laid the groundwork for clinical trials exploring stem cellrelated treatments for HIV/AIDS, Alzheimer's disease, the dry form of age-related macular degeneration, knee osteoarthritis and immune damage due to chemotherapy.

At our new Choi Family Therapeutic Screening Facility, investigators are testing up to 3,000 FDA-approved drugs a day on first-of-their-kind disease models that use reprogrammed and engineered cells directly from patients. Center researchers are exploring small molecule leads for amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease, and new screens will address a diversity of diseases, including cancer, deafness and bone fractures.

Building a world-class research team

Recent faculty recruits from Harvard University, Stanford University and John's Hopkins Medical School are enhancing our research and teaching programs, and forging new collaborations across USC's schools.

Dr. Megan McCain, a new faculty member in the USC Viterbi School of Engineering and our center, is devising new approaches to overcome the limitations of laboratory animals and traditional human cell culture, creating micro-scale mimics of human tissue. These socalled "organs on chips" provide new ways to study disease, develop new treatments and enhance the success rate of drugs moving into expensive clinical trials. Dr. Min Yu has succeeded in isolating rare and deadly circulating tumor stem cells that spread breast cancer to lung, bone and brain. The race is on to halt these cells in their circulatory tracks and to develop tailored therapies for individualized treatments.

Dr. Rong Lu is striving to improve bone marrow transplants, the first stem cell cure. An understanding of blood stem cell engraftment and expansion will provide predictive models to maximize the effectiveness of this lifesaving treatment.

Dr. Michael Bonaguidi studies rare stem cells in the brain's memory center that generate new nerve cells throughout life. These cells will provide new insights into a spectrum of neurodegenerative diseases, brain injuries, and mood and memory disorders.

Dr. Senta Georgia unites Children's Hospital Los Angeles (CHLA) with the center, pioneering new approaches to repurposing hormoneproducing cells in the intestine to replace those that are missing or non-functioning in diabetics.

The momentum continues: I look forward to recruiting two to three more faculty members in the coming year.

Leveraging investments

Our stem cell community extends beyond our laboratories. We are especially appreciative of the nearly 20 new Ambassadors for Stem Cell Research at USC, who have been inspired by the culture of innovation and outreach to join our efforts. The Ambassadors hail from all around the world and include leaders in medicine, venture capital, engineering and philanthropy.

Key gifts have ensured that USC's stem cell research center will continue to attract the best and brightest emerging talent. The USC Stem Cell Student/Postdoc Collaborative Challenge Grant Program, sponsored by our Ambassadors for Stem Cell Research at



USC, will provide seed funding for enterprising graduate students and postdoctoral fellows from multiple labs to enable their own development of mutually beneficial research partnerships.

Generous gifts from the The Broad Foundation and the Hearst Foundations launched USC Stem Cell's Society of Fellows, supporting exceptional senior and junior postdoctoral fellows. The first Broad Fellowship has already been awarded to Dr. Lori O'Brien, an exceptional postdoctoral research associate whose studies of kidney stem cells are unraveling the mysteries of kidney development to develop new regenerative therapies.

The Broad Foundation is also supporting innovative research projects and the center's state-of-the-art core facilities in imaging, therapeutic screening, flow cytometry, and stem cell isolation, culture and engineering. These facilities have an impact well beyond our center faculty, benefiting researchers across the entire university.

Fostering collaboration

Only by uniting researchers from across the disciplines can we translate our discoveries into cures. That's why the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research also serves as the heart of the USC Stem Cell initiative, uniting nearly 100 scientists, engineers and clinicians throughout the university and our stem cell colleagues at CHLA.

To advance the goals of USC Stem Cell, the Eli and Edythe Broad Innovation Awards at USC will award \$120,000 each to five innovative teams pursuing novel early-stage or translational projects. This critical seed support will then be leveraged to enable the research teams to compete for multi-year project funding from government and private sources.

To extend this spirit of team science even further, USC is hosting a Tri-institutional Stem Cell Retreat with our sister centers at UCLA



8

Andrew P. McMahon, PhD, FRS (Photo by Phil Channing)

and UCSF. Planned for May 2015 in Santa Barbara, the retreat will stimulate scientific discourse and enhance our external collaborative networks.

Training the next generation

Education and research are inseparable. Training the next generation of scientists is a must. This year, our Department of Stem Cell Biology and Regenerative Medicine has launched a revitalized PhD degree in Development, Stem Cells and Regenerative Medicine, and a firstof-its-kind Master of Science in Stem Cell Biology and Regenerative Medicine. I launched my own undergraduate course at the USC Dornsife College of Letters, Arts and Sciences in spring 2014. The center also continues to host a unique internship opportunity for talented high school students that is increasingly popular, and brings researchers from across the globe to our stem cell training courses.

USC's stem cell research center has also opened its doors to artists and scholars, many of whom have never before set foot in a lab. We recently invited students from the USC Roski School of Art and Design to find inspiration under microscopes, in petri dishes and in test tubes, and to bring their special design talents to energizing the center.

Another cross-disciplinary course challenged a small team of undergraduate students from the USC Viterbi School of Engineering to build a state-of-the-art optical projection tomography (OPT) microscope specially suited for imaging developing tissue samples. Nearing completion, the advanced 3D microscope will significantly enhance our imaging capabilities and will be integrated into the USC stem cell research center's Microscopy Core Facility.

In 2015, we will continue to break down boundaries between disciplines through a new undergraduate course about stem cells and science fiction. Dr. Gage Crump from USC's stem cell research center is leading spirited discussions about bringing extinct animals back to



life, conceiving embryos with three biological parents, and imagining a brave new future that currently only exists in literature, film and media.

In the years to come, USC will continue to shape our future as stem cell biology moves from discoveries towards cures.

