Seattle Children's

International Medical Services

西雅圖兒童醫院

國際醫療服務

Seattle Children's®
HOSPITAL · RESEARCH · FOUNDATION

Seattle Children's Is Ranked Among the Top U.S. Pediatric Hospitals

Seattle Children's, with more than 100 years of history, is consistently ranked as one of the nation's best pediatric hospitals. In 2012, U.S. News & World Report ranked Seattle Children's the sixth best pediatric hospital in the country. In addition to our overall ranking, we are highly ranked in the following specialties: cardiology and heart surgery, cancer and blood disorders, highly ranked bone marrow transplant program, neurology and neurosurgery, diabetes and endocrinology, gastroenterology and gastrointestinal surgery, orthopedics, pulmonology and neonatology. Seattle Children's has received world-class recognition for the craniofacial center and reconstructive pelvic medicine program.

What Sets Seattle Children's Apart

- Patients and families come to Seattle Children's from more than 70 countries to get superior care — many for complex or rare conditions.
- At Seattle Children's, doctors in nearly 60 pediatric subspecialties collaborate to provide the most advanced inpatient and outpatient diagnostic, medical, surgical and rehabilitative services.
- We are a teaching hospital for the University of Washington (UW) School of Medicine, which has one of the top 10 pediatrics programs in the country. Many of our doctors are UW professors.

This fantastic wood and glass sculpture, suspended in the Ocean Zone atrium, celebrates Pacific Northwest wildlife.

Each of the hospital's four zones — Forest, River, Mountain and Ocean — has original artwork to brighten the hospital experience.

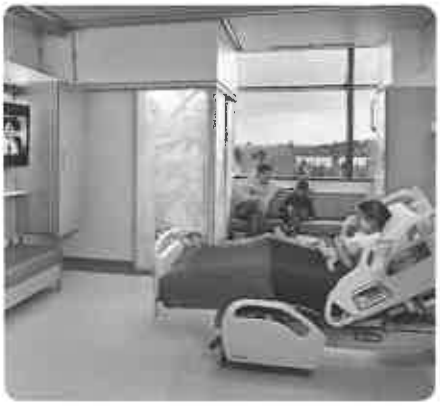
Seattle Children's state-of-the-art main campus covers 25 acres in the Laurelhurst neighborhood of Seattle, Washington. We have another 37 regional sites across four states and a large research institute that's a top recipient of National Institutes of Health funding.

西雅圖兒童醫院躋身美國頂級兒科醫院

擁有一百多年歷史的西雅圖兒童醫院，是全美最佳兒童醫院之一。根據《美國新聞與世界報導》雜誌，2012年我院被评为排名全美第6位的最佳儿童医院。 本院排名前茅的还有心臟內科和心臟外科，癌症治療專科，血液疾病，特別是骨髓移植医疗，腎臟病專科，泌尿外科，神經科和神經外科、糖尿病和內分泌科、胃腸病科和胃腸道外科、骨科、呼吸道科和新生小兒科。我們也擁有世界級的顱面整形外科及重建骨盆醫術专科。

西雅圖兒童醫院成為佼佼者的原因

- 世界各地70餘國的患者和家屬來到西雅圖兒童醫院接受卓越的醫療就诊与康复服务， 其中許多是複雜或罕見的病例。
- 在西雅圖兒童醫院，有近60多種兒科專科的醫生，专家通力合作，提供最先進的住院和門診医疗服务和診斷、內科、外科和復健服務。
- 本院是華盛頓大學(UW)醫學院的附屬醫院，擁有排名全美前十名的兒科专业。本院有很多醫生都是華盛頓大學的教授。

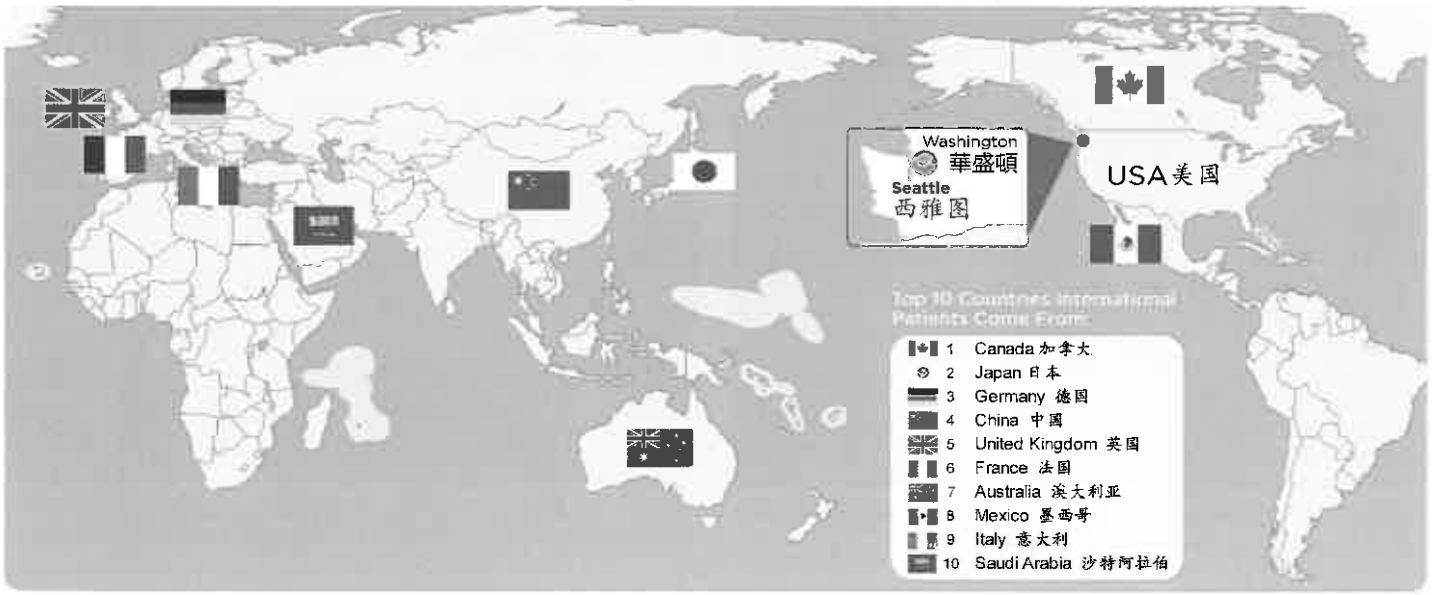


Patient room in the Cancer Care Unit of the new Building Hope addition.

The outdoor bamboo garden offers a place for quiet conversation and contemplation.

This is just one of Seattle Children's many state-of-the-art research facilities.

Seattle Children's is trusted by families from all over the world.



Seattle Children's Heart Center
Covering the Entire Spectrum of Cardiac Care

Seattle Children's Heart Center provides expert care for the full range of cardiac needs, from arrhythmia to acute issues requiring surgery or transplantation.

Catheterization
As a leader in interventional catheterization, we're developing new devices to help treat heart problems like septal defects and stenotic valves using less invasive alternatives to open heart surgery. We also perform electrophysiology studies and transcatheter ablation in our state-of-the-art cardiac catheterization labs.

Surgery
Our heart surgeons perform more than 500 operations a year, from straightforward repairs like closing a hole in the heart to the highly complex Norwood procedure for hearts with too few chambers.

Recent Seattle Children's Heart Center Innovations
- Using hybrid procedures that combine cardiac surgery with interventional cardiology to better serve patients with congenital heart defects
- Offering the latest pediatric ventricular assist devices and mechanical heart pumps designed for critically ill patients who are waiting for a heart transplant, including the Berlin Heart, CentriMag centrifugal pump, HeartMate II and SynCardia Total Artificial Heart
- Providing telemedicine services in which our cardiologists use live videoconferencing to assist echocardiogram procedures performed in remote locations

Leadership

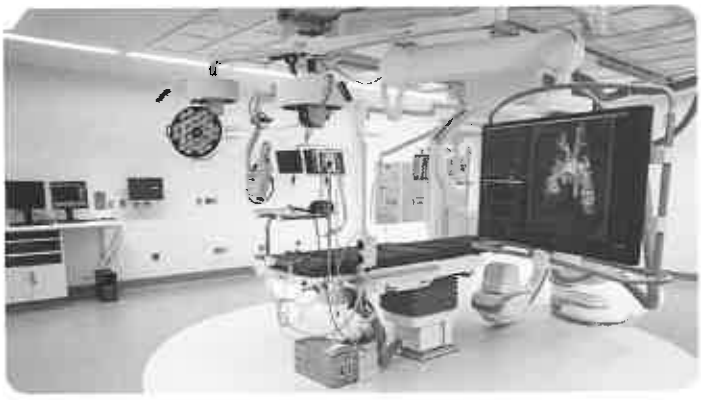
Jonathan M. Chen, MD
Division Chief, Congenital Cardiac Surgery
Co-Director, Heart Center

Academic title: Professor
Board certifications: Thoracic surgery, congenital cardiac surgery
Medical school: Columbia University College of Physicians and Surgery, New York
Residency: Surgery – general, New York Presbyterian Hospital, New York
Fellowships: Cardiothoracic Surgery, Columbia University Medical Center, New York; Ventricular Assistance – Cardiac Surgery, Columbia University Medical Center, New York; Congenital Cardiac Surgery, Morgan Stanley Children's Hospital, New York

Mark B. Lewin, MD
Division Chief, Cardiology
Co-Director, Heart Center
Director, Prenatal Diagnosis and Treatment Program

Academic title: Professor
Board certification: Pediatric cardiology
Medical school: Keck School of Medicine at University of Southern California, Los Angeles
Residency: Pediatrics, Children's Hospital of Los Angeles, Los Angeles
Fellowship: Pediatric Cardiology, Texas Children's Hospital, Houston

AJ Hwangbo (left) made a full recovery after a virus attacked his heart. With him are his little brother Alex, and mom, Yoo-Lee Yea.



Investments like our brand-new catheterization (cath) lab ensure Seattle Children's heart patients receive the best care possible.

西雅图儿童医院心臟中心

涵蓋全方位的心臟手術治療

從心律不整到需要手術或心脏移植的急症，西雅圖兒童醫院的心臟醫療中心皆能提供專業治療，滿足全方位的心臟醫療需求。

導管插入術

作為導管治療的領先者，我們正研發新的設備，以採用侵入性低於開心手術的替代方法來治療室間隔缺損和瓣膜狹窄等心臟疾病。我們也使用尖端的心導管實驗室來進行電生理學研究和經導管消融術。

手術治療。

我們的心臟外科醫生一年進行500多場手術，從簡單的心臟補洞到複雜精密的心室不全症諾伍德 (Norwood) 手術不等。

心臟中心的近期創舉

- 採用心臟手術與介入性心臟技術相結合的混合療法，為患有先天性心臟缺陷的患者提供更好的医疗服務
- 為等待心臟移植手術的重症患者提供最新的兒科心室輔助設備和機械心臟泵，包括柏林心臟輔助裝置、CentriMag離心泵、HeartMate II心室輔助裝置和SynCardia全人工心臟裝置等等
- 提供遠程醫療服務。我們的心臟病專家透過即時視訊會議，以協助在偏遠地區進行超音波心電圖檢查与会诊。

Cardiology patient Aimar Martinez Mendoza smiles shyly as she's held by her father, Ismael.

Dr. Rob Mazor leads the ventricular assist device program that keeps kids as healthy as possible while they await a new heart.

Drs. Jonathan Chen and Lester Permut perform cardiac surgery.

Seattle Children's Cancer and Blood Disorders Center
World-Renowned Cancer Care Up to Age 30

Leading-edge research by Seattle Children's hematologists-oncologists makes the newest treatment protocols available to our patients. We treat infants, children, adolescents and young adults up to age 21 for all cancers, and up to age 30 for select diagnoses.

Advanced Treatments
Seattle Children's provides chemotherapy, radiation therapy, surgery, hematopoietic cell transplants and other state-of-the-art interventions. Our nationally recognized surgical team includes bone tumor specialists, as well as neurosurgeons skilled at removing brain tumors.

Transplant Expertise
Seattle Cancer Care Alliance (SCCA) was founded by Seattle Children's, UW Medicine and Fred Hutchinson Cancer Research Center, which pioneered stem cell transplantation. We offer bone marrow, peripheral blood stem cell and cord blood transplants for cancer and nonmalignant diseases.

Cancer Center Highlights
- We are the only hospital in the Pacific Northwest and one of only a few in the U.S. that provide I-131-MIBG therapy for children with neuroblastoma.
- Seattle Children's is one of only a few pediatric hospitals that offer Phase I and Phase II clinical trials — such as our trials of T-cell therapy, a form of immunotherapy, for relapsed or refractory acute lymphoblastic leukemia and neuroblastoma.
- We offer proton beam therapy, which can treat many pediatric brain tumors, sarcomas and other cancers with fewer side effects, at SCCA Proton Therapy — the only proton therapy center for children in the Pacific Northwest, and one of only 13 in the U.S.
- Seattle Children's is the first hospital in the country with an inpatient unit dedicated solely to adolescents and young adults with cancer.

Leadership

Douglas S. Hawkins, MD
Associate Division Chief, Hematology/Oncology

Academic title: Professor
Board certification: Pediatric hematology-oncology
Medical school: Harvard Medical School, Boston
Residency: Pediatrics, University of Washington, Seattle
Fellowship: Pediatric Hematology/Oncology, University of Washington School of Medicine, Seattle

Bone cancer patient Alyssa Zoll keeps her sense of humor during clinical trials by wearing her pink eyelashed glasses.

One of the light-filled lounges in Building Hope offers Francisco Barron Jr. and his mother, Cecelia Rivas-Norris, a place to relax.

Dr. Julie Park, a national leader in neuroblastoma research, takes time to play with Tristan Estep, a recipient of I-131-MIBG therapy.

西雅图儿童医院癌症和血液疾病中心
30岁以下患者的癌症治療享譽全球

西雅圖兒童醫院血液科-腫瘤科醫生所進行的領先研究，讓我們的患者能獲得最先進的治療方案。我們為嬰兒、兒童、青少年和21歲以下的年輕人提供所有癌症治療，也治療30歲以下有特定診斷病例的特殊患者。

先進的癌症治療手段：
西雅圖兒童醫院提供化學療法、放射線療法、外科手術、造血細胞移植和其他先進的介入療法。我們全國知名的外科團隊囊括了骨腫瘤專家以及擅長移除腦部腫瘤的神經外科醫生。

移植專長。
西雅圖癌症治療聯盟 (SCCA) 由西雅圖兒童醫院、華盛頓大學醫學院和弗雷德哈欽森癌症研究中心聯合成立，本聯盟是幹細胞移植術的先創前鋒。本院為治療癌症和非惡性疾病提供骨髓、周邊血幹細胞和臍帶血移植。

癌症中心重點介紹
- 我們是美国西北太平洋地區為患有神經母細胞瘤的兒童提供I-131-MIBG療法的唯一醫院，也是全美12家提供此種療法的中心之一。
- 西雅圖兒童醫院是極少數提供一期和二期臨床試驗的兒科醫院之一，例如我們的T細胞療法試驗是一種免疫療法，用來治療復發性或難治癒的急性淋巴細胞性白血病和神經母細胞瘤。
- 我們提供能治療許多小兒腦腫瘤、肉瘤和其他癌症且副作用較少的質子療法，此療法在A ProCure中心的SCCA 質子療法部門進行（美国西北太平洋區唯一的兒童質子治療中心）。
- 西雅圖兒童醫院是全美首家專為青少年和年輕癌症患者成立专科住院病房的醫院。

Nurse Nate Stalsbroten stops in for a visit with teenage cancer patient Gailon Pursley.

Hematology-oncology specialist Dr. Akiko Shimamura shares an observation with a research colleague.

Seattle Children's Neurosciences
Nationally Recognized Neurology and Neurosurgery Expertise

Seattle Children's neurologists and neurosurgeons diagnose and treat a broad range of nervous system disorders, including cerebral palsy, epilepsy and brain tumors. Each year our neurosurgeons perform more than 600 surgeries, using the most advanced equipment and techniques.

Noteworthy in Neurosciences

- Our comprehensive epilepsy program for children and adolescents is the only one of its kind in the Pacific Northwest. Services include minimally invasive laser ablation surgery.
- We are a national referral center for children with Chiari malformation and craniosynostosis.