Sincerely,

AP. Lettel

Professor Andrew P. McMahon, PhD, FRS
W.M. Keck Provost Professor of Stem Cell Biology and Regenerative Medicine, and Biological Sciences
Director of the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC
Chair, Department of Stem Cell Biology and Regenerative Medicine
Chair of the Executive Committee, USC Stem Cell

Discovering the Future of Medicine

RESEARCH

Mouse skeletal system (Image by Lick Lai, PhD/McMahon Lab)

RESEARCH

The Eli and Edythe Broad Center for Regenerative Medicine at USC has 47 active research and education grants, including 14 new grants and contracts awarded in 2014. Support from government, academic, industry and private foundations include:

- American Heart Association
- Donald E. and Delia B. Baxter Foundation
- Biogen Idec
- The Broad Foundation
- California Institute for Regenerative Medicine (CIRM)
- Margaret E. Early Medical Research Trust
- EVOTEC
- A.P. Giannini Foundation
- Harvard Corporation
- Hearing Health Foundation
- Hearst Foundations
- March of Dimes
- Merck Sharp & Dohme Corporation
- National Cancer Institute
- National Institutes of Health
- National Heart, Lung and Blood Institute
- National Institute of Arthritis and Musculoskeletal and Skin Diseases
- National Institute on Deafness and other Communicative Disorders
- National Institute of Dental and Craniofacial Research
- National Institute of Diabetes and Digestive and Kideny Diseases
- National Institute of Neurological Disorders and Stroke
- Rainwater Charitable Foundation
- Sanofi Pharmaceuticals
- USC Ming Hsieh Institute for Engineering Medicine for Cancer
- USC Stem Cell Regenerative Medicine Initiative
- Wright Foundation
- Zhongmei Group

Total grant and contract-based research funding for 2014: \$11,512,995

Collaborative, Disease-focused Research Teams Regenerative Medicine Initiative Awards

Carmen A. Puliafito, MD, MBA — dean of the Keck School of Medicine of USC — provided \$1.2 million in Regenerative Medicine Initiative (RMI) awards to three disease teams to take early steps towards stem-cell based therapies for certain forms of deafness, bone defects and pediatric leukemia. These awards are part of USC Stem Cell, the university-wide initiative in regenerative medicine spearheaded by Andrew P. McMahon, PhD, FRS, and led by the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC. The center continues to support these and other multi-investigator, multidisciplinary research collaborations to turn scientific discoveries into patient cures.

- Neil Segil, PhD, and Justin Ichida, PhD, from USC's stem cell research center are working with Takahiro Ohyama, PhD, and Radha Kalluri, PhD, from the Keck School's Department of Otolaryngology to eventually cure deafness. They have used cellular reprogramming to create inner ear cells, including sensory hair cells. The death of these delicate structures, which humans and other mammals cannot regenerate, is the most common cause of deafness.
- Gage Crump, PhD, and Francesca Mariani, PhD, from USC's stem cell research center are collaborating with Jay R. Lieberman, MD, surgeon and chair of the Keck School's Department of Orthopaedic Surgery, to discover new ways to repair human bones. They plan to tap into the potential of special cartilage cells that can transform themselves into bone-producing cells called osteoblasts. The research team hopes to show that these cells can heal severe bone damage more effectively than current therapeutic approaches.
- Gregor Adams, PhD, from USC's stem cell research center has teamed up with Fatih Uckun, MD, a professor in the Keck School's Department of Pediatrics who heads the translational research in leukemia lymphoma at the Children's Center for Cancer and Blood



Diseases of Children's Hospital Los Angeles (CHLA), to develop a new therapy for the most common form of cancer in children and adolescents, which is called B-precursor acute lymphoblastic leukemia. They are developing a new medicine to target a defective gene that results in the production of an abnormal form of the protein CD22, which causes cancer stem cells to proliferate and resist chemotherapy. To accelerate their progress, they're also working with Jianjun Cheng, PhD, an associate professor of materials science and engineering at the University of Illinois at Urbana-Champaign and an affiliate with the NCI Alliance for Nanotechnology in Cancer.

Human amniotic epithelial cells (Image courtesy of the Miki Lab)



Publications

The 17 faculty members at the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC, and in the Department of Stem Cell Biology and Regenerative Medicine published 54 papers in top journals, including *Nature, Cell, Cell Stem Cell, Developmental Cell, Development,* and the *Proceedings of the National Academy of Sciences (PNAS).*

Highlights

Brain, Nerves and Senses

Roberta Diaz Brinton, PhD, from the USC School of Pharmacy, USC Viterbi School of Engineering and Keck School of Medicine of USC and **Lon S. Schneider, MD, MS**, from the Keck School and USC Davis School of Gerontology are conducting a Phase I clinical trial for Alzheimer's disease. They are evaluating the safety and tolerable dosage of allopregnanolone, a natural brain steroid known to promote the generation of new brain cells, reduce amyloid levels and restore cognitive function in mice.

Michael Bonaguidi, PhD, from the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC is tapping into the potential of neural stem cells within the adult brain. These stem cells can generate more stem cells or form new neurons and supporting cells, offering a possible avenue for treating symptoms associated with Alzheimer's disease and other brain dysfunctions. *bonaguidilab.usc.edu*

Cheng-Ming Chuong, PhD, from the Keck School is researching how hair stem cells might reverse male pattern baldness. By plucking 200 hairs in a specific pattern and density, he can induce 1,000 replacement hairs to grow.

David Cobrinik, MD, PhD, from CHLA and the Keck School is growing 3D human eye structures from stem cells. This research is elucidating how the mutation of a tumor-suppressing gene called RB1 can lead to the formation of retinoblastoma, a childhood eye tumor.

"My approach is actually to learn what the brain can do and what it cannot do in terms of repair and regeneration, and to learn the lessons of what it can do, identify what it can't do and overcome those limits." —Michael Bonaguidi, PhD



David R. Hinton, MD, from the Keck School and **Mark S. Humayun, MD**, **PhD**, from the Keck School and USC Viterbi are putting retinal cells derived from stem cells into the eyes of patients with the atrophic, or dry type of age-related macular degeneration (AMD) in a Phase I clinical trial. The project is supported by nearly \$40 million in funding from the California Institute for Regenerative Medicine (CIRM).

Justin Ichida, PhD, from the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC is seeking treatments for amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease. His lab is testing FDA-approved drugs on neurons formed by reprogramming skin cells from patients with ALS. Although these patient-derived neurons display the disease's signature degeneration, the Ichida lab has already found several FDA-approved drugs that keep the neurons alive in the petri dishes — and might do the same in patients. *ichidalab.usc.edu*

Kris Kobielak, MD, PhD, from the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC is studying stem cell development into hair, skin, sweat glands and nails. This research can shed light for regenerative treatments for skin burns and certain forms of baldness, and may also help in understanding how some cancers form.

Wange Lu, PhD, from the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC is studying neural stem cell self-renewal and differentiation, pluripotency and somatic cell reprogramming. *wangelulab.usc.edu*

Neil Segil, PhD, from the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC aims to treat deafness through the regeneration of the sensory cells of the inner ear. His current research is focused on inner ear development, maintenance and sensitivity to noise, certain antibiotics and chemotherapy agents. *segillab.usc.edu*

Qi-Long Ying, PhD, from the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC is focusing on understanding how embryonic stem cells decide whether to self-renew or to differentiate. *yinglab.usc.edu*

Muscles and Skeleton

Ruchi Bajpai, PhD, from the Ostrow School of Dentistry of USC and the Keck School is addressing a congenital disorder known as CHARGE syndrome. She is studying the development and genetics underlying this disease by differentiating stem cells into the so-called "neural crest cells" that form many parts of the brain and face.

Yang Chai, DDS, PhD, director of the Center for Craniofacial Molecular Biology at the Ostrow School, is exploring a possible way to treat a rare congenital disorder that causes babies to have fused skulls that can't grow normally. Chai has found that the skull joints, known as sutures, contain a special population of stem cells that can help maintain and repair the skull.

Gage Crump, PhD, from the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC is using zebrafish to understand how faces develop and can be rebuilt following severe injuries. His findings are helping explain a variety of human craniofacial birth defects and providing novel insights into how to better stimulate bone repair in patients. *crumplab.usc.edu*

Scott E. Fraser, PhD, from the Department of Stem Cell Biology and Regenerative Medicine, USC Dornsife College of Letters, Arts and Sciences, and USC Viterbi has a long-standing interest in the imaging and molecular analysis of intact biological systems, and has been developing new technologies for novel assays. His current research centers on the high-resolution imaging of embryonic zebrafish and analysis of craniofacial development in avians and mice. He conducts this research at four shared imaging facilities: the Translational Imaging Center (TIC), the Center for Electron Microscopy and Microanalysis



(CEMMA), the Translational Biomedical Imaging Laboratory (TBIL), and the MRI Center. *fraserlab.usc.edu*

Francesca Mariani, PhD, from the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC is delving into the molecular control of normal skeletal development and maintenance. She focuses specifically on the role of growth factors on the development and regeneration of the mammalian skeleton. *marianilab.usc.edu*

C. Thomas Vangsness, Jr., MD, from the Keck School is planning a phase I/IIa clinical trial in which he will inject stem cells directly into the knees of 100 patients with osteoarthritis. The injections will contain a special population of adult stem cells called "mesenchymal stem cells (MSCs)," which have the ability to differentiate into bone cartilage, muscle, tendon and other connective tissues. These cells also help reduce inflammation, which often is the cause of pain. In a related study, Vangsness previously showed evidence that a single, high-dose stem-cell injection following arthroscopic meniscus knee surgery could provide pain relief and aid in meniscus regrowth.

Heart, Lung and Blood

Gregor B. Adams, PhD, from the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC is focusing on the hematopoietic stem cell niche in the bone marrow. In particular, he is examining how stem cells migrate to this niche, and either selfrenew or differentiate.

Paula Cannon, PhD, from the Keck School and her collaborators are genetically modifying blood-forming stem cells to cure HIV/AIDS. Along with principal investigator (PI) John Zaia and co-PI David DiGiusto from the Beckman Research Institute of City of Hope and Sangamo Biosciences, Cannon is a co-PI on a \$14.6 million CIRM grant funding this research. The approach is inspired by the "Berlin patient," a man cured of both HIV and leukemia through a bone marrow transplant from a donor with a gene mutation that confers natural immunity to HIV. In collaboration with Sangamo BioSciences, Zaia is the PI on an additional \$5.6 CIRM strategic partnership grant for the ongoing clinical trial portion of the project.

Ellen Lien, PhD, from CHLA and the Keck School is researching cardiac vasculature and heart regeneration after injury.

Rong Lu, PhD, from the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC is "barcoding" individual blood stem cells by labeling them with a genetic marker. This allows her to observe individual cells' contributions to forming blood, which could determine strategies for more effective blood transfusions or bone marrow transplants. *ronglulab.usc.edu*

Megan McCain, PhD, from the Department of Stem Cell Biology and Regenerative Medicine and USC Viterbi is pioneering "organs on a chip." To overcome the limitations of using laboratory animals or human cells in petri dishes to study human disease, McCain's laboratory engineers these dynamic micro-scale mimics of human heart tissue. *livingsystemsengineering.usc.edu*





Henry Sucov, PhD, from the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC is researching the cellular and molecular basis of cardiovascular development and the etiology of congenital cardiovascular defects, and addressing how these insights can be extended to regenerative therapies for adult heart disease. *sucovlab.usc.edu*

David Warburton, MD, from CHLA and the Keck School studies lung development and disease, which can have both genetic and environmental causes, such as smoking or pollution. He also researches infant mortality in Ulaanbaatar, Mongolia, which consistently tops the list of cities with the worst air pollution in the world.