Leadership

Sidney M. Gospe, MD, PhD
Division Chief, Neurology
Program Director, Neurology Education
Program Director, Neurology Residency

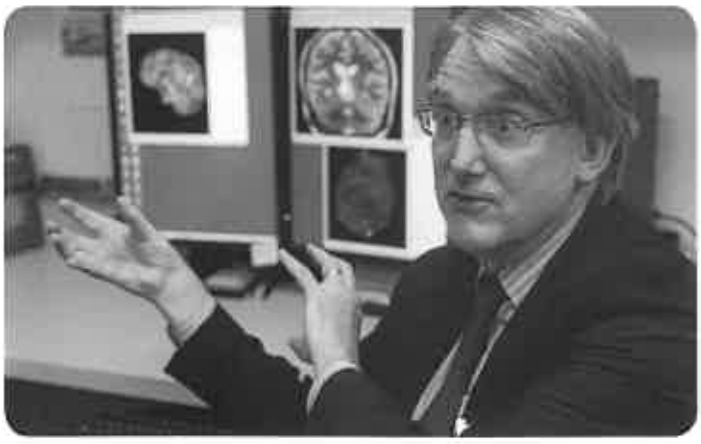
Academic title: Professor
Board certifications: Neurology with special qualification in child neurology, pediatrics
Medical school: Duke University, Durham
Residencies: Pediatrics, Baylor College of Medicine, Houston; Child Neurology, Baylor College of Medicine, Houston

Jeffrey G. Ojemann, MD
Division Chief, Neurosurgery
Director, Epilepsy Surgery
Co-Director, Epilepsy Program

Academic title: Professor
Board certification: Neurological surgery
Medical school: Washington University School of Medicine, St. Louis
Residency: Neurological Surgery, Barnes Jewish Hospital, St. Louis
Fellowships: Neurological Surgery, St. Louis Children's Hospital, St. Louis; Neurological Surgery, University of Washington School of Medicine, Seattle

Neurosurgeon Dr. Amy Lee laughs with patient Skylar Druffel and Skylar's mom, Christy, during a clinic visit.

Teenager Sara O'Neill is a patient at the region's first pediatric multiple sclerosis clinic located at Seattle Children's.



Neurologist Dr. Rusty Novotny is a national leader in techniques that produce 3-D images of patients' brains.

西雅图儿童医院神經科
全國知名的神經科和神經外科專業

西雅圖兒童醫院的神經科和神經外科醫生為廣泛的神經系統障礙--包括腦性麻痺、癲癇和腦腫瘤提供診斷和治療。我們的神經外科醫生運用最先進的設備和技術每年進行超過600場手術。

值得一提的神經科重點

- 我們是西北太平洋地區唯一一家為兒童和青少年提供癲癇病全面的会診治療的醫院。服務包括鐳射微創消融手術。
- 我們是小腦扁桃體下疝畸形和顱縫早閉兒童的全國轉診中心。

We have an extremely low shunt failure rate for for hydrocephalus patients, like Justus Fucillo, 2.

Tristan Carroll, 8, was having up to 50 seizures a day until Dr. Russell Saneto prescribed a high-fat, low-carb ketogenic diet in combination with medication.

Stage Atkins was born with severe developmental disabilities. His family gets physical and mental support from Seattle Children's.

Daniel Kelley's recent epilepsy surgery left the 3-year-old free from seizures and with his motor skills intact.

Seattle Children's Craniofacial Center
The Most Comprehensive Craniofacial Team in the Country

At Seattle Children's, the craniofacial team includes more than 50 healthcare providers from 19 specialties who treat cleft lip and palate, craniosynostosis, craniofacial microsomia and other complex conditions.

Craniofacial Areas of Focus

- Cleft lip and palate is the most common craniofacial condition we treat. Our team has the specialized training to use nasoalveolar molding, which means fewer surgeries and better outcomes.
- Our program is the largest in the country. Each year we see about 80 new patients with craniosynostosis and perform about 90 craniosynostosis surgeries, including endoscopic strip craniectomies.
- We have over 35 years of experience in interdisciplinary care for craniosynostosis.
- Each year 15 to 20 new patients with 22q11.2 deletion syndrome come to us for treatment.

Leadership

Michael L. Cunningham, MD, PhD
Division Chief, Craniofacial Medicine
Medical Director, Craniofacial Center

Academic title: Professor
Board certification: Pediatrics
Medical school: University of Washington, Seattle, University of Vermont College of Medicine, Burlington
Residency: Pediatrics, University of Washington School of Medicine, Seattle
Fellowship: Neurodevelopmental Disabilities, Seattle Children's, Seattle

Richard Alan Hopper, MD
Division Chief, Plastic Surgery
Surgical Director, Craniofacial Center

Academic title: Associate professor
Board certification: Plastic surgery
Medical school: Memorial University of Newfoundland, St. John's, Newfoundland
Residency: Plastic Surgery, University of Toronto, Toronto
Fellowship: Surgery – Craniofacial, New York University Medical Center, New York

Dr. Michael Cunningham with patient Joseph Veliz in the craniofacial clinic.

Wendy Nicone, child life specialist, holds a doll wearing a craniofacial halo, used to explain procedures to young patients.

Craniofacial patient Mason Cirrotti-Calruso, receiving care for a cleft lip and palate, is comforted by father, Seth.

西雅图儿童医院 顱面整形中心

全美最佳，最全方位的顱面整形治療團隊

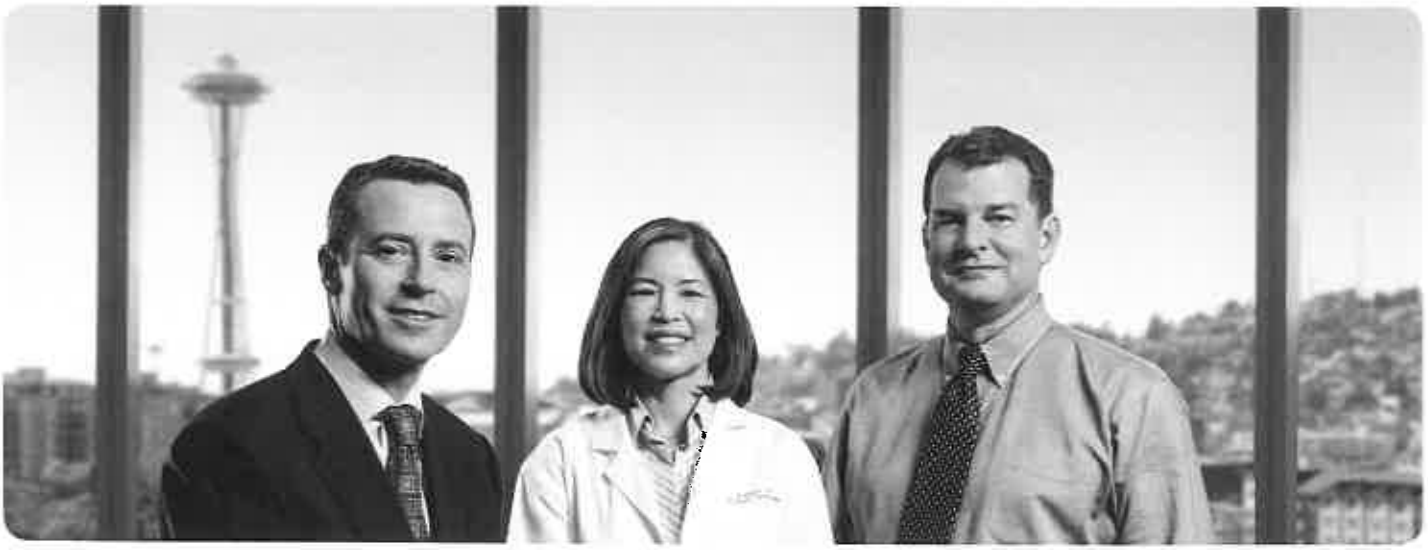
西雅圖兒童醫院的顱面整形治療團隊由來自19個專科的50多位醫師組成，負責治療唇齶裂、顱縫早閉、顱顏小臉症和其他複雜病症。

顱面整形領域的焦點

- 唇齶裂是我們最常治療的顱面問題。我們的團隊受過鼻腔齒槽成型療法的專業訓練，代表著手術次數的減少以及更好的術後效果。
- 我們在顱縫早閉的跨科治療方面擁有35年以上的經驗。本專科是全美國規模最大的。我們每年接診約80位顱縫早閉患者，進行約90個顱縫早閉手術，包括內窺鏡帶狀顱骨切除術。
- 每年有15到20個22q11.2 缺失症候群的新患者來本院接受治療。

Dr. Hitesh Kapadia, craniofacial orthodontist, and Dr. Richard Hopper, craniofacial surgeon, collaborate closely on a case.

Tumors covered the neck, face and ear of Shakira Locke, 5, before successful treatment with a blood pressure medication.



Craniofacial specialists Dr. Richard Hopper, Dr. Kathy Sie and Dr. Michael Cunningham are just three of the many Seattle Children's professionals who have dedicated their lives to helping children with abnormalities and injuries affecting the skull and face.

Seattle Children's
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美国西雅图
儿童医院 – 医学研究院 – 基金会

International Medical Services 国际医疗服务

International Patient Services: 国际患者服务

At Seattle Children's, we provide the highest quality specialty medical services to patients from more than 70 countries. All international patients should have both medical and financial approval prior to scheduling of services. Please fill out the International Intake Form located at www.seattlechildrens.org. Our services include providing help with the following:

西雅图儿童医院为世界各地70多个国家的儿童提供最高质量的医疗服务。国际患者需要预先经过注册，通过病例医审和财务审核。请在www.seattlechildrens.org 注册。我们的服务包括：

- Information about services, programs and physicians
- Medical cost estimates and billing arrangements
- Identification of a physician to meet each patient's unique needs
- Appointment scheduling, including consultations and follow-up care
- Facilitation of communications with physicians, family and friends at home
- Interpretation services in multiple languages
- Transportation and accommodation

- 主治医生介绍，专科业务介绍，
- 医疗费用估计，收费安排
- 根据具体病例确认主治医生
- 预约门诊时间和有关服务
- 协调与医生的交流和咨询
- 提供翻译服务
- 协助安排交通和住宿

International Fellowship Programs: 国际医生进修培训项目

Seattle Children's Hospital is a teaching hospital associated with University of Washington School of Medicine. We have international residents and fellowship programs jointly with UW.

西雅图儿童医院是华盛顿大学医学院附属教学医院。欢迎国际医生加入我们的进修培训项目。

International Observer Programs: 国际医生观察进修培训项目

International physicians who meet requirements related to English-language skills, medical specialty, patient referrals, and tuition obligations are welcome to our 1- to 3-month International Observer Program.

欢迎国际医生加入我们的国际医生1 到 3个月的观察进修培训项目. 需要满足的条件：英文，对口专科，协同引介患者，承担培训费用。

International Referral / Sister Hospital Programs: 国际患者引介医院 / 友好医院项目

At Seattle Children's, we work with a worldwide patient referral network and sister hospitals. We welcome international hospitals to join our network and establish sister hospital relationships!

西雅图儿童医院与世界各地医院建有患者引介服务网和友好医院交流关系。欢迎加入！

Contact: 联系我们

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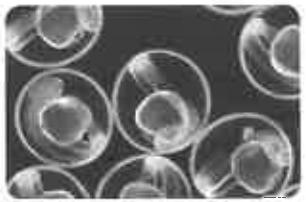
Phone: 1-206-987-1700
www.seattlechildrens.org

Seattle Children's Research Institute

Improving the Health of Children Worldwide



Seattle Children's®
HOSPITAL • RESEARCH • FOUNDATION

Located in downtown Seattle's biomedical corridor, Seattle Children's Research Institute has grown to 330,000 square feet in just six years. But square footage isn't the whole story. Our facilities are designed and equipped to support pioneering research where medical science flourishes.

The research institute's combination of technology, facilities and unique expertise enables scientists to contribute to the pediatric care and cures of tomorrow in ways not possible elsewhere.

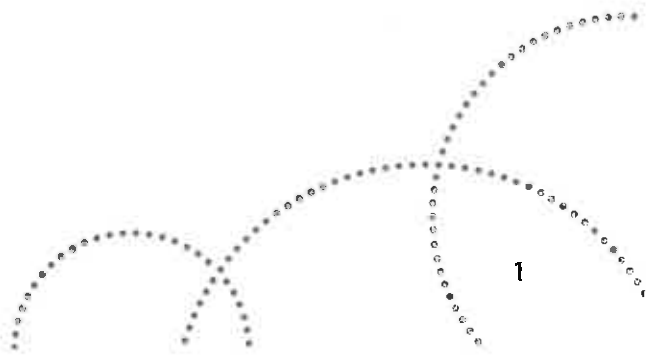
"Because of the new treatments developed at Children's, my daughter lived an extra 10 years. Those were the most beautiful years of my life. She learned to ride a horse, she went to college. She never would have had those years."

— Mom of a cystic fibrosis patient

The health issues our doctors and nurses see every day in our medical center inspire the investigations that result in better outcomes for children all over the world.

Seattle Children's Research Institute

Improving the Health of Children Worldwide



RESEARCH INSTITUTE CENTERS AND PROGRAMS

- Ben Towne Center for Childhood Cancer Research
- Center for Child Health, Behavior and Development
- Center for Clinical and Translational Research
- Center for Developmental Biology and Regenerative Medicine
- Center for Developmental Therapeutics
- Center for Genetics and Development
- Center for Global Infectious Disease Research
- Center for Immunity and Immunotherapies
- Center for Integrative Brain Research
- The Treuman Katz Center for Pediatric Bioethics
- The Science Adventure Lab

Seattle Children's Research Institute: A World Leader in Research

At Seattle Children's, delivering world-class care is a vitally important part of our mission. We strive to improve that care through research that helps prevent, treat and eliminate childhood disease. That's why Seattle Children's Research Institute was founded.

Our renowned research institute's investigators generate innovative ideas, undertake breakthrough studies, conduct clinical research studies and introduce new medical practices that are impacting pediatric care throughout the world.

A history of lifesaving discoveries

Our research starts at the bedside, where our clinicians see opportunities to improve patient care every day. They carry those needs to the research lab, where investigators make discoveries that advance the practice of pediatric healthcare.

This approach has propelled Seattle Children's toward important breakthroughs in:

- **Cancer** — pioneering therapies like pediatric bone marrow and stem cell transplants and immunotherapy.
- **Cystic fibrosis** — revolutionizing treatment by developing an inhalable antibiotic that brings the bacteria-fighting medicine directly to where it's needed.
- **Sudden infant death syndrome (SIDS)** — identifying the syndrome and developing prevention efforts that dramatically reduce SIDS deaths.

Phenomenal research growth

In 2003, Seattle Children's incorporated research into our mission, making it a high institutional priority and sparking phenomenal growth. Our research institute, established in 2007, is now one of the nation's top five pediatric research organizations, as measured by National Institutes of Health (NIH) funding.

This funding — coupled with our state-of-the-art research campus and our collaborations with leading health organizations — is attracting top scientists from around the world. Our workforce of more than 1,100 people is researching hundreds of diseases, conditions and health issues as we work to bring the next wave of pediatric health discoveries to life.

Research Institute Fast Facts

The research institute is one of the nation's top five pediatric research centers and is among the fastest growing pediatric research organizations in the United States.

- $46 million in federal research funding (2013)
- $76 million total research funding (2013)
- A workforce of more than 1,100 people
- 330,000 square feet of lab, clinical research and office space.

"I find joy every day in working with highly principled and brilliant researchers, educators and clinicians who all seek to make the world a healthier place for children."

— Dr. F. Bruder Stapleton, Senior Vice President and Chief Academic Officer, Seattle Children's

Collaboration in Pursuit of Cures

OUTSTANDING TALENT

The research institute's partnerships with the University of Washington and Fred Hutchinson Cancer Research Center enable it to attract world-renowned researchers. Other strengths include our long-term financial commitment to research, our facilities and our ability to help improve clinical outcomes for patients around the world.

To accelerate progress, the research institute is organized into nine centers. These centers follow a collaborative model: researchers work closely with one another, with clinicians at Seattle Children's Hospital and with colleagues at partner institutions like the University of Washington and Fred Hutchinson Cancer Research Center.

Uniting experts in different disciplines

Our innovative "open lab" design eliminates walls between labs and makes it easier for researchers from different disciplines to share insights as they unravel medicine's most complex problems.

For example, our Center for Integrative Brain Research includes experts in genetics, brain circuitry and molecular biology who work together to understand all aspects of brain disorders like autism and epilepsy. This collaborative approach sets the stage for comprehensive new treatments and potential cures.

World-class facilities spur advances

Our 330,000 square feet of lab, clinical research and office space includes:

- **A state-of-the-art "therapeutic cell production core"** that is one of only three pediatric facilities in the country that meets FDA requirements for manufacturing therapies.

- **A zebrafish aquatics facility** where researchers use zebrafish — tiny fish that rapidly regenerate damaged tissue — to pursue stem-cell therapies that enable tissues to repair themselves.
- **A Pediatric Clinical Research Center** that provides outpatient beds, nurses and other services for clinical research studies involving patients.

Integrating research and clinical care

In 2012 we embarked on an ambitious process to help deliver on the overarching strategy of Seattle Children's current strategic plan: **to ensure every child has the opportunity to directly or indirectly benefit from research**. We have benchmarked best practices, surveyed key stakeholders and audited our infrastructure, and we are now beginning to implement our vision to make research studies and outcomes more visible throughout our hospital environment.

"We are committed to developing the facilities and infrastructure our researchers and staff need to find solutions to pediatric medicine's most daunting challenges."

— Dr. Jim Hendricks, president of Seattle Children's Research Institute

Collaborating with world-class partners

We accelerate discoveries and develop new clinical practices by collaborating with leading health and science organizations, including:

- Allen Institute for Brain Science
- Centers for Disease Control
- Cystic Fibrosis Foundation
- Fred Hutchinson Cancer Research Center
- Institute of Translational Health Sciences (ITHS)
- Kineta
- PATH
- Seattle BioMed
- Seattle Cancer Care Alliance
- University of Washington
- Washington Global Health Alliance

Ben Towne Center for Childhood Cancer Research

CENTER MISSION

To translate scientific discoveries into therapies that cure pediatric cancer with minimal side effects and improve the lives of childhood cancer survivors.

Revolutionizing cancer treatment

The Ben Towne Center for Childhood Cancer Research is spearheading an immunotherapy approach to treating cancer that may eventually eliminate the need for chemotherapy, radiation and surgery. The key is to genetically equip an individual's own immune system to recognize cancer cells as dangerous so cancer might be eliminated from the body, just the same as the common cold.

Advancing innovative therapies through clinical research studies

The center's world-class investigators pursue potential cures by:

Building on a history of advances. Dr. Michael Jensen led the first FDA-authorized research of T-cell immunotherapy in adults with lymphoma and brain tumors as well as in children with recurrent neuroblastoma.

Developing new therapies. Dr. Jensen is collaborating with colleagues in the Center for Clinical and Translational Research and the Cancer and Blood Disorders Center clinical program to conduct clinical research studies using T-cell therapies to treat pediatric patients with a variety of types of cancer.

Director
Michael Jensen, MD

Associate Directors
Haim Burstein, PhD
Leslie Kean, MD, PhD

Areas of Focus
- Immunotherapy
- Translational research
- Therapeutic cell production

Research Partners
- Ben Towne Pediatric Cancer Research Foundation
- Fred Hutchinson Cancer Research Center
- University of Washington

Partnering with world leaders. Seattle Children's researchers work with colleagues at Fred Hutchinson Cancer Research Center and the University of Washington to accelerate the progress of developing innovative new treatments for cancers that afflict children.

Manufacturing therapies in a leading-edge facility

Seattle Children's recently designed and opened a multimillion-dollar therapeutic cell production core at the Ben Towne Center for Childhood Cancer Research in downtown Seattle. This facility gives our investigators the opportunity to have new therapies manufactured under FDA guidelines for clinical research studies at Seattle Children's Hospital.

> *"We have the technology, we have the knowledge, we have the research. Seattle Children's is the place and now is the time to make a great leap forward.*
>
> *— Dr. Mike Jensen*

Center for Child Health, Behavior and Development

CENTER MISSION

To find new ways to promote health and development so that all children can reach their physical, intellectual and emotional potential.

The science of growing up healthy

The Center for Child Health, Behavior and Development is a national leader in conducting innovative clinical and health-outcomes research. The center brings together a diverse and talented group of research scientists driven to find answers to some of the most critical and challenging children's health issues. Investigators work with families, communities, schools and healthcare providers to translate research findings into actions that improve children's lives.

New insights enhance children's well-being

The center has a broad array of research disciplines, from studies that focus on specific disorders such as craniofacial anomalies to national topics such as measuring the quality of pediatric healthcare. Several current research initiatives include:

Benefiting early childhood. Drs. Dimitri Christakis, Pooja Tandon and Michelle Garrison are exploring ways to optimize preschool children's cognitive, social, physical and emotional development by focusing on parenting education, interactive play, physical activity, and sleep.

Improving autism treatment. Our investigators are pursuing diagnosis and treatment innovations that will help children with autism lead more productive and satisfying lives. One recent study by Dr. Bryan King showed that an antidepressant commonly prescribed for children with autism does not improve their symptoms and has negative side effects.

Developing a new approach to chronic pain. Dr. Tonya Palermo is improving the outcome for kids with chronic pain. She was the first to develop a Web-based tool that combines cognitive behavior and relaxation techniques with other pain management skills and that can be used by teens and families anywhere there is Internet access.

Supporting adolescent health. Researchers are also embarking on significant studies of adolescent health and behavior, aimed at meeting adolescents where they are and understanding the pressures they face today. Their important work addresses teen depression and substance abuse.

- Dr. Megan Moreno is using Facebook to identify and track when college students are at risk for substance-related harm.
- Dr. Laura Richardson is studying whether collaborative care can help adolescents with depression get better care, faster.
- Dr. Cari McCarty is comparing the effectiveness of two different school-based preventive interventions for young adults designed to reduce depression and improve their relationships.

"Today's children face a broad array of challenges. Our group is applying cutting-edge science to help children overcome them."

— Dr. Dimitri A. Christakis

Director

Dimitri A. Christakis, MD, MPH

Areas of Focus

Health
- Child and adolescent mental health
- Patient safety
- Pediatric obesity
- Quality of pediatric healthcare

Behavior
- Media and aggression
- Fetal alcohol syndrome
- ADHD

Development
- Autism
- Craniofacial abnormalities
- Kindergarten readiness

Pain Management

Research Partners

- Group Health Cooperative
- Public Health - Seattle and King County
- RAND Corporation
- Seattle Public Schools
- University of Washington
- U.S. Department of Health and Human Services

Center for Clinical and Translational Research

CENTER MISSION

To translate laboratory discoveries into innovative treatments that improve children's lives. The center will advance clinical research by focusing on new methods to conduct better research and by mentoring clinical scientists to become tomorrow's leaders.

Translating laboratory discoveries into lifesaving therapies

The Center for Clinical and Translational Research uses clinical research — the process of testing and refining innovations until they are safe and effective in people — to develop therapies for many pediatric diseases and disorders.

Developing next-generation treatments

The center's researchers are analyzing outcomes, generating research ideas and working on clinical research studies designed to improve pediatric medicine and child health. Our research includes:

Improving quality of life. Dr. Bonnie Ramsey and others continue their groundbreaking research to develop better treatments for cystic fibrosis.

Defending children against viruses. Led by Dr. Janet Englund, our investigators are spearheading new ways to help children ward off the flu and other viruses.

Advancing new leukemia treatments. Each year, thousands of children with cancer can't find a suitable donor for a potentially lifesaving bone marrow transplant. Dr. Colleen Delaney is pioneering a technique that uses stem cells from umbilical cord blood as a viable substitute.

Improving pain management. Dr. Gary Walco is on a mission to make every hospital experience as painless as possible. He and his colleagues are advancing various techniques — such as improved patient education and better methods of giving shots — for making everything from surgery to blood draws less painful.

Collaborations incubate discoveries

The center is home to the child health branch of the Institute of Translational Health Sciences (ITHS), which was created to help researchers from Seattle Children's, the University of Washington, Fred Hutchinson Cancer Research Center and other regional health organizations translate discoveries into therapies.

> *"Every clinician sees something that could change their patients' lives. The center's job is to help them carry those observations into bench research and make discoveries that improve clinical care."*
>
> *— Dr. Bonnie Ramsey*

Director

Bonnie Ramsey, MD

Associate Directors

- Douglas Hawkins, MD
- Margaret Rosenfeld, MD, MPH

Areas of Focus

- Clinical research studies in children
- Academic and industry partnerships
- Development and testing of novel devices
- Comparative effectiveness research
- Epidemiology and biomarker research

Research Partners

- Ben Towne Center for Childhood Cancer Research
- Cystic Fibrosis Foundation
- Duke Clinical Research Institute
- Fred Hutchinson Cancer Research Center
- Institute of Translational Health Sciences
- University of Washington

Center for Developmental Biology and Regenerative Medicine

CENTER MISSION

To restore children's health after injury through repair, regeneration or replacement of tissues, cells and organs.

Helping the body repair itself

Researchers at the Center for Developmental Biology and Regenerative Medicine are studying how the body responds to injury at the molecular, cellular, tissue and whole-organ levels and are developing innovative therapies to help the body repair itself.

Healing children through innovation and discovery

The center's team is pursuing cutting-edge treatments for damage caused by childhood developmental abnormalities (such as craniofacial malformation) and illnesses (such as kidney disease or heart disease). Our research could improve child health by:

Preventing birth defects. Dr. David Beier studies mutations that cause birth defects, with the goal of understanding the fundamental biological processes that are disrupted in these disorders.

Repairing craniofacial abnormalities. Drs. Michael Cunningham, Timothy Cox, Anne Hing, Daniela Luquetti and A. Murat Maga research the molecular, genetic and developmental causes of craniofacial malformations. Their research could lead to new techniques that help correct developmental abnormalities.

Using stem cells to correct heart defects. Drs. Mark Majesky and Lisa Maves investigate molecular, biological and genetic approaches to heart formation. Their research could lead to new therapies for heart repair without invasive surgery or transplant.

Collaborations fuel progress toward treatments

The center's members work in an open lab environment, allowing doctors and researchers to collaborate with experts in a wide range of disciplines. This collaborative approach fuels advances in our common search for causes and treatments of childhood illnesses.

> *"I am delighted to be part of an institution with the level of commitment, energy and resources that I see in the donors, the research institute and the hospital. Seattle Children's provides a collaborative environment where researchers work together across benches to find cures, and I enjoy participating in its culture of scientific excellence."*
>
> *— Dr. David Beier*

Director
David Beier, MD, PhD

Areas of Focus
- Developmental biology
- Stem cell and regenerative medicine
- Myocardial Regeneration Initiative
- Genetics and genomics

Research Partners
- Fred Hutchinson Cancer Research Center
- Kidney Research Institute
- University of Washington
- University of Pittsburgh
- Brigham and Women's Hospital

Center for Developmental Therapeutics

CENTER MISSION

To use studies of childhood diseases and child development to learn fundamental principles that can be translated into improvements in children's health.

Pioneering therapies for a variety of disorders

Motivated by problems seen in clinical settings, the Center for Developmental Therapeutics researchers develop safe and effective treatments and preventive measures that improve children's lives. Our expert team is pioneering revolutionary therapies for Kawasaki disease, mitochondrial diseases, prematurity and stillbirth, thoracic disorders, and environmental exposures.

Pediatric advances with global impact

Researchers at the Center for Developmental Therapeutics are working to improve prevention and treatment of pediatric diseases and conditions by defining fundamental principles and understanding molecular mechanisms. Our innovative research pushes scientific boundaries to improve child health around the world by:

Saving newborns from respiratory distress. Drs. Tom Hansen, Peter Richardson, and Charles "Skip" Smith have developed a low-cost, low-maintenance, and easy-to-use respiratory support apparatus, Seattle-PAP, for use in resource-limited healthcare settings. Seattle-PAP has the potential to save the lives of hundreds of thousands of newborns each year throughout the world.

Improving diagnosis of mitochondrial diseases. The center's world-class program uses gene sequencing and genetic studies to improve diagnosis of mitochondrial diseases. Our researchers — including Drs. Philip Morgan, Margaret Sedensky, Sihoun Hahn and Albert Quintana — also study how to tailor care for patients with mitochondrial defects.

Pursuing healthier births in low-resource countries. Working with the Global Alliance to Prevent Prematurity and Stillbirth (GAPPS), the center's team studies mechanisms underlying stillbirths and preterm births while raising awareness of these problems.

Advancing therapeutic approaches. Dr. Michael Portman and his team have introduced medications that reverse injury to the heart muscle, and have developed therapies that improve outcomes for children with Kawasaki disease.

Improving outcomes for premature infants. The lungs of many premature infants are underdeveloped and collapse due to the lack of adequate surfactant. Supported by a Grand Challenges Exploration Grant from the Bill & Melinda Gates Foundation, a team led by Dr. Charles "Skip" Smith is pursuing the development of an affordable, appropriate, artificial surfactant called GenExSurf. GenExSurf shows great promise for use in developing countries, as it can be produced at a very low cost and may not require a cold chain for transportation.

> *"We work to improve health around the world by discovering and tailoring therapies that are appropriate to the age, size, and stage of development of children, using tools ranging from molecular to mechanical."*
>
> *— Dr. Charles "Skip" Smith*

Director

Charles "Skip" Smith, PhD

Areas of Focus

- Bioinformatics
- Cardiovascular development and function
- Developmental toxicology
- Lung development and function
- Mitochondrial diseases
- Obesity, nutrition, exercise and diabetes
- Prematurity and stillbirth

Research Partners

- Bill & Melinda Gates Foundation
- GAPPS
- PATH

Center for Genetics and Development

CENTER MISSION

To advance the understanding of the genetic basis of disease, with the goal of improving treatment and developing cures.

Improving diagnosis and treatment of childhood disorders

The Center for Genetics and Development is creating a future where doctors can use genetic information to identify, plan for and potentially correct genetic defects and the disorders they cause.

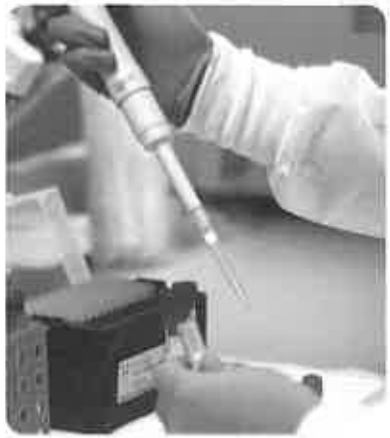
Advancing breakthrough technologies and techniques

As our researchers work to mitigate and potentially cure pediatric disorders, their groundbreaking work includes:

Developing advanced sequencing techniques. Center director Dr. Michael Bamshad and his colleagues helped develop exome sequencing, a breakthrough technique that accelerates the process of identifying genes that cause disorders.

Pinpointing the causes of genetic disorders. Researchers in the center identified the genetic variations that trigger Kabuki syndrome and Miller syndrome. Now they're working to identify the mutations behind a variety of lung diseases, heart defects and other disorders.

Answering complicated ethical questions. New sequencing approaches radically increase the amount of genetic information known about research participants and raise questions about how that information could alter patients' lives. The center's team, which includes a full-time ethicist, is considering these questions now to lay the foundation for future best practices.



Director
Michael J. Bamshad, MD

Areas of Focus
- Advanced sequencing technologies
- Gene identification
- Bioethics
- Mendelian disorders

Research Partners
- Institute of Translational Health Sciences
- University of Washington

Investigating ways to repair defective genes

Knowing which genes and gene mutations may trigger a disorder helps doctors diagnose the condition, anticipate which health problems a patient might develop and counsel parents about their child's coming health challenges. Center researchers are taking their discoveries one step further by translating them into real-world therapies — such as techniques for repairing or replacing defective genes — that improve children's lives.

> *"In 10 or 20 years, we'll have genetic knowledge that will allow us to know whether kids are at risk for conditions like autism before they're even born. This will lead to new treatments that reduce the impact of — and potentially cure — health problems affecting children throughout the world."*
>
> *— Dr. Michael Bamshad*

Center for Global Infectious Disease Research

CENTER MISSION

Through scientific discovery we will understand, treat, prevent and cure infectious diseases affecting people across the globe from neonatal to adult stages of life. Our research teams will develop effective solutions so children can grow up to be healthy adults.

Developing new strategies against infectious diseases

The Center for Global Infectious Disease Research translates basic biology into strategies for diagnosing, treating and preventing infectious diseases and conditions that impact people locally, nationally and globally.

International initiatives for healthier children

The center aims to develop new antibiotics, vaccines and antiviral agents. Our researchers are:

Taking aim at a global health threat. Dr. Timothy Rose is leading a multidisciplinary team of researchers to investigate how the virus that causes Kaposi's sarcoma — one of the most common pediatric cancers in Africa — spreads and turns cancerous.

Preventing mother-infant HIV transmission. Dr. Lisa Frenkel is a nationally recognized researcher focusing on human immunodeficiency virus (HIV) with a specific interest in preventing mother-to-infant transmission. In addition to developing less expensive approaches to optimize care in low-resource communities, her group is also performing studies to help determine how infections persist at low levels during treatment, which could form the basis of new approaches to cure HIV infection.

Developing an Internet-based outbreak tracking system. Dr. Scott Weissman is studying the growing public health threat of antibiotic resistance in bacteria and developing innovative ways to identify and monitor the spread of difficult-to-treat infections.

Co-Directors

Lisa M. Frenkel, MD

Timothy Rose, PhD

Areas of Focus

- Infectious diseases in acutely and chronically ill patients
- Global health
- Natural history of infectious diseases
- Discovery and testing of antimicrobial agents
- Vaccine discovery and evaluation
- Respiratory infections in childhood
- Improving treatment of disease
- Stillbirth and premature birth

Research Partners

- Bill & Melinda Gates Foundation
- BioTraces
- Cystic Fibrosis Foundation
- Enertechnix, Inc.
- Fred Hutchinson Cancer Research Center
- GAPPS
- Global WACh
- Institute of Translational Health Sciences
- Micronics, Inc.
- North Coast Biologics
- PATH
- Seattle BioMed
- University of Washington

"For us, every single day is something new — a new question to answer, a new problem to solve, a new discovery to make. Advancing science isn't easy; it can be a long process. But every day we come to work to improve the quality of children's lives — that's what drives us."

— Dr. Timothy Rose

Center for Immunity and Immunotherapies

CENTER MISSION

To harness the immune system's power to prevent, treat or cure life-threatening childhood diseases.

Pursuing cures for immune disorders

Millions of children develop life-threatening infections because their immune system fails to protect against invading viruses or bacteria. Many other children suffer from diabetes, arthritis and related conditions when their immune system turns against the body. The Center for Immunity and Immunotherapies pursues new ways to understand, treat and cure these life-threatening conditions.