Digestion and Metabolism

Senta Georgia, PhD, from the Department of Stem Cell Biology and Regenerative Medicine and CHLA is working to induce intestinal stem cells to make insulin by "turning on" key genes. The goal is to use these insulin-producing intestinal cells to treat diabetes. *georgialab.usc.edu*

Tracy Grikscheit, MD, from CHLA, the Keck School and USC Viterbi is growing small and large human intestines in the laboratory for the first time, supported by \$6.4 million in grants from CIRM. Her approach is relatively simple: take discarded human intestine from the operating room, break it up and put it on a felt-like, biodegradable tube in a special machine. Before long, this forms new intestine, which she hopes to reconnect to the digestive tracts of patients with injured or diseased intestine.

Toshio Miki, MD, PhD, from the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC is exploring how to make functional liver cells from stem cells, particularly placenta-derived stem cells. The long-term goal is to transplant these liver cells into patients.

Kidney and Urinary System

Andrew P. McMahon, PhD, FRS, director of the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC and chair of the executive committee of USC Stem Cell, is exploring the regulatory processes that construct, maintain and repair mammalian organ systems with a principal focus on the central nervous system, skeleton and kidney. *mcmahonlab.usc.edu*

Cancer

Valter Longo, PhD, from USC Davis is exploring the benefits of fasting, which inhibits the genes responsible for both aging and overall growth. Clinical trials are currently underway at the USC Norris Comprehensive Cancer Center, Mayo Clinic and elsewhere to explore whether fasting can improve outcomes in patients receiving chemotherapy for lymphoma as well as breast, prostate and colorectal cancers. He's also conducting a clinical trial exploring whether a five-day fast can stimulate stem cell-based regeneration of multiple organ systems.

"By understanding the unique biology of each individual patient's cancer, we can develop targeted drug therapies to slow or even stop their diseases in their tracks." —Min Yu, MD, PhD

Alan S. Wayne, MD, from CHLA and the Keck School works on immunotherapy for patients with the most common form of childhood cancer, acute lymphoblastic leukemia, or ALL. In a recent clinical trial, his team engineered patients' immune cells to recognize and attack leukemia, and two-thirds of the children experienced complete remission.

Min Yu, MD, PhD, from the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC and USC Norris Comprehensive Cancer Center recently isolated breast cancer cells circulating through patients' blood streams and kept these cells alive in petri dishes. She is using these cells to identify mutated cancer strains and the right drugs to target them — ushering in personalized treatments for breast cancer patients. *yulab.usc.edu*



Building a World-Class Research Team

FACULTY

Brain organoid derived from ALS patient stem cells (Image by Lisa Nguyen, Yaoming Wang and Angeliki Nikolakopoulou/Ichida and Zlokovic labs)

FACULTY

USC Stem Cell Affiliated Faculty

USC Stem Cell is a collaborative and multi-disciplinary effort working to translate the potential of stem cell research into the clinical imperative of regenerative medicine. The initiative brings together 93 research and clinical faculty members from across USC, including:

- Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC
- Keck School of Medicine of USC
- The Saban Research Institute of Children's Hospital Los Angeles
- USC Roski School of Art and Design
- USC Marshall School of Business
- USC Viterbi School of Engineering
- Ostrow School of Dentistry of USC
- USC Davis School of Gerontology
- USC Dornsife College of Letters, Arts and Sciences
- USC School of Pharmacy

Promotions

Henry Sucov, PhD, earned promotion to full professor, with a primary appointment in the Department of Stem Cell Biology and Regenerative Medicine.

His lab focuses on the cellular and molecular basis of cardiovascular development and the etiology of congenital cardiovascular defects, and addresses how these insights can be extended to regenerative therapies for adult heart disease.

Sucov serves as faculty director of USC's new Master of Stem Cell Biology and Regenerative Medicine program, and has been awarded the designation of "master teacher" by the Keck School. He has been recognized several times by the American Heart Association (AHA), and is a member of the AHA's Research Council. *sucovlab.usc.edu*



Recruitments

Rong Lu, PhD, is studying what makes one blood stem cell outcompete another, which has ramifications for improving bone marrow transplants and preventing blood cancers.

As a postdoctoral scholar at Stanford University, Lu came up with the idea of "barcoding" individual blood stem cells by labeling them with a genetic marker. This allows her to observe individual cells' behavior, interactions, self-renewal or differentiation, and contributions to forming blood.

"The most important reason I came to USC is the people here," said Lu. "The stem cell department is growing, and everybody's having new ideas and really being interactive and collaborative. You can feel the energy here." *ronglulab.usc.edu*

Min Yu, MD, PhD, is finding new cures for breast cancer. Recruited in conjunction with the USC Norris Comprehensive Cancer Center, Yu filters out circulating breast cancer stem cells from billions of other blood cells to understand how the disease spreads and stop it in its tracks.

If perfected, her technique could eventually allow doctors to use cancer cells isolated from patients' blood to monitor the progression of their diseases, pre-test drugs and personalize treatment plans accordingly.

"Our director Andy McMahon has a vision of uniting the bioengineering and medical fields, and applying basic science to clinical science," said Yu, who completed her postdoctoral work at Harvard University and Massachusetts General Hospital. "He's very passionate about helping young faculty start their labs and set up collaborations, so I'm excited to join." *yulab.usc.edu* **Michael Bonaguidi, PhD**, is studying individual neural stem cells within the adult brain. These stem cells have the potential to spawn more stem cells, or to form new neurons and their critical supporting cells, called astroglia. He is already collaborating with scientists at USC's Zilkha Neurogenetic Institute (ZNI) to explore the extent of these cells' natural regenerative capabilities following brain injury or disease.