Advanced therapies disarm disease

Center researchers study disorders that yield extraordinary insights into how the immune system operates. This helps the center pursue therapies in the same way that previous immune discoveries led to new drugs for arthritis and cancer. Our researchers are:

Developing novel gene therapies. Led by Drs. Dåvid Rawlings and Andy Scharenberg, the center pioneers techniques that replace or repair the malfunctioning genes behind immune disorders. These therapies are being tested in clinical research studies and will have a major impact on pediatric genetic diseases.

Rapidly identifying immune diseases. Drs. Troy Torgerson and Hans Ochs have developed unique approaches to rapidly identify patients with immune diseases. They provide testing for patients worldwide via the Immunology Diagnostic Laboratory. This lab also works with the state newborn screening lab to identify infants with life-threatening immune diseases.

Promising new hemophilia treatments. Dr. Carol Miao is developing gene therapy and immunomodulation strategies for treating hemophilia in children. Currently, hemophiliacs must visit the hospital during bleeding crises. The new therapy could eliminate bleeding episodes, increase quality of life and decrease medical costs.

Director
David J. Rawlings, MD

Areas of Focus
- Cellular therapeutics
- Gene therapy and repair
- Immune monitoring
- Molecular diagnostics

Research Partners
- Benaroya Research Institute
- Fred Hutchinson Cancer Research Center
- Seattle Cancer Care Alliance
- University of Washington

A global reputation

The center has developed a global reputation in identification of the genetic causes of immune disorders and understanding how such changes promote disease. Center researchers have contributed to breakthroughs in two additional areas of importance:

- A better understanding of both rare and common immune disorders such as lupus, inflammatory bowel disease, multiple sclerosis and Type 1 diabetes – leading to new biomarkers, treatments and drugs to control these disorders.

- Advancements in the science of genome editing and reprogramming that will enable the human immune system to actually heal itself. These technologies hold the promise of a permanent solution to conditions that are now considered incurable, ranging from immune deficiency to sickle cell disease to AIDS.

"As a parent and a physician, I am continually amazed by the capacity of our patients and their families to adapt to the challenges of living with a chronic immune-system disease. As a physician-scientist, I am driven by the challenge to make this battle less difficult by whatever means possible — now and in the future."

— Dr. David Rawlings

Center for Integrative Brain Research

CENTER MISSION

To understand the mechanisms beneath pediatric neurological, neurodevelopmental and neuropsychiatric disorders to lay the foundation for innovative treatments, prevention strategies and potential cures.

A transformational approach to neurological disorders

The Center for Integrative Brain Research brings together experts from distinct areas to understand all facets of a disease. By sharing knowledge at the genetic, molecular, cellular, network and behavioral levels, our researchers unlock how these facets spawn disorders — setting the stage for comprehensive treatments and potential cures.

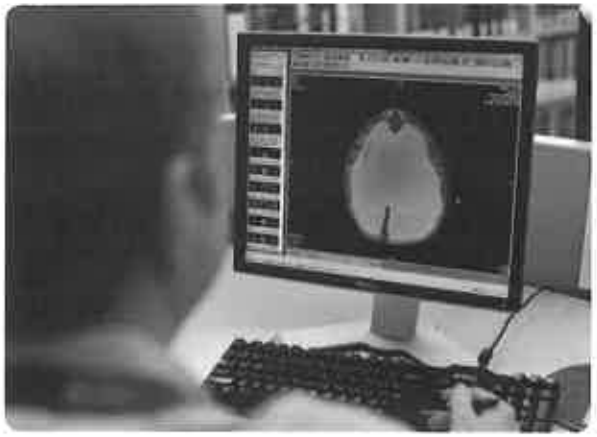
Pursuing breakthroughs with a world-class team

The center has assembled renowned neuroscientists who bring established expertise, funding and an eagerness to work together. Their work could improve patient outcomes by:

Improving diagnostic techniques. Dr. Rusty Novotny combines images from different systems (like PET, MRI and CT scans) to create a clearer view of what happens in the brain, and to improve epilepsy diagnosis and treatment.

Understanding early brain development. By investigating the genetic basis of brain malformation and the cerebellum's early development, Drs. William Dobyns and Kathleen Millen advance diagnosis and potential treatment of complicated brain disorders.

Exploring impulse control disorders. Dr. Susan Ferguson unravels the complexities of the neural pathways beneath impulse control disorders to help get to the root of ADHD, Tourette's, addiction, eating disorders, anxiety and depression. Her team has developed technologies to study how these disorders affect behavior.



Director
Jan "Nino" Ramirez, PhD
Associate Director
Elizabeth Aylward, PhD

Research Partners

- Allen Institute for Brain Science
- Fred Hutchinson Cancer Research Center
- Institute of Translational Health Sciences
- University of Washington

Tackling breathing disorders. Our researchers identified key mechanisms behind sudden infant death syndrome, sleep apnea and other breathing disorders — a key step toward innovative new treatments.

Training future neuroscience leaders

We are passionate about training the next generation of leading neuroscientists. The center encourages faculty to teach and mentor new scientists and clinicians. This ensures a constant flow of new ideas that keep our work at the forefront of science.

> *"Our center is different because we have scientists from many disciplines working together to cure childhood neurological disorders. The vision was to have people exchanging ideas that aren't generated in a typical environment where you only talk to people in your own discipline. If you can work on the same floor, you can talk and exchange ideas."*
>
> *— Dr. Nino Ramirez*

The Treuman Katz Center for Pediatric Bioethics

CENTER MISSION

To improve the lives of children and their families by enhancing ethical deliberation in pediatric healthcare and research.

Director
Benjamin S. Wilfond, MD

Areas of Focus
- Genomics
- Global health
- Immunizations
- Research ethics
- End of life
- New technologies

Framing complex ethical questions for better decisions

The first program in the country to focus exclusively on pediatric issues, the center serves as a national resource for addressing the complex bioethical issues affecting families, healthcare institutions and society. Our team provides practical guidance to research and clinical teams, hospital leadership and families who are facing difficult decisions where there is ethical uncertainty or disagreement.

Training the next generation of bioethicists

The center is committed to training clinicians for academic careers in bioethics. By engaging the next generation of scholars, teachers and consultants, we help establish the best practices and approaches that guide ethical decision making.

"At a time when the ethical landscape is getting more complicated, we are helping guide parents, researchers and providers through today's complex ethical challenges."

— Dr. Benjamin Wilfond

The Science Adventure Lab

Advancing health through science education

The Science Adventure Lab brings authentic, interactive science experiments to students in a custom-built, state-of-the-art mobile laboratory. Scientists from Seattle Children's Research Institute lead hands-on experiments and students become health investigators in a true-to-life lab setting. The program is intended to offer innovative science experiences, encourage healthy behaviors and increase interest in science and healthcare careers.

Real-world lessons with life-changing possibilities

The curriculum is designed to inspire a passion for science, promote better health and encourage the type of critical-thinking skills needed for today's science careers. Teaching modules use inquiry-based learning, the scientific method and skills such as observation, measurement, prediction and testing.

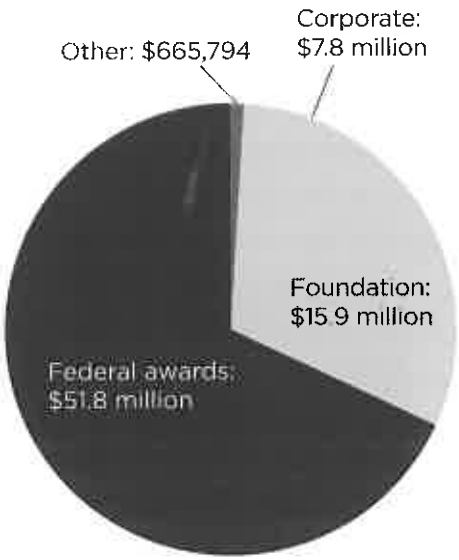
PROGRAM MISSION

To work in partnership with teachers, schools and communities to deliver innovative educational experiences that inspire a passion for science among school-age children and promote better health among the youth of Washington state.

Director
Amanda Jones, PhD

Diverse Funding Supports Lifesaving Research

Total research awards in 2013: $76.2 million



Less than half a cent of every healthcare dollar in the U.S. is spent on pediatric research.

A broad combination of funding sources fuels research institute progress toward better treatments and potential cures. Most of our funding comes via grants from the federal government, private corporation grants and philanthropic gifts.

Help create a healthier future for all children

Our ability to attract federal funding moves our science forward and helps us draw and retain world-class researchers.

Philanthropic support, however, provides essential funding for a variety of needs, including seed money for innovative research projects. It enables cutting-edge researchers to generate preliminary results that attract funding from the NIH or other large entities.

Thanks to the generosity of our community, we are accelerating research that will advance the practice of pediatric medicine in our region and across the globe. Our supporters range from major foundations to individuals, families and guilds — all of them motivated by the goal of improving the lives of children.

> *"Every child is touched by pediatric research. It's an investment in the future of our children, not only here in Seattle, but throughout the Pacific Northwest and around the world. Our donors believe in what Seattle Children's can accomplish and want to be part of something that will improve the world around them."*
>
> *— Dean Allen, Chair, Research Institute Advisory Board*

How you can help

Give now. People have many reasons for giving. You may have had a personal experience with Seattle Children's, or you may simply be interested in the well-being of all children. Your donation will provide hope where it truly makes a difference.

Become a Research Champion. Becoming a Research Champion is a meaningful way to sustain our groundbreaking research. Individuals and family foundations can become Research Champions by donating $1,000 or more to research in one calendar year. Organizations can join with a gift or grant of $2,500 or more. We offer members the opportunity to engage with world-renowned scientists and fellow Research Champions through social and scientific events.

Join or start a research guild. Get together with friends, family and co-workers and turn an activity you love into a way to support research at Seattle Children's.

I AM A SEATTLE CHILDREN'S RESEARCH CHAMPION

> *"I'm a strong supporter of Children's and became a Research Champion this year because research is the way we find cures and improve life for children and their families. The idea that every child should grow up free of illness or injury is truly significant — and research is a way to make that a reality. I believe that people coming together as a community to support research can have a powerful effect locally, regionally, and beyond. As an individual, this gives me the opportunity to have a broad and enduring impact. I like that."*
>
> *— Susan Mask, Hospital Trustee, 2013 Research Champion*

Hope. Care. Cure.™

Hope. Care. Cure.™

Our Mission: We believe all children have unique needs and should grow up without illness or injury. With the support of the community and through our spirit of inquiry, we will prevent, treat and eliminate pediatric disease.

Seattle Children's®
HOSPITAL • RESEARCH • FOUNDATION

MISSION BAY HOSPITALS

Care for Children, Women and Cancer Patients

This next-generation hospital complex at Mission Bay is uniquely designed to meet the needs of children, women and cancer patients. It sets a world-class standard for patient- and family-centered health care, safety, sustainability and translational medicine.

UCSF Medical Center

UCSF Benioff Children's Hospitals

Message from the CEO

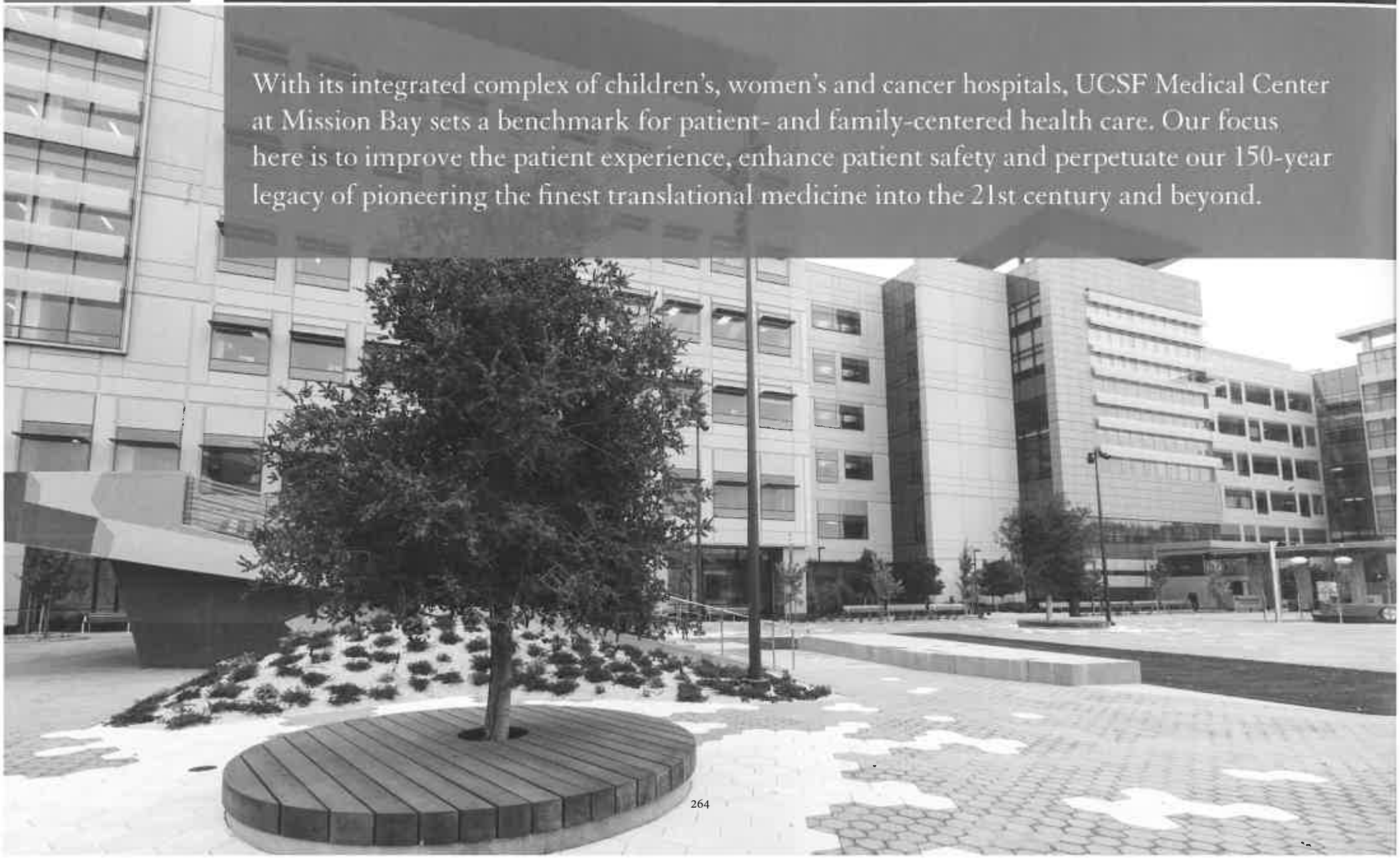
UCSF Medical Center at Mission Bay profoundly advances our ability to fulfill our mission as a public hospital, providing high-quality health care that will meet the future needs of the entire Bay Area.

Now that we have clinical care facilities side by side with our research enterprise at Mission Bay, UCSF physicians and scientists in the forefront of cancer medicine and women's and children's health will be able to more readily translate discoveries into next-generation therapies and cures.

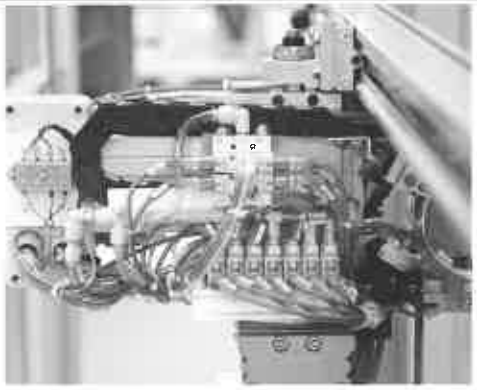
Mark R. Laret
Chief Executive Officer
UCSF Health
UCSF Medical Center
UCSF Benioff Children's Hospitals

Our Vision

With its integrated complex of children's, women's and cancer hospitals, UCSF Medical Center at Mission Bay sets a benchmark for patient- and family-centered health care. Our focus here is to improve the patient experience, enhance patient safety and perpetuate our 150-year legacy of pioneering the finest translational medicine into the 21st century and beyond.



A media platform is available to all inpatients, enabling them to order room service, video chat with co-workers and classmates, post to social media accounts, pick from an expansive selection of movies, email their clinical team and more.

TO ACHIEVE OUR VISION

After listening closely to our patients, we've done – and will continue to do – everything possible to consistently meet their needs, from ensuring the finest, safest and most up-to-date medical care to creating a supportive hospital experience that allows people to maintain touch with their lives outside of the clinical setting.

MEDICAL ADVANCES

Our new hospitals are on the same campus as UC San Francisco's world-renowned research enterprise, so physicians and scientists in the vanguard of cancer medicine and women's and children's health can accelerate the translation of laboratory discoveries into next-generation therapies and cures.

SAFETY

We've implemented evidence-based patient safety protocols, efficient electronic health records and sophisticated technologies from robotics to imaging, while incorporating the highest standards of energy efficiency, seismic safety and sustainability.

TEAM-BASED CARE

Our integration of cancer, women's and children's hospitals in one place facilitates team-based care for conditions that often require experts from multiple fields.

COMFORT

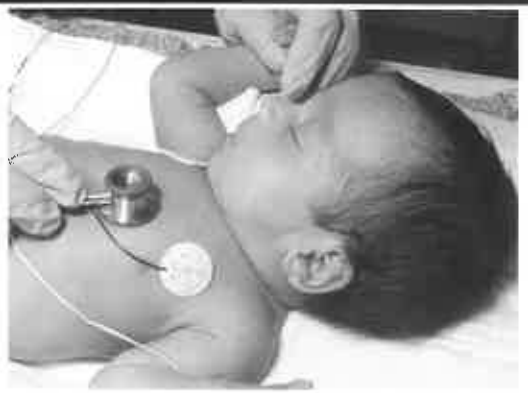
Our bright, family-friendly rooms, intimate green spaces and innovative art and child life programs create a uniquely humane environment that engages and supports entire families throughout the healing process.

UCSF Benioff Children's Hospital San Francisco

Here at the only dedicated children's hospital in San Francisco, some of the world's finest clinicians deliver advanced pediatric, emergency and specialty outpatient care in a physical space that celebrates healing and the special needs of children.

An atmosphere of sophisticated and colorful whimsy greets families as they enter the new hospital. Every room is private, with huge windows that welcome natural light. Loved ones can stay overnight in comfort right in the patient's room. For families with patients under age 18 who come to the hospital from 50 or more miles away, the Ronald McDonald House can provide a home away from home.

Our state-of-the-art medical helicopter – Bear Force One – is available 24/7 to respond to hospital referrals within a 150-mile radius of Mission Bay.



LEADERSHIP IN CHILDREN'S HEALTH

UCSF Benioff Children's Hospital San Francisco:

- Is among the nation's best children's hospitals in nine pediatric specialties.*
- Is a leader in fetal diagnosis and treatment, including having performed the first successful fetal surgery.
- Cares for more than 1,000 infants each year in what was one of the first neonatal intensive care nurseries in the world.
- Delivers specialized treatment for infants who show signs of brain damage, in the first neurointensive care nursery in the United States.
- Is among the largest bone marrow transplantation centers for children in North America.
- Delivers the most advanced care for childhood stroke from experts at the UCSF Pediatric Stroke and Cerebrovascular Center.

*U.S. News & World Report, Best Children's Hospitals 2015-16

CHILD LIFE PROGRAMS

Because young patients can require frequent or lengthy stays (weeks or even months), our nationally recognized Child Life Department helps children and teens find their time with us comforting, stimulating and life-affirming. Our child life spaces include:

- **Marie Wattis School**, a dedicated, accredited San Francisco Unified School District classroom
- A **Creative Arts Studio** for dance, music and other forms of live performance, which is staffed by a creative arts therapist and artists-in-residence
- A **Digital Arts Studio** with multimedia workstations, private listening rooms and technically advanced equipment
- A **Playroom** with toys, board games, puzzles, books and arts-and-crafts materials
- A **Teen Lounge** with foosball, crafts, board games and video games

UCSF Betty Irene Moore Women's Hospital

Our women's hospital offers a full array of services tailored to the unique biology and health concerns of women across their life spans – from puberty to menopause and beyond.

We offer outstanding women's surgical care for benign and cancerous conditions, and state-of-the-art perinatal care in a 36-bed birth center with nine deluxe labor and delivery suites.

Our 36-bed birthing center is adjacent to UCSF Benioff Children's Hospital San Francisco and UCSF Bakar Cancer Hospital, enabling patients to have immediate access to other specialized services.

LEADERSHIP IN WOMEN'S HEALTH

UCSF:

- Created the first in vitro fertilization program in the Bay Area.
- Revolutionized the field of prenatal diagnosis, proving the safety and accuracy of tests now routinely used to screen for birth defects.
- Founded one of the first birth centers in the nation.
- Launched www.breastcancertrials.org, the first website designed to help breast cancer patients find clinical trials for which they may be eligible.
- Was designated the first National Institutes of Health (NIH) Specialized Center of Research on Lower Urinary Tract Function in Women.

PREGNANCY AND CHILDBIRTH

For women experiencing both normal and high-risk pregnancies, we provide team-based care, which can include certified nurse-midwives, expert obstetricians and leading neonatologists, depending on the needs of your pregnancy and your preferred approach.

CANCER CARE

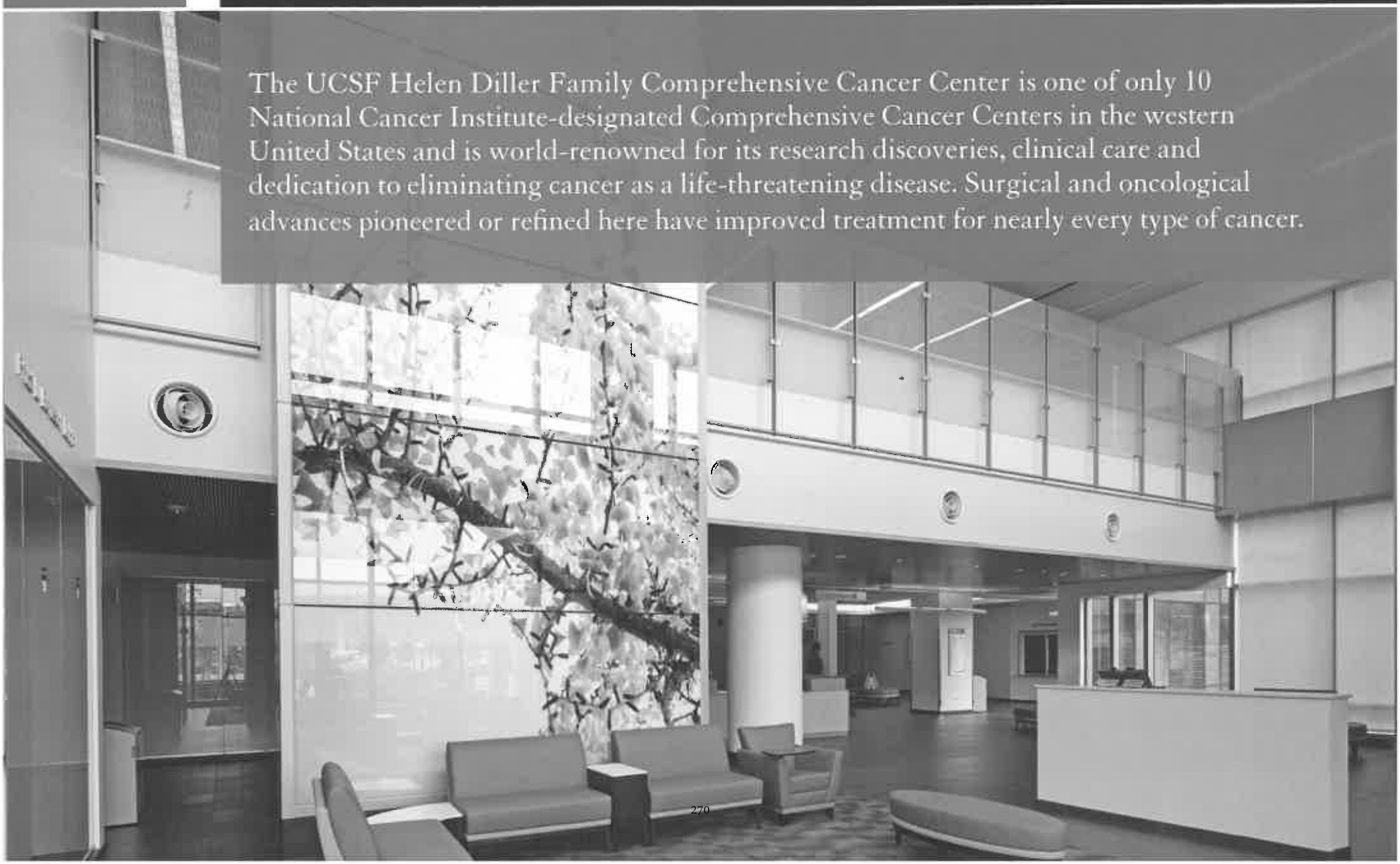
Women with cancer have access to specialists who understand women's distinct needs – as well as to new diagnostic tests and treatments that help specialists personalize care to individual biology and preferences.

A HEALING ENVIRONMENT

Expansive two-story atria, intimate meditation spaces, soft color schemes, exceptional artwork and patient rooms that maximize the use of natural light and offer views of our city and gardens support the emotional and spiritual aspects of healing.

UCSF Bakar Cancer Hospital

The UCSF Helen Diller Family Comprehensive Cancer Center is one of only 10 National Cancer Institute-designated Comprehensive Cancer Centers in the western United States and is world-renowned for its research discoveries, clinical care and dedication to eliminating cancer as a life-threatening disease. Surgical and oncological advances pioneered or refined here have improved treatment for nearly every type of cancer.



Patient-friendly imaging scan suites are tailored for both children and adults, enabling them to virtually experience a Golden Gate sunset or a cable car ride around San Francisco.

INTEGRATING RESEARCH AND CLINICAL CARE

As a part of the UCSF Helen Diller Family Comprehensive Cancer Center, our new 70-bed UCSF Bakar Cancer Hospital builds on the center's tradition of excellence. The close proximity to the UCSF Helen Diller Family Cancer Research Building, which is co-located on the Mission Bay campus, facilitates collaboration between scientists and physicians, thus speeding the latest evidence-based treatments to patient care.

SUPPORTIVE SERVICES

We also know that healing requires more than the finest science. Symptom Management and Integrative Medicine are just two of our supportive care services. The Ida & Joseph Friend Cancer Resource Center enables patients to access community services, a large network of peer support volunteers, support groups and educational programs. And the Ernest H. Rosenbaum MD Art for Recovery program provides the opportunity to express through art the intense feelings that can arise during a life-threatening illness.

LEADERSHIP IN CANCER CARE

The UCSF Helen Diller Family Comprehensive Cancer Center:

- Ranks consistently among the very top cancer care centers in the nation, according to the "Best Hospitals" survey from U.S. News & World Report.
- Ranks fifth nationally in the size of its National Cancer Institute Cancer Center Support Grant, resulting in research at UCSF that has led to multiple Nobel Prizes and forms the basis for some of today's most promising cancer studies.
- Developed a new class of targeted chemotherapy drugs, called immunoliposomes, designed to reduce treatment toxicity and increase effectiveness.
- Pioneered and proved the effectiveness of a mapping technique that allows for the safe removal of tumors near language pathways in the brain.
- Refined greatly the risk associated with certain cancers, leading to treatment with fewer side effects - or, in some cases, no treatment at all, just careful monitoring.
- Routinely uses minimally invasive, robotic-assisted surgical procedures for cancers of the prostate, kidney, bladder, ovaries and other organs. In the hands of expert surgeons, this approach can facilitate faster recovery and discharge from the hospital than more traditional approaches.
- Is at the forefront of molecular research that promises to make it possible to more precisely develop cancer treatments for individual patients.

Innovative Spaces That Optimize Care and Create Community

While expert clinicians will always be at the center of effective care, many other factors contribute to the complex processes of healing and recovery. From our original vision through implementation, we've paid close attention to everything that can help restore our patients' health and well-being.

THE ART PROGRAM

We are committed to integrating art into the fabric of UCSF Medical Center at Mission Bay. Our art program, which consists of internationally renowned artists and local community and patient artists, supports our mission – caring, healing, teaching, discovering – and creatively conveys UCSF's preeminence in advancing health worldwide™.

The hospital complex uses 50 percent less energy than the average US hospital and integrates water-efficient technology that reduces water use by 40 percent.

ENHANCED CLINICAL CARE AND PATIENT SAFETY

Throughout the new medical center, we've implemented a number of advances that:

- Prevent hospital-acquired infections by making every room a single-bed room, with hand-washing sinks and hand-sanitizer dispensers near entryways. One-hundred-percent fresh air circulates throughout the hospital at all times.
- Reduce the risk of medical errors by helping reduce staff fatigue with well-lit, efficiently laid-out workspaces.
- Facilitate faster response times through decentralized nurses' stations, which keep nurses closer to their patients, and electronic real-time locating systems for necessary medical equipment.

A HEALING AND SUPPORTIVE ENVIRONMENT

In our patients' rooms, enormous windows offer views of the bay, the city or the hospital's gardens. Recessed entries create semiprivate "front porches" for family-doctor consults. Sleeper couches and lockable storage cabinets for personal belongings ease overnight stays.

Outdoor balconies and terraces enable patients, their families and staff to experience fresh air and sunlight from within every patient care unit. Gardens and a vehicle-free, pedestrian-friendly public plaza add to the hospitals' green space. Other patient amenities include meditation rooms, private consult rooms, valet parking, on-demand food service and family living areas with showers, laundry facilities and kitchens.

STATE-OF-THE-ART TECHNOLOGY FOR TODAY AND TOMORROW

Our spacious operating rooms are fully integrated to optimize technology interfaces throughout the hospitals and beyond. Connections with other areas of the facility speed test results and clinical insights to the OR table. User-friendly monitors enable clinicians to view a remarkable array of patient information, including images of radiology or lab results and real-time patient data.

As part of our efforts to reduce health care costs and maximize efficiency, a fleet of TUG mobile robots transport food, linen, waste, equipment and supplies.

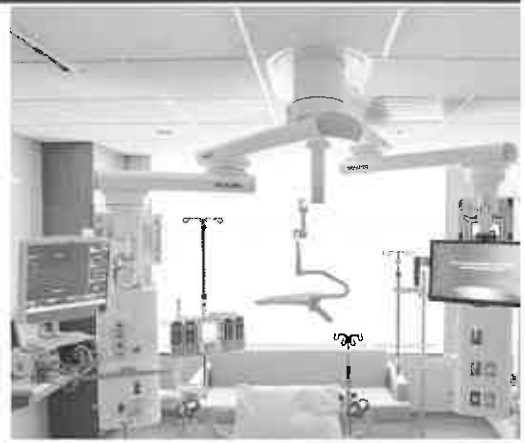
INTERACTIVE PATIENT CARE

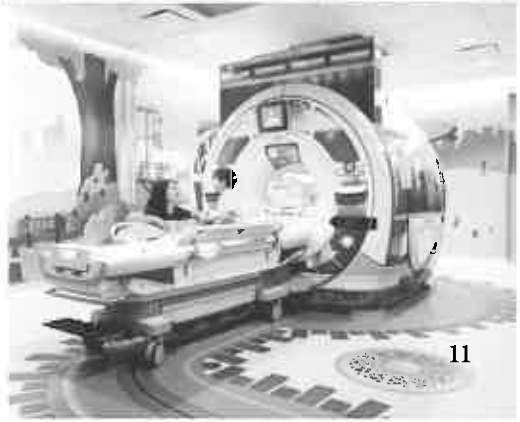
Large, smart displays coupled with bedside tablet computers are in the patient rooms as part of Oneview interactive patient care system, a hub for education and entertainment.

All patients can use the Oneview system to consult with clinicians, learn about their medical conditions and treatment plans and order meals. Children can continue their studies with classmates. Adults can stay in touch with faraway relatives and friends.

IMAGING SUITE

In the new children's hospital, children undergo CT scans and MRIs in a specialized imaging suite that allows them to select a theme of sights and sounds, thereby transforming their diagnostic visit into an adventure tailored to their particular interests. This minimizes their anxiety and restlessness, resulting in better-quality scans.





Innovative Spaces That Optimize Care and Create Community (cont.)

UCSF RON CONWAY FAMILY GATEWAY MEDICAL BUILDING

The new medical center provides a continuum of care through specialty outpatient services housed in UCSF Ron Conway Family Gateway Medical Building at the north end of the complex. The six-story building has clinics for everything from dialysis to pelvic reconstructive surgery, from pediatric oncology to cardiac care. With 126 exam rooms, 10 outpatient procedure rooms, 18 specialty rooms such as audiology booths, five dialysis stations and 36 infusion bays, this facility can accommodate more than 120,000 visits annually from women, children and cancer patients. The building is also the home of San Francisco's only regularly operating hospital helipad.

LEED GOLD MEANS ENVIRONMENTAL SUSTAINABILITY

UCSF Medical Center at Mission Bay integrates best practices in sustainable architecture to create a hospital complex that enhances the healing, health, safety and well-being of our patients, while also preserving our environment. By conserving water, improving energy performance, incorporating healthy building materials and more, we are the first facility of our size in the US to receive LEED (Leadership in Energy and Environmental Design) Gold certification.

FOURTH STREET PUBLIC PLAZA CONNECTS US TO OUR COMMUNITY

We worked with the City and County of San Francisco to transform Fourth Street from a busy vehicular thoroughfare to a dynamic, car-free public plaza that includes:

- A multipurpose, tree-lined promenade for pedestrians and bicyclists
- A raised amphitheater for outdoor events and concerts
- A bench walk well suited to lounging in the sun
- A peaceful tree grove for relaxing breaks

The plaza is the crowning touch on an intimate, innovative and expansive community of healing and restoration.

UCSF BENIOFF CHILDREN'S HOSPITAL SAN FRANCISCO is named in honor of Marc and Lynne Benioff, whose generosity helped build a new home for UCSF Benioff Children's Hospital at Mission Bay. The Benioffs' goal is that the state-of-the-art facility serve as the most advanced children's hospital in the world, providing patient-centered care, supporting the translation of medical research into clinical practice, developing the next generation of medical technology and training the caregivers of the future who will advance health care worldwide.