To search for potential drugs that encourage neural stem cells to either last longer or make particular types of cells, Bonaguidi has joined forces with **Justin Ichida**, **PhD**. Ichida is leading the newly opened Choi Family Therapeutic Screening Facility, where scientists can test potential drugs on reprogrammed stem cells from patients.

"For me, I think the sky is the limit at USC," said Bonaguidi, who completed his postdoctoral work at Johns Hopkins University. "It's in a tremendous growing phase right now, and that's made very obvious by the substantial investment in stem cell research, neuroscience and imaging." *bonaguidilab.usc.edu*

Joint Appointments

Senta Georgia, PhD, a principal investigator at the Saban Research Institute of Children's Hospital Los Angeles (CHLA), recently earned a joint appointment in the Department of Stem Cell Biology and Regenerative Medicine.

Her research aims to induce intestinal stem cells to make insulin, a hormone that lowers blood sugar concentrations. The ultimate objective is to use these cells to treat both Type 1 and Type 2 diabetes.

"The things that could happen in my lab could some days be exhilarating, because I'm the only person in the world that knows this," said Georgia. "And we have a goal that we're working towards. We might really be interested in the science and the biology of it, but in the bigger picture, we are interested in helping people, and so that means a lot." *georgialab.usc.edu*



Megan McCain, PhD, a principal investigator in the Department of Biomedical Engineering at the USC Viterbi School of Engineering, also recently earned a joint appointment in the Department of Stem Cell Biology and Regenerative Medicine.

Recently named to the MIT Technology Review list of "35 Innovators Under 35," McCain uses tissue engineering to understand how diseases such as heart failure develop on the cell and tissue level. She constructs micro-scale mimics of human tissues, known as "organs on chips," that can enable researchers to screen drug toxicity using engineered human heart tissues on a chip. She has already created "hearts on chips," and will soon begin producing "kidneys on chips" in collaboration with **Andrew P. McMahon, PhD, FRS**, director of USC's stem cell research center.

"Due to tremendous advances over the last couple of decades in microfabrication, materials science, stem cell biology and imaging, it is really an exciting time to be a tissue engineer," said McCain. *livingsystemsengineering.usc.edu*

Awards and Recognitions

- Stem Cell Australia Visiting Scholar Award: Gage Crump, PhD
- Donald E. and Delia B. Baxter Foundation Faculty Scholar Award: Justin Ichida, PhD
- Powell Foundation Research Award: Megan McCain, PhD
- MIT Technology Review List of "35 Innovators Under 35": Megan McCain, PhD
- American Heart Association's 10 Top Cardiovascular Disease Research Advances in 2014: Gang Wang, MD, Megan McCain, PhD, et al. publication in *Nature Medicine*
- USC Ming Hsieh Institute for Engineering Medicine for Cancer Award: Min Yu, MD, PhD



Expanding State-ofthe-art Facilities

CORE FACILITIES



Kin-Chung and Amy Choi, philanthropists and lead supporters of the Choi Family Therapeutic Screening Facility (*Photo by Cristy Lytal*)



Supporter Lucia Choi takes a tour of the new screening facility. (*Photo by Cristy Lytal*)



Justin Ichida, PhD, director of the Choi Family Therapeutic Screening Facility (*Photo by Cristy Lytal*)

CORE FACILITIES

Established in 2006, the Eli and Edythe Broad CIRM Center for Regenerative Medicine and Stem Cell Research at USC is the hub for highly specialized technical expertise and equipment that promotes stem cell research throughout the university.

Choi Family Therapeutic Screening Facility choiscreening.usc.edu Opened March 2014

As part of USC's stem cell research center, the Choi Family Therapeutic Screening Facility officially opened in May 2014. The facility offers a "disease in a dish" approach to help scientists make more accurate predictions about which potential drugs will effectively treat disease before launching expensive and laborious human clinical trials.

The approach involves reprogramming patients' stem cells into their disease-affected cell types. This allows scientists to populate petri dishes with neural cells from patients with neurodegenerative diseases, inner ear cells from patients with hearing loss or balance disorders, and other cell types relevant to a wide variety of medical conditions. These "diseases in a dish" can then be used to test the effects of potential drugs on a patient's actual cells.

The facility comprises extensive chemical libraries, state-of-theart screening equipment and trained technicians — which support researchers across the university. A new automated high content imaging system (ImageXpress Micro System) was recently added to the facility.

This new facility will result in discoveries that will transform patient care in our lifetime.

Since the opening of the facility, there have been 11 investigators from six different departments/centers (USC's stem cell research center, the



USC Norris Comprehensive Cancer Center, the Zilkha Neurogenetic Institute, the Department of Microbiology and Immunology, the Department of Opthalmology, and the Department of Cell and Neurobiology) using the facility. Two complete screens were performed in the facility, and two others are ongoing.

Competition for free small molecule screens:

To encourage translational research at USC, Andrew P. McMahon, PhD, FRS, director of USC's stem cell research center, and Stephen Gruber, MD, PhD, MPH, director of the USC Norris Comprehensive Cancer Center, sponsored three screens at the new Choi Family Therapeutic Screening Facility. Three teams of USC stem cell researchers won the coveted prize — the opportunity to test thousands of drug candidates or chemicals for the potential to help patients.

- Gage Crump, PhD, and Francesca Mariani, PhD, two principal investigators at USC's stem cell research center, are testing a variety of chemicals to see which ones encourage cartilage progenitors to develop into "ossifying chondrocytes," a special type of cell that promotes bone growth. Such chemicals would hold promise for healing large fractures in patients.
- A team led by **Shou-Jiang Gao, PhD**, professor of Molecular Microbiology and Immunology at the USC Norris Comprehensive Cancer Center, is seeking new treatments for a group of tumors and cancers caused by Karposi's sarcoma-associated herpesvirus, or KSHV. His team has finished screening the entire library collection and identified several compounds that inhibit cancer cell growth but have no effect on healthy cells.
- A team led by **Amy S. Lee, PhD**, professor of Biochemistry and Molecular Biology at the USC Norris Comprehensive Cancer Center, is using the screening facility in their quest for potential drugs that affect the expression of GRP78, a protein that plays a major role in the growth of a wide variety of cancers, and the normal survival of neurons.