The UCSF BETTY IRENE MOORE WOMEN'S HOSPITAL is named in honor of Betty Irene Moore, a patient safety pioneer and advocate. The generosity of Bay Area residents Gordon and Betty Moore helped fund the region's first women's hospital and advance the innovative initiatives of the UCSF National Center of Excellence in Women's Health. The Moores' leadership and philanthropy have profoundly influenced health care practices throughout the United States.

The UCSF BAKAR CANCER HOSPITAL was named in recognition of philanthropists Gerson Bakar's and Barbara Bass Bakar's long-standing commitment to support cancer programs and research at UC San Francisco. Located adjacent to a state-of-the-art cancer research building, the facility brings clinicians and researchers together to not only develop new treatments, but also bring these treatments to the patient's bedside more rapidly.

The UCSF RON CONWAY FAMILY GATEWAY MEDICAL BUILDING is named in honor of angel investor and philanthropist Ron Conway, his wife, Gayle, and their sons, Ronny, Topher and Danny. The Conway family's generosity helped fund the outpatient medical building at UCSF Medical Center at Mission Bay, a facility noteworthy for the connection it provides between the high-quality inpatient medical care provided at the three specialty hospitals and the groundbreaking continuing care that is provided to outpatients.

UCSF Medical Center

UCSF Benioff Children's Hospitals

The Mission Bay hospitals are comprised of:

UCSF Benioff Children's Hospital San Francisco
1975 Fourth Street
San Francisco, CA 94158

UCSF Betty Irene Moore Women's Hospital
1855 Fourth Street
San Francisco, CA 94158

UCSF Bakar Cancer Hospital
1855 Fourth Street
San Francisco, CA 94158

UCSF Ron Conway Family Gateway Medical Building
1825 Fourth Street
San Francisco, CA 94158

Website: www.ucsfmissionbayhospitals.org | **Phone:** 415-353-3000 | **Maps and directions:** www.ucsfhealth.org/pathway

UCSF Medical Center and UCSF Benioff Children's Hospitals strive to provide equal access to our facilities and services for our patients with disabilities. For more information or assistance, please call Patient Relations at 415-353-1936.

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Salk **Calendar**

SEPTEMBER

22 Back to Basics Lecture

24 San Diego Salkexcellerators private dinner

OCTOBER

11 Salk Science & Music Series
featuring Vadym Kholodenko

28 San Diego Salkexcellerators private reception
and scientific presentation

NOVEMBER

8 Salk Science & Music Series
featuring Asi Matathias & Victor Stanislavsky

DECEMBER

2 Salk Women & Science

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August 2015
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One on one with... Beverly Emerson

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Dear Friends,

WITH CALIFORNIA'S DROUGHT PERPETUALLY IN THE HEADLINES, it's an opportune time to note the advancements made by Salk scientists who specialize in plant biology. The feature story in this issue of *Inside Salk* reveals how teams in the labs of **Joanne Chory** and **Joseph Noel** are identifying some of the tools, such as genetic variations and molecular mechanisms, that plants use to adapt to environmental challenges. Theirs is vitally important work that too often does not receive the spotlight. But a burgeoning global population combined with the disruptive changes to our climate means that such work is critical to human survival.

I might add that one of the oldest trees in the world—a 5,000-year-old specimen that has withstood many droughts, along with pests, disease and erratic changes in climate—continues to survive here in California. It's living—and thriving—proof there is hope for plants and for us.

You'll find that advancements in neuroscience comprise many of our other recent discoveries. **Martyn Goulding** has mapped circuitry in the spinal cord that facilitates balance; **Dennis O'Leary** demonstrated the amazing plasticity of neurons; **Ronald Evans** identified a metabolic protein that impacts both physical and mental activities; and **Sreekanth Chalasani** added to our understanding of how chemical signals influence risk-taking behaviors. **Juan Carlos Izpisua Belmonte**, who earned publication in three top biomedical journals—*Cell*, *Nature* and *Science*—in the space of a few weeks, devised a method to eliminate the transmission of mitochondrial disease and tied the aging process to deterioration of DNA packaging.

Additional recent achievements at Salk include **Inder Verma**'s development of an "immune system-in-a-dish" that offers hope for those with blood disorders, and **Kathy Jones'** investigation into a cellular pathway that directs the growth of stem cells, a process that is key to regenerative therapies.


William Brody

The volume and significance of these advancements speak to the level of science taking place here at the Institute. It is work that is recognized beyond our walls, and I'm proud to congratulate **Dennis O'Leary** and **Joseph Ecker** on their election to the American Academy of Arts and Sciences; **Vicki Lundblad** to the National Academy of Sciences; **Joanne Chory** to the American Philosophical Society; and **Nicola Allen** on being named a Pew Scholar. Our investigators strive to be at the very forefront of science and I hope you'll find, as I do, that their stories make for inspiring reading.

William R. Brody

William R. Brody, MD, PhD
President, Salk Institute
Irwin Mark Jacobs Presidential Chair

ON THE COVER

Regions around the world are experiencing drought and desertification due to climate change. Plant biologists at Salk are discovering ways to help plants—and us humans—adapt to new environmental extremes.

Plants have adapted to Earth's extremes. Can they help humans adapt to climate change?

Seeds of Change

HIGH IN THE WHITE MOUNTAINS OF CALIFORNIA, anchored to a rocky slope by its gnarled roots, is a tree older than Methuselah.

Now knotted and twisted with age, the tree sprouted from seed hundreds of years before the Egyptians built the great pyramids. It was roughly 3,000 years old when Julius Caesar was born and 4,000 years old when Genghis Kahn ruled the Mongol Empire. The ancient arbor, a bristlecone pine, predates its famous California neighbor, "Methuselah," another bristlecone named after the Bible's longest-lived man and once thought to be the oldest tree in the world.

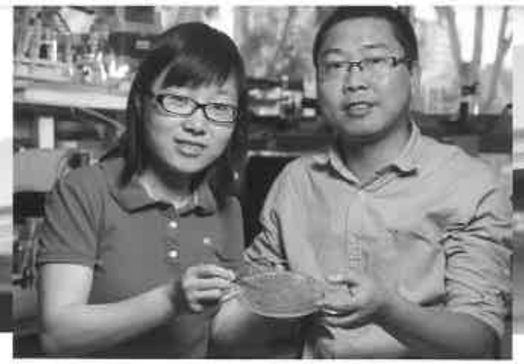
Over its 5,064-year lifespan, the pine has experienced droughts as bad, if not worse, than the one currently parching California and other parts of the American West. It has lived through long snowy winters, insect invasions, lightning storms, raging forest fires, torrential rains—a litany of ordeals. The tree's life is an epic tale, but what can we humans learn from a weathered old tree? Perhaps the most poignant lesson is this: to stay in one place requires remarkable flexibility. To survive is to adapt.

"With our nomadic tendencies, we rely on our mobility for our survival," says **Joanne Chory**, director of Salk's Plant Molecular and Cellular Biology lab. "If our current location gets dicey, we can make tracks for another. For plants, though, location is destiny. Because of this, they have developed a wide range of tools for adjusting to whatever their environment throws at them."

It is these tools, a range of genetic programs, molecular devices and versatile chemistry plants deploy like the blades of a Swiss Army knife, that Chory and other Salk plant biologists are intent on cataloging and describing. In this quest, they are propelled by curiosity, the scientist's driving force. But another powerful motivation is necessity—the need to ensure the longevity of *Homo sapiens*.

Jianyin Huang observes seedlings grown in a high-light chamber. Her research could help develop new high-light tolerant crop varieties.

California's bristlecone pines are some of the oldest trees in the world.



Jianyan Huang and Xiaobo Zhao explore how plants cope with stress from excess light and heat.

Crunch Time for Farmers

To understand what's at stake, it helps to consider that the global human population recently topped 7 billion and is expected to reach 10 billion in just 35 years. This population crush equates to crunch time for farmers. More people means surging demand for the myriad of products plants provide, from food on the table to the shirts on our backs. United Nations experts predict that agricultural yield must double in the next two decades to meet the demands for natural resources. And as the pressure on farms constantly increases, weather patterns are increasingly inconstant. Thanks to global climate changes, some regions are experiencing extreme drought and desertification, while others are experiencing violent storms and flooding.

"In California right now, everyone's focused on the drought, and for good reason, but water stress is only one kind of stress plants experience," says Chory, who is also a Howard Hughes Medical Institute Investigator and holder of Salk's Howard H. and Maryam R. Newman Chair in Plant Biology. "These old bristlecone pines, exposed on the side of a mountain, have seen extremes of all sorts—really hot, really cold, lots of water, no water.

"Agricultural crops grow in more moderate conditions," she adds, "but they still have to cope with various kinds of stressors, and farmers have to make sure they plant the right varieties for the climate, or they'll end up with a poor yield or dead crops. With rapid climate change, a great challenge is for our agricultural practices to keep up with environmental extremes."

This is where science can help. One of the great breakthroughs in science was the discovery that when farmers breed for certain desirable characteristics, they are selecting for certain genetic patterns. A recent study published in the journal *Cell*, for instance, identified a specific gene, COLD1, that confers cold tolerance to domesticated rice grown in Japan, where temperatures can be too chilly for wild rice species. Finding a gene that helps a plant survive cold stress helps explain what was going on under the hood as farmers drove rice cultivation further north. It might also help in the development of new varieties of cold-tolerant rice or convey cold tolerance to other crops through genetic engineering.

As Chory points out, a single plant can experience a range of extremes over its lifetime, or even over the course of a year. **Joseph Noel**, another Salk plant biologist and longtime collaborator with Chory, notes that there are trade-offs in a plant's ability to tolerate certain types of stress.

"A plant that is highly drought resistant isn't going to grow as well in a rainy year," says Noel, holder of Salk's Arthur and Julie Woodrow Chair and also a Howard Hughes Medical Institute Investigator. "Ideally, a farmer would be able to look at the climate forecast for the upcoming growing season—which have gotten much more accurate—and pick a crop variety that's optimized for the predicted weather. It would work sort of like getting a yearly flu shot, where the vaccines are developed based on informed predictions. It won't work all the time, but on average, you'd come out with better results and more sustainable crop yields."

Plants, Proteins and Possibilities

In a new line of research, Noel's lab is exploring a related concept: how plants respond to subtle variations in drought. Specifically, he's studying a plant hormone called abscisic acid (ABA) that, among other things, turns on a plant's emergency response program during drought. When the roots sense the soil is drying out, they release ABA, which travels through the stems to the leaves. There, the hormone closes the stomata, the openings in the leaves that exchange oxygen for carbon dioxide. This conserves the plant's water stores, as water vapor can escape from the open stomata. Scientists knew that ABA signaled the stomata to close by flipping molecular switches known as PYR/PYL receptors, 14 varieties of which are found in *Arabidopsis thaliana,* a mustard plant that serves as a model for plants in laboratory research. Initially, scientists thought the interactions seemed to be all-or-nothing in that ABA bound all versions of the receptor, switching them all on when it was present. In recent studies however, Noel's team believes they've uncovered a more complex relationship, one in which alternate forms of the ABA bind some, but not all, of the PYR/PYL receptors, and bind some receptors more tightly than others.

"Looking at this through the lens of evolution and adaptation, it could mean that this gives you a range of different responses to dry soil," says Noel. "We thought the ABA drought response function was an on-off switch, but maybe it's more like a dimmer switch, where you can dial in a precise response to water stress. Back to that idea of precision agriculture: the farmer could pick the appropriate variety of plant based on its ABA profile and match it to climate forecasts."

In another project, **Charisse Crenshaw,** a postdoctoral researcher in Noel's lab, has teamed up with Salk Associate Professor **Tatyana Sharpee**, an expert in computational biology and neuroscience, to study the flexibility of a plant's genome in responding to its environment. Plants have apparently repurposed a few basic protein designs to serve multiple functions, exploiting a biochemical phenomenon called "promiscuity."

Crenshaw's focus is on the largest class of natural products, called terpenoids, which are responsible for plant defenses and a

Joanne Chory

Chanelle Crenshaw studies the functionality of a plant's genome in responding to its environment.

number of other functions, including generating aromas that attract bees or deter plant-eating organisms. Oranges, for instance, produce a terpenoid called valencene that smells like...well, oranges. Terpenoids also give mint and lemongrass their distinctive scents. Small changes in the genes responsible for a subclass of terpenoids, known as terpene synthases, allow these enzymes to output diverse chemicals that protect the plant against a range of different foes, including bacteria, fungi and insects. Crenshaw hopes to shed light on the origins, evolutionary history and driving forces responsible for this vast diversification of function.

Crenshaw and Sharpee study a terpene synthase from tobacco called 5-epi-aristolochene synthase (TEAS) that helps generate a natural antibiotic, capsidiol, to protect the plant from mold during wet periods. The plant generates TEAS based on instructions in its DNA, and variations in that gene among different plants result in terpene synthases with different shapes. The plants produce versions of TEAS that best help them defend themselves in their local environment. In other words, plants have learned how to combat antibiotic resistance long before we humans even knew antibiotics existed. In the laboratory, Crenshaw and colleagues generated 500 versions of TEAS by mixing and matching mutations that were identified in nature much like others have identified specific mutations in various human cancers. Tweaking the DNA code altered the sequence of amino acids, which in turn changed the enzyme's properties when the long chain of amino acids folds into a three-dimensional structure. When Crenshaw tested the heat tolerance of the different TEAS mutants the results were surprising.

Working with Sharpee and University of California, San Diego graduate student Jonatan Aljadeff to apply theoretical models borrowed from physics to analyze the data, Crenshaw found that many combinations of the mutations she introduced had modest effects on the thermal stability of the molecules. For instance, most of the proteins were stable up to 40 degrees Celsius (or 104 Fahrenheit), within some range. But this wasn't always the case. Some of her tiny tweaks led to huge shifts in thermal stability, with some of the proteins capable of withstanding temperatures of up to 53 degrees Celsius (127 Fahrenheit).

"Most variations of TEAS have similar characteristics, so it's almost as if there is a mechanism keeping the thermal stability of the protein close to the status quo," she says. "But then you've got these occasional non-linear effects that pop up, where the proteins are stable at temperatures way outside of the norm. So, resilience to even higher temperatures can be accessed through relatively few DNA sequence mutations. And this is possible without plants losing their ability to synthesize critical natural chemicals used for protection and improved growth."

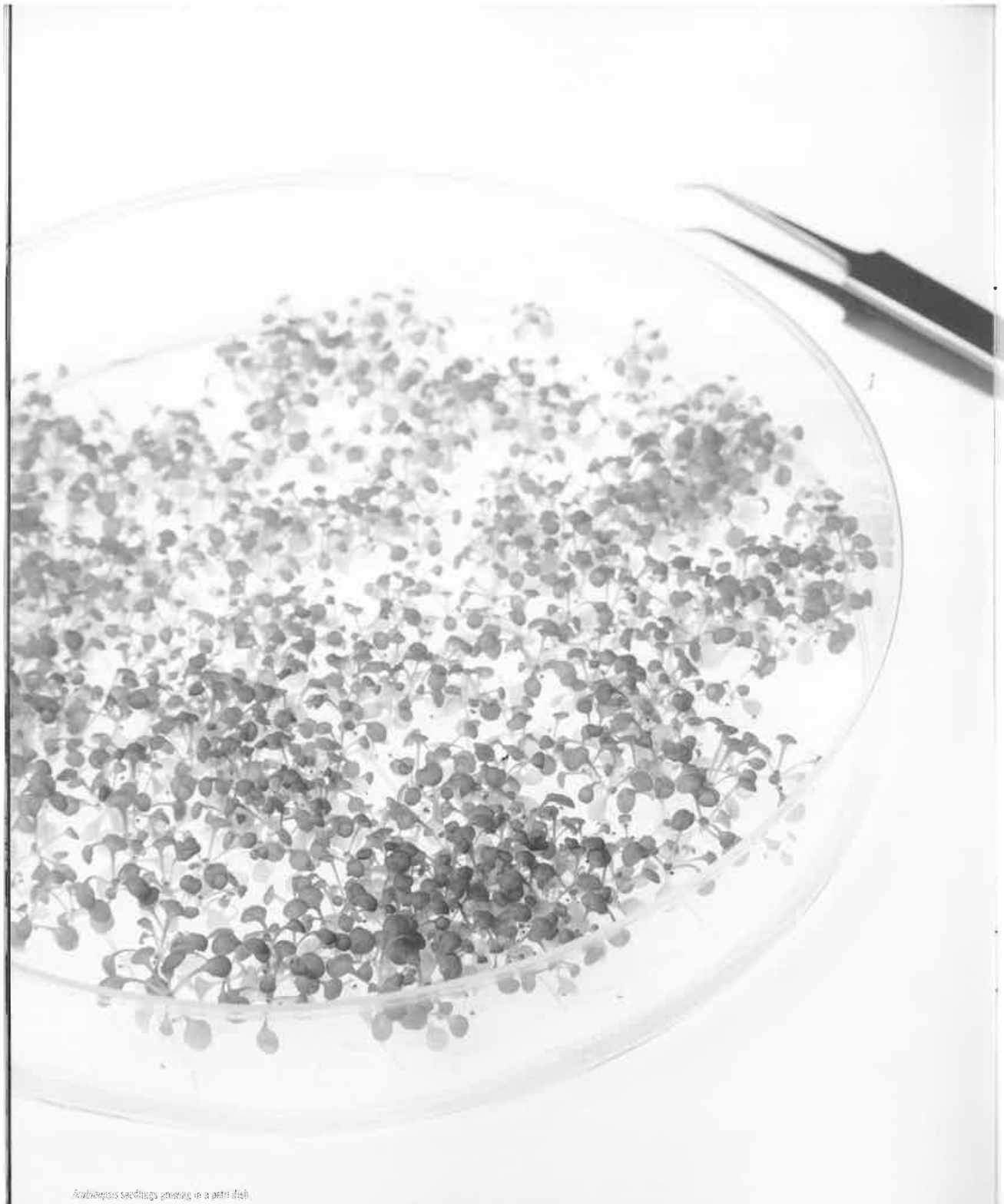
"I'm really interested in exploring what's possible," Crenshaw adds. "The potential in the plant genome to adapt to wide variations in climate is vast. I believe this is the power and promise of understanding plant evolution to help us adapt to changing climates across the globe."

Some Like it Hot

Crenshaw's quest to plumb the possible is really an extension of something humans have been doing for thousands of years. Because we have always relied on plants for our survival, it's a good bet that we humans have eaten (or gingerly tasted) every plant we've encountered. Many of those we liked, we've modified to our tastes. In the case of the wild cabbage, for instance, humans selecting for different desirable characteristics turned a single species, *Brassica oleracea*, into a smorgasbord of crops that includes broccoli, cauliflower, kale and Brussels sprouts. Corn is another prime example. Corn has long been a food staple in the Mexican culture of the Baja California region near the Salk Institute. The modern corn used by Mexican families to make tortillas and tamales is a far cry from the primitive maize plant, which produced a single, spindly cob covered in tiny kernels. First domesticated 10,000 years ago by ancient farmers, millennia of artificial selection have produced the robust, completely domesticated varieties that produce multiple large cobs per plant—each covered in juicy, pea-sized kernels.

In other cases, plants we use for food didn't need any coaxing to survive—even when we moved into less than hospitable climates. Those Mexican families mentioned earlier also eat wild prickly pear cactus. This thorny emblem of the desert is a great example of a plant that can survive in an extreme environment. In addition to being dry, deserts are also extremely hot and sunny, and as a result cacti and other desert plants are fine-tuned to these conditions. These adaptations are the result of millions of years of natural selection, but what if domesticated crop varieties could be conferred similar properties through traditional breeding or genetic engineering? If so, it might improve crop yield during hot, dry climate swings or allow crops to be introduced to new regions—for example, wheat could be grown in a more arid climate than is now possible. The first step to answering the question is to untangle the molecular pathways and genes that are activated when a plant is stressed by heat and high light—exactly the challenge that Joanne Chory's team is currently tackling.

In the cells of a plant's leaves, organelles known as chloroplasts are responsible for photosynthesis, the conversion of light energy into chemical energy necessary for the plant to survive. The energy captured is used to convert carbon dioxide from the air into high-energy compounds like glucose and starch. One of the byproducts of



Arabidopsis seedlings growing in a petri dish

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photosynthesis is oxygen, which is released as a waste product and creates the atmosphere we oxygen-breathing creatures require to roam the Earth.

Because chloroplasts are so essential to a plant's survival, it is critical for a cell to be informed about their functional state and for the cell's nucleus, its control center, to operate in concert with the chloroplasts. The nucleus contains the majority of the plant's DNA, but the chloroplasts also contain a short strand of DNA. Chloroplasts were once independent microorganisms, but somewhere along the line were incorporated into plant cells. Chloroplasts contain about 117 genes, 87 of which are code for proteins involved in directing chloroplast function.

In previous groundbreaking research with *Arabidopsis*, Chory's team discovered how the nucleus and chloroplasts communicate about the production of the photosynthesis machinery. Parts of the system are built in the chloroplast and other parts are built in the nucleus, but the final molecular complexes are assembled in the chloroplasts. They found that signals sent from the chloroplasts to the nucleus helped coordinate this complex process. In another study, Chory and her collaborators identified a gene that is a key player in signaling between the chloroplasts and nucleus. That discovery laid the groundwork for exploring precisely how plants respond to stress, since coordinating cellular responses to protect and repair chloroplasts is critical to a plant's survival. It also suggested an avenue for augmenting a plant's resilience to environmental stressors.

More recently, **Jesse Woodson**, a staff scientist in Chory's lab, has identified a mechanism in plant leaves that tells cells to recycle chloroplasts damaged by extreme heat, light or other stressors. By removing the damaged chloroplasts, this system theoretically prevents the entire cell from dying.

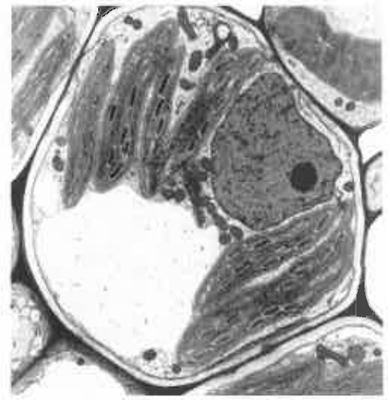
"Maintaining an existing cell takes less energy than generating an entirely new one, so this could be a damage control strategy for plants," says Chory.

In another ongoing line of research, **Xiaobo Zhao**, a postdoctoral researcher in Chory's lab, found that a certain gene mutation made plants more sensitive to heat stress. He is now exploring whether amplifying the expression of the normal form of the gene might make plants more heat resistant. "One goal is to identify the entire pathway by which plants respond to heat stress," Zhao says. "There are general stress mechanisms that are triggered by a number of different stressors, whether it's a cold snap or a hungry insect, but we think we've found a gene that is specifically involved in heat stress. We are also hoping to find ways to control a plant's heat response, so it could grow efficiently in hotter climates, and this gene is a promising lead."

A Bright Future

On a related front, the Chory lab is searching for a switch that controls plants' response to light intensity that is especially high. Plants have evolved to Earth's particular light cycle and to the light conditions found at the longitude and latitude they call home. Farmers often grow crops that originate in climates that are very different from that of their farms. In places like Australia, Africa, Mexico and the southwestern United States crops have to contend with sunlight that is particularly intense—more intense than many plants need or can withstand.

"When there is more light than the plant needs, the excitation energy exceeds the capacity of the photosynthetic apparatus, which results in a buildup in leaves of reactive oxygen molecules such as hydrogen peroxide," says **Jianyan Huang**, the postdoctoral researcher leading the study. "These molecules trigger a stress response to the high light conditions. If the plant's response isn't adequate, the excess reactive oxygen can damage the plant—for instance, damage to chloroplasts and the loss of chlorophyll results in the leaves turning pale, a phenomenon known as bleaching."



Chloroplasts (green), the living solar panels within a plant cell, can be damaged by extremes of temperature and light.

One way a plant responds to extreme light conditions is to put the brakes on its photosynthesis system. When reactive oxygen molecules start to build up, the plant cells reduce the size of the light-harvesting complex in chloroplasts to relieve the oxidative stress. It's akin to removing the solar panels from your roof on an extremely sunny day to prevent damage to your house's electrical system.

In ongoing experiments, Huang is trying to identify molecules that trigger the high light stress response by activating certain genetic programs in plant cells. She's screening a collection of 2,000 *Arabidopsis* transcription factors, proteins that control which genes are turned on or off. She has identified a number of possible candidates from the collection, and she's currently testing to see whether they are capable of activating genes known to be involved in the high light stress response. Her experiments have turned up some promising results, including identifying several proteins that appear to switch on the high light response. Similar to Zhao's work, her findings could lead to a way to develop agricultural crops that can be farmed in places where high light periods are a threat.

"Our work in *Arabidopsis* and other model organism plants sets the stage for identifying the same genes and molecular pathways in crops," says Chory. She notes, for example, discoveries made in *Arabidopsis* have been instrumental in the development of tomatoes rich in carotenoids, naturally occurring pigments that give vegetables their yellow, orange, and red hues. In addition to providing color, carotenoids such as beta-carotene, lycopene, lutein and zeaxanthin are important dietary nutrients. Another variety of tomato developed separately contains high levels of anthocyanins, plant pigments that are antioxidants and have been shown to extend life in mice with cancer. Tomatoes high in anthocyanins are more purple than red—owing to the bluish color of the anthocyanin molecules.

Scientists in academic institutions and biotech companies are also working to develop drought-tolerant crops, both through traditional crossbreeding and through genetic engineering. For instance, the Drought Tolerant Maize for Africa project has generated 153 new varieties of drought-tolerant maize. In early field trials, these varieties yielded 30 percent more under drought conditions compared to commercially available varieties under normal rainfall conditions. Another project, organized by the African Agricultural Technology Foundation in Nairobi hopes to have a transgenic variety of drought-resistant maize available for African farmers as soon as 2016.

"At Salk, we're not in the business of developing new crops, but we find the genes and pathways that are responsible for the stress response and which can be leveraged to improve agriculture," says Chory. "The more we know about the plants we rely on, the more resilient we humans will be as a species. Change is coming, that much you can be sure of. The big question is how we will respond."

One on One with...
Beverly Emerson

ENORMOUS FOSSILS IN GLASS CASES AND A DUO of plastic dinosaurs adorn biologist Beverly Emerson's study at the Salk Institute. Though the décor may seem unrelated to Emerson's study of processes that underlie cancer, the fossils and dinosaurs have common themes with the deadly disease: evolution and diversity in nature.

Rather than viewing tumors as originating from a single mutated cell that goes awry, Emerson looks at how cancer develops its own diverse "society" (a tumor) that is stubbornly resistant to threats such as chemotherapy.

Emerson came to the Salk Institute in 1987, where she has made seminal discoveries showing how enzymes can remodel chromosomes in normal cells or how this process goes awry to allow cancer to thrive. Her current efforts are focused on combating early cancers (such as breast cancer) and managing the cellular diversity that is required for drug resistance in established tumors. Emerson also has a personal interest in health, particularly around the philosophy of food and self care.

What was your path to becoming a scientist?

When I was young, I wasn't interested in science. I wanted to be a boxer or an artist. My dad was both, as well as a diesel mechanic, but I never quite grasped how engines worked. Instead, I was my father's sparring partner. Due to Dad's excellent coaching, I retired undefeated at age 8!

After retiring from the ring, I continued my artistic endeavors by painting and wood carving. As an undergraduate at the University of California, San Diego, a class on molecular biology riveted my attention to science, saving me from a career as a mediocre artist. I was struck by the elegance of how genes were regulated and the logic of transcriptional and biological circuitry, like a machine itself. Those concepts have hooked me ever since.

My dad taught his children to be freethinking and not tolerate bullying, while my mom was very optimistic and thought everything was possible. Each parent had a great sense of humor and neither liked hierarchy. I carried these traits into science: follow your own path and don't look for others' approval, as well as a belief that everything will work out, even if there are long downtimes for experiments to succeed.

Do you feel a connection between art and science?

Every successful scientist I know is also highly creative in an artistic way. The best scientists see not only the importance and significance of what they're doing, but also the beauty of it. It doesn't have to be uncovering a major principle. Just finally understanding a small question or achieving a little yet vexing technical feat has a beauty to it.

People think of science as being very dry, but meticulous and repetitious experiments are the medium scientists have to use: it is their particular paintbrush or musical instrument. When you make a discovery, the beauty of it is thrilling. They call that the "aha" moment, but it's more than that. There's a sense of the aesthetic in one's discovery and in nature.

Why is cancer so drug resistant?

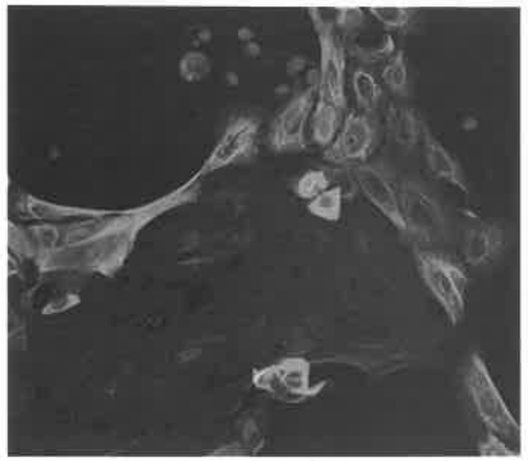
When we keep challenging cells without killing all of them with one chemotherapy drug, cancer develops a specific mechanism to survive. This is like if a town has a flood every week—eventually, the survivors adapt and learn to become expert swimmers. Now, if you're hit with unexpected threats—for cells, a cocktail of chemotherapy drugs, or for people, a natural disaster—there are usually still some that remain because cells and people are diverse in their capabilities to maximize survival.

We liken drug resistance to evolution. Our studies and those of others show that nature has programmed cells to be diverse to ensure survival in harsh conditions. I had trouble wrapping my head around this because, while there is beauty in nature striving for life at every level, drug-resistant metastatic cancer cells are our enemy. Somehow, nature is not distinguishing between the driving force for normal cells versus cancer cells to survive.

How are cancer cells like "angry, ostracized people?"

A simple way to think about cancer is that it starts from a single, mutated cell that takes on a life of its own and begins to metastasize. But perhaps a more accurate view is that cancer exists as part of a community within a larger ecosystem. A damaged cell can sit in your body forever and never wreak havoc. It's when the relationship between one cell and its community breaks down that the formation of tumors begins.

Some of the first genes to go awry in cancer are those that control the ability of cells to contact each other, called cell adhesion. Now, if you're a stressed cell and lose contact with your neighbors, you have a very different relationship with your environment. Like an angry person that's been ostracized from a community, that cell forgets its social contract in a sense and begins to act erratically.



Immunostaining shows the organization of different types of normal human mammary cells, which will be compared against precancerous and tumor-causing cells.

One area of cancer that we do not understand that relates to this "community" of the body is the higher-order communication between our overall physiology and control of metastasis. Some patients with cancer, for example, simply waste away (cachexia), as if the higher-order operating system had made the calculation for the body to give up. This mind-body relationship to one's health is a poorly understood area but worth exploring.

How do you de-stress?

I love to snorkel in Cancun and recently tried the flying trapeze—it was a lot of fun. I enjoy travel, from eating a giant gelato in Italy, hiking in New Zealand, getting a camel kiss in Jordan and riding a yak in the Himalayas. At home, I regularly cycle, go to the gym and take our large, loveable but unruly dogs hiking in nearby canyons as a courtesy to our neighbors.

Aside from those activities, I have recently focused on a holistic approach to food in the last few years. What started as a scientific interest in reading all the strange stuff listed on food labels and seriously wondering how this was affecting my epigenome grew into an ethical philosophy for me.

"The best scientists see not only the importance and significance of what they're doing, but also the beauty of it."

Beverly Emerson and Fernando Lopez-Diaz

When did you start to think more deeply about food and consumption?

On a trip to D.C. about ten years ago, I walked by a poster that opened my eyes to the conditions in which factory farm-raised animals are kept. That was an epiphany for me and greatly raised my compassion and awareness about the connection between ethical treatment of animals, contamination-laced produce, artificial foods and diet-based human disease. I never thought I'd be interested in food books, but I started to read about corporate-controlled food politics in books like *What to Eat* by Marion Nestle and *In Defense of Food* by Michael Pollan.

I also was inspired by *French Women Don't Get Fat* by Mireille Guiliano whose central message is to give yourself lots of variety, take the time to buy and prepare only the best stuff, and bother to put a flower on the table just for you. In this way, grocery shopping can become a reflection of a life philosophy.

In the end, we still don't understand why some people are able to overcome disease—like cancer—and others don't. We rely on our bodies to take care of ourselves so we must treat our bodies with respect.

You've mentored dozens of young scientists. What knowledge do you try to impart to them?

Being a mentor has been both my greatest joy and my greatest frustration. You see some people who have intelligence and work hard, but are held back from reaching their full potential by fear: either fear of failure or of peer review upon completion of their project. It's a given that to be a successful scientist you need several traits: intelligence, dedication, perseverance, optimism, willingness to accept criticism. You quickly learn as an advisor that the best people have all of these qualities and I am just cultivating them for that extra mile.

My own mentors—Peter Geiduschek from when I was a UCSD undergraduate, Robert Roeder during my graduate work at Washington University and Gary Felsenfeld from my postdoctoral studies at the NIH—were almost as important to me as my parents in influencing my growth and development.

You've given several talks on women in science. What are your thoughts on the landscape today?

I think things are better for women and minorities, but the culture still needs to improve. In general, it's easy to be generous to a person junior to you, but the glass ceiling really comes into play when women reach higher levels. At these levels, the more enlightened leaders willingly step aside and remove barriers to elevate qualified and deserving individuals who are underrepresented. The "boys' club" culture at a professional level is an embarrassing anachronism.

My advice to women scientists is not to put up with the glass ceiling. If your institute or company isn't providing you with opportunities for fair advancement, go to another organization. Sometimes—and this is the case for all scientists—you have to take a step back from the daily grind of grants and papers to look at the system you operate in and see if it's good for you and serves your best interests.

Any parting thoughts to living the life of a scientist?

In my own experience, I can delineate three stages to becoming a scientist. The first is embracing the culture: I observed as a naive undergraduate in Dr. Geiduschek's lab how no sacrifice was too great for the good of one's experiment. I was very impressed by the dedication of people who routinely came back to the lab at 2 a.m. to optimize their experiment.