The group has finished its first round of screening and identified several compounds that might be used to treat cancer or slow neurodegenerative diseases.

Other successes to date:

• Justin Ichida, PhD, is testing FDA-approved drugs on motor neurons formed by reprogramming skin cells from patients with amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease. The Ichida lab has already found several FDA-approved drugs that keep the motor neurons alive in the petri dishes — indicating possible therapeutic benefit.

Human chemical induced pluripotent stem cell (iPSC) colony (*Image courtesy of the Ichida Lab*)





Circulating tumor cells isolated from the peripheral blood of a breast cancer patient (*Image courtesy of the Yu Lab*)



Mouse lung (Image by Gohar Saribekyan and Lisa Rutledge/ McMahon Lab)



Liver stem cells (Image courtesy of the Ying Lab)

Flow Cytometry Core Facility

flow.usc.edu

The Flow Cytometry Core supports 132 faculty from six USC schools: medicine, pharmacy, engineering, dentistry, gerontology, and letters, arts and sciences. The facility's 15 outside academic and industry clients include Caltech, CHLA, Western University, City of Hope, Chromologic, Deton Corp, Epeius Biotechnologies, Neumedicines, Novogenix and Sanguine Biosciences.

Several machines (Aria I and Aria II cell sorter, The MoFlo Astrios) received upgrades and repairs and are now in active service.

Microscopy Core Facility

microscopy.usc.edu

With initial funding from the Hearst Foundations, the Microscopy Core Facility is equipped with a wide range of cutting-edge microscopes, which allow researchers to study high-resolution cellular dynamics in diverse systems such as mouse embryos, living zebrafish and human stem cell cultures. Seventy-five active users from 40 labs used the Microscopy Core Facility last year. In addition, 13 new users were trained to use the confocal microscopes.

Stem Cell Core Facility

stemcellcore.usc.edu

The Stem Cell Core Facility serves as the center of excellence at USC for all uses of human embryo stem cells. The core provides researchers with the ability to generate patient-specific induced pluripotent stem cells and to genetically engineer these and other cell types. This facility offers comprehensive support and is a central hub for technical expertise, resources and state-of-the-art technology for researchers working with stem cells. Last year, the Stem Cell Core Facility offered 16 courses to 120 students, including 38 local high school students.

Training the Next Generation

EDUCATION

Stem cell-inspired oil painting by USC Roski School of Art and Design alumna Kristen Chen

EDUCATION

Department of Stem Cell Biology and Regenerative Medicine, Keck School of Medicine of USC

stemcelldept.usc.edu

With the transformative recruitment of chair Andrew P. McMahon, PhD, FRS, USC established a new Department of Stem Cell Biology and Regenerative Medicine, which is spearheading new multidisciplinary educational initiatives across the university.

Doctorate in Development, Stem Cells and Regenerative Medicine

pibbs.usc.edu

USC's stem cell research center is the home of a doctoral degree in development, stem cells and regenerative medicine. This unique program incorporates a re-vamped curriculum that emphasizes hands-on training, critical thinking about the literature and extensive laboratory experience working with embryos and stem cells.

More than 40 PhD students from the Keck School participate in this program, with support and partnership from affiliated faculty at CHLA, the Ostrow School of Dentistry, and USC's Biochemistry Department.

Master of Science in Stem Cell Biology and Regenerative Medicine

scrm.usc.edu

USC welcomed its inaugural class of more than 35 master's students to the first program of its kind in the United States with the goal of providing a deep education in stem cells and regenerative medicine to scientists, clinicians, policymakers, entrepreneurs and others in the field. The opportunities at this biomedical frontier attracted an accomplished inaugural class from all reaches of the globe — with two-thirds of the students from the United States and one-third from abroad. Many students have earned previous master's or medical degrees, and have gained prior research experience in the labs of top stem cell scientists. At USC, these students are pursuing course work in developmental and stem cell biology, human embryology, regenerative medicine, and the translational and therapeutic aspects of stem cell technology. They are also donning lab coats and gaining hands-on experience with stem cells. During an optional second year, selected students will be invited to further develop these lab experiences into independent research projects. The program will prepare graduates for applying to medical or PhD programs, entering the growing stem cell pharmaceutical or regulatory domains, or engaging in other academic, clinical or business efforts.

"Our goal is to train our students to become the select group of leaders who will chart the course of the medicine of the future — regenerative medicine," said Department Director Andrew P. McMahon, PhD, FRS.

Inaugural class of students in USC's Master of Science in Stem Cell Biology and Regenerative Medicine Program (Photo by Cristy Lytal)



Courses Offered at the Keck School of Medicine of USC Microanatomy Course in Medical Education

As part of a mandatory course for incoming first-year medical students, faculty from the stem cell research center lead a semester-long course in microanatomy to empower students with knowledge in cellular biology. In addition, several laboratories at the center host medical students and fellows for hands-on stem cell and regenerative medicine research.

Regenerative medicine seminars for each body system

In this innovative seminar series for medical students, a USC stem cell researcher teams up with a clinician to give an overview of each body system. This gives the next generation of doctors an awareness of the medicine of the future — regenerative medicine.

Undergraduate Courses

USC Dornsife College of Letters, Arts and Sciences From Stem Cells to Regenerative Medicine Taught by Professor Andrew P. McMahon, PhD, FRS

Nineteen students signed up for this new spring semester course, which focuses on the underpinnings of development, maintenance and repair of body systems from worms to man. Students discussed the critical experiments that frame the current view of animal organization, and the application of knowledge-gained to the goals of regenerative medicine. Students also read groundbreaking papers from the primary literature.