The second phase of becoming a scientist is as a graduate student, when you are becoming a journeyman who masters the craft of being an accomplished experimentalist. This often requires doing things over and over for years to learn to solve a problem rigorously.

Thirdly, once you've mastered your craft, you develop self-confidence and judgment. Not only can you do the experiments at this point, you can figure out which problems are worth exploring. As a postdoc at the NIH and later a faculty member, I learned to trust and follow my passion.

Ultimately, living the life of a scientist has been a wonderful journey of self-discovery and a golden opportunity to share my professional life with many outstanding people.

Next generation:

Laura Tan

WHEN LAURA TAN GOT A REQUEST to present a two-minute elevator pitch on her work to faculty and high-end donors, she got a little nervous. When she heard that actor/director Robert Redford and Salk Board Chair Irwin Jacobs were expected to be in the audience, she got excited.

"It was really, really fun," says Tan, a research associate in the Laboratory of Neuronal Structure and Function led by **Paul Sawchenko**. "With two minutes, you really can't get into detail. You are giving a teaser trailer like a movie, just giving little snippets so they come talk to you afterwards."

As it turned out, Jacobs and Redford missed Tan's talk—which included a PowerPoint slide of Fort Knox to represent how impenetrable the brain can be—but rather than be crestfallen, Tan channeled her customary ebullience into the rest of the evening. Several attendees—people she would probably not have met otherwise—approached her to learn more about her work on how the brain perceives and processes stress signals. And she did get to chat with Jacobs and Redford at the evening reception, where Redford requested meeting the postdoctoral researchers.

"It's kind of nice to be a rock star in research for two minutes," says Tan. Game to try anything—be it stopping a fast break in lacrosse or landing her alto to a choir—Tan is fueled in part by the three cups of coffee she drinks every day and in part by an insatiable curiosity for what makes the brain tick, particularly when it's under siege by stress. For the past year, she has turned her considerable energy to studying stress and its effect on Alzheimer's disease.

One of the problems with treating Alzheimer's is that drugs have difficulty crossing the blood-brain barrier, a highly selective fortress that keeps pathogens out of the brain by separating circulating blood from the brain's extracellular fluid in the central nervous system. That makes delivering a beneficial central nervous system drug in a pill or blood injection difficult, as it has to flow through the entire body with perhaps little, or none, of the drug getting into the brain. It can create toxicity problems along the way affecting the liver, heart, digestive tract and more. And the stress receptor Tan is targeting exists outside of the brain as well, creating more complications for treatment.

If the brain is like Fort Knox, says Tan, the rest of the body is like the Kentucky countryside. "We could go in with planes and tanks to try and get to the gold in Fort Knox, but it would destroy most of Kentucky in collateral damage, which is extraordinarily bad because I like bourbon," she jokes. "In this metaphor, drugs designed for the brain can destroy the body and never even reach their target."

Tan is investigating alternative ways of delivering drugs that block corticotropin-releasing factor (CRF) receptors that are both efficacious and targeted to the brain and that do not require invasive procedures (such as brain surgery) for the treatment and prevention of Alzheimer's disease.

"We are using a sneaky Ocean's 11 approach where we are coming in through the back door," Tan says. "We are going with a smaller team. We are getting in and out with the gold without destroying anything outside."

To accomplish this, Tan uses an intranasal administrator, similar to an asthma inhaler, to deliver drugs precisely to the upper olfactory region of the nasal cavity in her mouse models. Neurons in the mucous membrane that lines the nasal cavity send their axons through the skull to the brain, the same pathway that gives humans their sense of smell. Using this non-invasive route, Tan and her colleagues have been able to show that it can transport lower doses of drugs—in this case, a compound that binds to one receptor—across the blood-brain barrier, thereby sparing peripheral tissues from exposure.

"CRF was discovered at Salk in **Wylie Vale**'s lab in 1981," Tan says. "The fact we are pursuing this feels organic. It's a very Salkian thing to do."

Tan, 33, hails from Mississauga, the sixth largest city in Canada. Her father, a chemical engineer, and her mother, a social worker, never pushed her toward a science career, but she was inspired by her uncle, Larry Tan, who discovered the first acellular vaccine for pertussis. The vaccine contains cellular material but not whole-cell bacterium to invoke an immune response to create antibodies in the patient.

Tan always thought she would be a medical doctor until her senior year at the University of Toronto when she got her first taste of lab life and was hooked. Up to that point, she felt her studies had been all about memorizing and regurgitating information.

"We do that here, too, but I feel we are creating the knowledge," Tan says. "I don't have to be the encyclopedia, but I do have to use the encyclopedia and then apply it to what I'm doing. I like science because I get to ask the questions I want to ask."

Characteristically, Tan plunged head first into the sprawling 50,000-student experience of the University of Toronto. In addition to biology and humanities coursework, she organized an intramural sports program, playing on more than 100 teams. The "Laura A. Tan Award" was created to honor her contribution to athletics at the college.

Graduating with distinction in zoology/biology with a minor in classical civilizations, Tan remained at the University of Toronto to earn her PhD in neuroscience. She did her doctoral studies under David Lovejoy, a former Salk postdoctoral researcher in Vale's lab.

When she began casting her net for a postdoctoral position, Tan was initially attracted to Europe. Then fate intervened in the form of an advisor who told her, "If you want culture, go to Europe. If you want science, you go to the United States."

Taking that advice to heart, Tan reached out to Salk, and Sawchenko specifically because of his reputation as a good mentor and his mastery of anatomy.

"It was such a good fit," she says. "I remember emailing Paul and getting a response back in three hours. That was one of the greatest feelings."

Tan joined Salk in 2011 and slipped into Institute life like a hand into a glove—organizing

"She is the kind of individual who enlivens a workplace, embodying a most rare combination of scholarly acumen, a strong work ethic and social conscience."

–Paul Sawchenko

www.salk.edu

Image courtesy of Alina Scipione

networking opportunities for researchers and volunteering for a plethora of other Institute events. Almost immediately upon arriving at Salk, she answered an internal bulletin board ad to join a softball team formed by **Inder Verma**'s lab. She encouraged her three colleagues to follow suit.

"We knew nobody in that lab. We just showed up and suddenly, we are all the best of friends," she says. "So much so that everyone thinks I'm in the Verma lab."

To relieve the stress she gets from studying stress, Tan also doodles. Many of her cartoons have a central theme of her in the lab being menaced by chocolate chip cookies and muffins, which bear a striking resemblance to a stain she employs when counting cells—the background is beige and the cells are dark brown.

"I was terrified of chocolate chip cookies for awhile," she says.

Sawchenko describes Tan as a "true Renaissance woman," a highly creative and productive scientist who is also an accomplished athlete, chef and chorister with a schedule that exhausts him just thinking about it.

"From day one, she has been the unquestioned leader of my laboratory group, heading up not only collegial interactions within our group and between our lab and others at the Institute, but also spearheading such activities as our participation in science outreach to local high school students and holiday food collection drives," Sawchenko says. "She is the kind of individual who enlivens a workplace, embodying a most rare combination of scholarly acumen, a strong work ethic and social conscience."

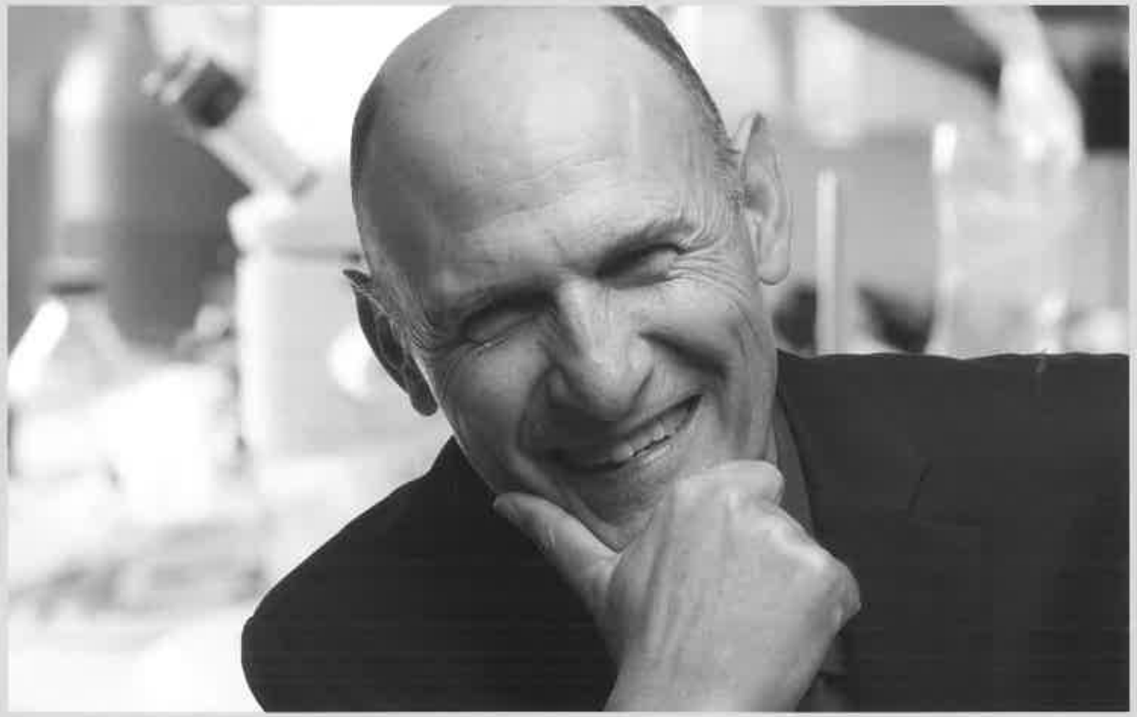
At the Institute, Tan has learned that she likes, and is good at, mentoring the newer researchers. She embraced recruiting volunteers for Explore Salk earlier this year, taking her cue from another research associate, **Amy Rommel**.

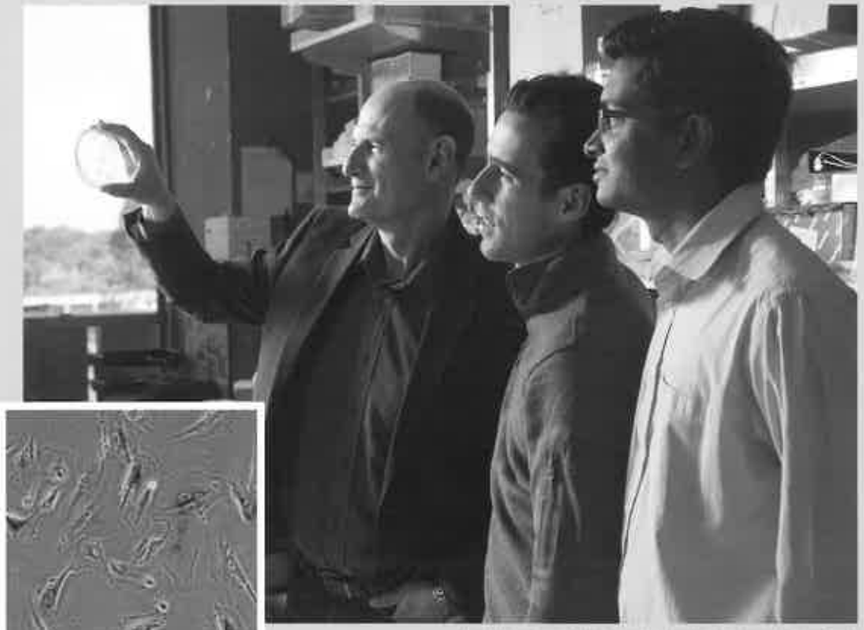
"I always think of her as my prototype," she says. "It's like, 'If I can be a little bit more like Amy, I'm doing okay.'"

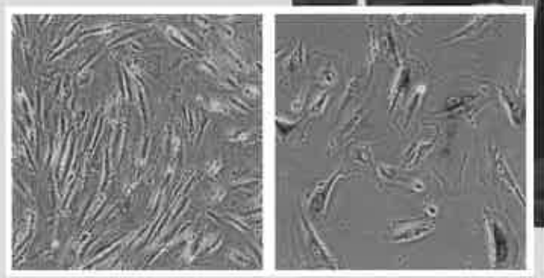
Beyond the bench, Tan's life is equally full tilt.

She plays defense for the San Diego Lacrosse Club at nearby Doyle Park during the summer and at tournaments in Los Angeles, Las Vegas, Arizona and Hawaii, among other places. She discovered the club on Facebook and has been playing with the all-woman team since the day after she arrived in town. Tan also sings as an auxiliary member with Sacra/Profana, an eclectic local choir that frequently accompanies the San Diego Symphony, including for its Summer Pops concert paying tribute to Broadway shows such as *Wicked*, *Rock of Ages* and *Les Miserables*. And in her spare time, she bakes. Chocolate milk stout cupcakes with peanut butter buttercream are her signature sweet.

Four years into her time at Salk, Tan still marvels at her good fortune. "There is something about being surrounded by good people and the building itself," she says. "Sometimes, I come in to work and give the Salk walls a pat as if to say, 'Hey, hi friend. Nice to see you.'"



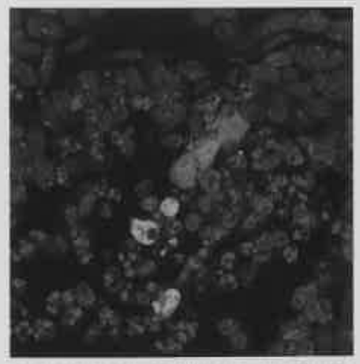




This image shows normal human cells (left) and cells that are genetically modified to model Werner syndrome (right), which show signs of aging.

Evan Wu, Juan Carlos Izpisua Belmonte, Alejandro Ocampo and Pradeep Reddy

Izpisua Belmonte
garners international attention for string of major discoveries



A novel type of human stem cell is shown in green integrating into the surrounding cells of a blastocyst mouse embryo. The stem cell holds promise for one day growing replacement functional cells and tissues.

» **View video:** www.salk.edu//insidesalk/0815/belmonte

SALK PROFESSOR JUAN CARLOS IZPISUA BELMONTE AND HIS RESEARCH team received worldwide media attention earlier this year for a string of groundbreaking discoveries reported in top science journals.

The papers, which shed light on fundamental problems in aging, mitochondrial disease and regenerative medicine, were covered in *TIME* magazine, *The Washington Post*, *Scientific American*, *New Scientist* and *The Guardian*, to name just a few.

The first of the discoveries to be announced was published April 23 in *Cell*. In that paper, the scientists reported a new method of preventing the transmission of mitochondrial diseases in mice using gene-editing technologies.

For thousands of women around the globe carrying a mitochondrial disease, having a healthy child can be a gamble. This set of diseases affect mitochondria, tiny powerhouses that generate energy in the body's cells and are passed exclusively from mother to child.

Women wishing to prevent their children from inheriting mitochondrial diseases have typically relied on preimplantation genetic diagnosis to pick the healthiest embryos, but that is no guarantee of having a healthy baby. In a mouse study, Izpisua Belmonte's lab developed a simple technique to eliminate mitochondrial mutations from eggs or early embryos, which has the potential to prevent babies from inheriting mitochondrial diseases.

"Currently, there are no treatments for mitochondrial diseases," says Izpisua Belmonte, a professor in Salk's Gene Expression Laboratory and holder of the Roger Guillemin Chair. "Our technology may offer new hope for mitochondrial disease carriers."

In the second study, detailed later the same month in *Science*, the lab focused on Werner syndrome, a genetic disorder that causes people to age more rapidly than normal. People with the disorder suffer age-related diseases early in life, including cataracts, type 2 diabetes, hardening of the arteries, osteoporosis and cancer, and most die in their late 40s or early 50s.

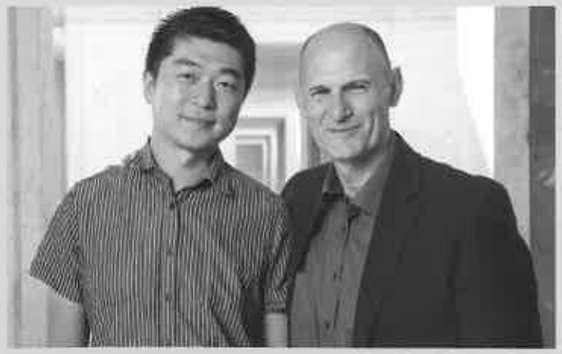
By studying Werner syndrome, the team found that the aging process for humans is tied to the deterioration of tightly packaged bundles of cellular DNA. The discovery could eventually lead to methods of preventing and treating age-related diseases such as cancer, diabetes and Alzheimer's.

In early May, the team reported in *Nature* the discovery of a novel type of pluripotent stem cell—cells capable of developing into any type of tissue—whose identity is tied to their location in a developing embryo. This contrasts with stem cells traditionally used in scientific study, which are characterized by their time-related stage of development.

The researchers dubbed this new class of cells "region-selective pluripotent stem cells," or rsPSCs for short. The rsPSCs were easier to grow in the laboratory than conventional human pluripotent stem cells and offered advantages for large-scale production and gene editing (altering a cell's DNA), both desirable features for cell replacement therapies.

Collaborating with the labs of Salk Professors **Joseph Ecker** and **Alan