USC Viterbi School of Engineering

Microscope Design and Construction Taught by Seth Ruffins, PhD

This special one-time offering brought together a small crossdisciplinary team of undergraduate students from USC's Viterbi School of Engineering to build a state-of-the-art optical project tomography microscope for imaging biological samples. Students participated in all aspects of the microscope design, construction and verification, and learned how to work as members of a professional team. The advanced 3D microscope is now being integrated into the USC stem cell research center's Microscopy Core Facility, where it will enable stem cell researchers to better understand gene expression and tissue morphology.

USC Roski School of Art and Design

Advanced Drawing Advanced Ceramics Special Project and Design Art and Technology Taught by faculty from the USC Roski School of Art and Design

USC Stem Cell is partnering with the USC Roski School of Art and Design to bring art students into its laboratories. While scientists improve their ability to communicate with non-scientists, art students learn the beauty of science through hands-on research, creating stem cell-inspired works of art to cap their experience. To date, art students have produced a series of sculptures, paintings, animation and design installations inspired by USC's stem cell research center.



Students from the USC Roski School of Art and Design (Photo by Lillian McKibbin)



Training Courses

California Institute for Regenerative Medicine (CIRM) Bridges Training Grant

With support from a CIRM Bridges Training grant, USC Stem Cell hosted undergraduate and graduate students from California State Universities and city colleges. After a one-week stem cell laboratory training course, students were placed in laboratories to conduct research under the guidance and mentorship of principal investigators and postdoctoral students.

USC Early Investigator High School (EiHS) Program in Stem Cell Research and the USC CIRM Science, Technology and Research (STAR) Program

Thirty-eight local high school students spent their summer vacations in a very unusual place: USC's stem cell research center. Over the course of the summer, the high school students participated in either a 10-day training course or eight-week research internship, working hands-on with human stem cells in USC's world-class laboratories. Under the mentorship of USC faculty and graduate students, the students learned about the latest advances in regenerative medicine and explored stem cells, ethics and public policy. This year's participants were selected from Harvard-Westlake School, Lifeline Education Charter School, Chadwick School and Bravo Medical Magnet High School, and many received scholarships. On graduation day, the students shared their transformative summer experiences with their mentors, friends, parents and teachers by presenting scientific posters and by contributing articles to the program's new EiHS Journal, which published its inaugural issue this year. To date, 100% of past participants are pursuing a college education, and most of them intend to pursue careers in medicine or research.

Stem Cell Core Training Facility

Sponsored by a CIRM Core Facility grant, the Stem Cell Core Facility offers a broad range of educational services including technical protocols, one-on-one customized training and a week-long course covering human pluripotent stem cell culture techniques.

Engaging our Communities

COMMUNICATION AND OUTREACH

-

Community guests at Stem Cell Awareness Day. (*Photo by Cr<mark>isty Ly</mark>tal*)

COMMUNICATION AND OUTREACH

In 2004, the people of California created the California Institute for Regenerative Medicine (CIRM) to dispense \$3 billion in voter-approved dollars to fund stem cell research in the state. The public support of stem cell research through Proposition 71 as well as continued philanthropic and grant support has enabled USC's researchers to spearhead important new research programs and develop new therapeutic approaches.

Educating the public on our advances in regenerative medicine and stem cell research is central to our mission and vital for continued progress and support. To this end, USC's stem cell center hosted events, provided lectures to academic institutions, and utilized print, web and social media to engage our community in the advances in stem cell research.

Last year, USC's stem cell center was proud to host CIRM for several public events including:

- Meet the New CIRM President Reception, June 2014
- Stem Cell Awareness Day and Open House, October 2014
- CIRM's 10 Year Anniversary Media Event, November 2014



Local community guest at Stem Cell Awareness Day (Photo by Cristy Lytal)

Visit from General David H. Petraeus

As part of the Dean's Distinguished Lecture Series, David H. Petraeus, PhD, retired four-star general and former CIA director, visited the USC Health Sciences Campus in November 2014 to see for himself what the view is like on the front lines of the life sciences revolution.

Petraeus — who also serves as the Judge Widney Professor at USC and Chairman of the KKR Global Institute — started his morning at the Eli and Edythe Broad CIRM Center for Regenerative Medicine and Stem Cell Research at USC.

Center Director Andrew P. McMahon, PhD, FRS, and Screening Director Justin Ichida, PhD, welcomed Petraeus to the Choi Family Therapeutic Screening Facility, which is testing FDA-approved drugs on motor neurons formed by reprogramming skin cells from patients with amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease. Military veterans are more likely than civilians to suffer from this fatal disease.

Professor of Research Neil Segil, PhD, is collaborating with Ichida to apply a similar approach to hearing loss, which afflicts many who have served in the military. They've used cellular reprogramming to create inner ear cells which they will use to search for drugs that ameliorate hearing damage.

"This has to be the Delta force of health science campuses," said Petraeus.



Graduate student Kimberley Babos shows General Petraeus the Choi Family Therapeutic Screening Facility. (Photo by Steve Cohn)



Public Lectures and Presentations

USC's Executive Roundtable Group Andrew P. McMahon, PhD, FRS Paula Cannon, PhD Bob Klein, USC Stem Cell Ambassador and author of Proposition 71 San Francisco, California February 2014

South China University of Technology Alumni Association Qing Liu, PhD Los Angeles, California February 2014

University of Seoul Seoul National University Qi-Long Ying, PhD Seoul, South Korea May 2014

Inha University Hospital International Symposium Gage Crump, PhD Seoul, South Korea June 2014

California Club Justin Ichida, PhD Los Angeles, California July 2014 Long Beach USC Alumni Association Henry Sucov, PhD Long Beach, California July 2014

California State University RISE-MARC Program Senta Georgia, PhD Los Angeles, California July 2014

Keck School of Medicine of USC Alumni and Supporters

Dean Carmen A. Puliafito, MD, MBA Andrew P. McMahon, PhD, FRS San Francisco, California October 2014

Department of Biological Sciences, California State University, Los Angeles Andrew P. McMahon, PhD, FRS Los Angeles, California October 2014

Rotary Club of Santa Paula Justin Ichida, PhD Santa Paula, California October 2014 Additive Manufacturing Technology Research Institute Qing Liu, PhD NanSha, GuangZhou, China October 2014 California State University San Bernardino CIRM Bridges Program Senta Georgia, PhD San Bernardino, California November 2014

Ambassadors for Stem Cell Research at USC Andrew P. McMahon, PhD, FRS Bob Klein, USC Stem Cell Ambassador and author of Proposition 71 Los Angeles, California November 2014



Articles and Videos

USC Stem Cell website stemcell.usc.edu/news-archive	66 articles 14 videos 1 animation
External media outlets featuring	Forbes
USC Stem Cell news	Fox News
	Medical Daily
	Medical News Today
	NIH Research Matters
	CIRM's Stem Cellar
	Eurekalert
	Phys.org
	MedicalxPress
	redOrbit
	Futurity
USC Publications featuring	Trojan Family Magazine
USC Stem Cell news	Daily Trojan
	USC News
	Keck Medicine Magazine
	USC Norris Cancer Report
	HSC News
	Keck School of Medicine of USC
	Dean's Report

т

Web and Social Media Analytics

Keck School of Medicine websites broadstemcell.usc.edu stemcelldept.usc.edu	1,224,616 sessions 3,716,678 pageviews average session duration 00:02:22
USC Stem Cell website stemcell.usc.edu	22,883 sessions 55,837 pageviews average session duration 00:02:09
Lab websites bonaguidilab.usc.edu crumplab.usc.edu fraserlab.usc.edu georgialab.usc.edu ichidalab.usc.edu livingsystemsengineering.usc.edu marianilab.usc.edu mcmahonlab.usc.edu ronglulab.usc.edu segillab.usc.edu sucovlab.usc.edu wangelulab.usc.edu yinglab.usc.edu yulab.usc.edu	14,679 sessions 54,967 pageviews average session duration of 00:03:08
Core facilities websites choiscreening.usc.edu flow.usc.edu microscopy.usc.edu stemcellcore.usc.edu Master's program website	2,727 sessions 12,051 pageviews average session duration 00:03:04
scrm.usc.edu	15,808 pageviews average session duration of 00:03:25
USC Stem Cell Facebook facebook.com/uscstemcell	525 likes

Т



Leveraging Investments PHILANTHROPY

Zebrafish scales stained to show calcified structures (*Image by Camilla Teng/Crump Lab*)

PHILANTHROPY

Ambassadors for Stem Cell Research at USC stemcell.usc.edu/ambassadors-for-stem-cell-research

USC Stem Cell recruited nearly 20 Ambassadors for Stem Cell Research at USC. The ambassadors hail from everywhere — San Diego to San Francisco, Hawaii to Beijing — and include leaders in medicine, venture capital, engineering, real estate, wealth management and philanthropy.

In November 2014, USC Stem Cell's inaugural Ambassadors dinner in downtown Los Angeles featured special guest Bob Klein, author and architect of Proposition 71, the California Stem Cell Research and Cures ballot initiative. USC Stem Cell looks forward to hosting many more exciting Ambassador events in 2015.

Klein joined Professor Andrew P. McMahon, PhD, FRS, director of USC's stem cell research center, in providing an overview of past and present milestones in California stem cell research, including two USC-related, multi-institutional, state-funded clinical trials set to begin in 2015: a macular degeneration treatment that may prevent age-related blindness (pioneered by Mark Humayan, PhD, MD, and David Hinton, MD); and a genetic modification technique that may lead to the first cure for HIV/AIDS (innovated by Paula Cannon, PhD).

Following these remarks, guests discussed the economic impact of Proposition 71; the future applications of stem cell research for preventative medicine, treatment and cures; and the ripple effect of the California Institute for Regenerative Medicine (CIRM). CIRM is the catalyst behind 13 countries currently collaborating with California institutions, 2,500 peer-reviewed articles being published since 2004, and 10 human clinical trials initiated within 10 years.



As advocates and supporters, the ambassadors play a pivotal role in fulfilling the mission to revolutionize medicine through the discovery, translation and clinical application of stem cell research.

Through their support, USC Stem Cell has invested in new interdisciplinary, disease-focused research initiatives, promoted the careers of promising junior faculty and postdoctoral fellows, established new core facilities to find better drugs for debilitating diseases, and provided inner-city youth with hands-on laboratory experience.

Philanthropic Support stemcell.usc.edu/support

USC Stem Cell is deeply grateful for its philanthropic supporters, who gave more than \$2.75 million in 2014 to support core facilities, seed innovative research projects and promote education and outreach initiatives including our special high school educational program. Recent gifts from The Broad Foundation, the Hearst Foundations and the Choi family have had a tremendous impact on the center and university overall. These notable gifts helped launch the Broad and Hearst Fellowship Awards, the Eli and Edythe Broad Innovation Awards and the Choi Family Therapeutic Screening Facility, ensuring that the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC will maintain its leadership role in regenerative medicine and stem cell biology, inspire a new generation of investigators devoted to this crucial area of research and, most importantly, ensure that future patients reap the rewards of lifesaving cures that are the dreams of today and the realities of tomorrow.

Eli and Edythe Broad CIRM Center for Regenerative Medicine and Stem Cell Research at USC

1425 San Pablo Street Los Angeles, CA 90033-9080 323-442-1013 stemcelldev@usc.edu *stemcell.usc.edu*

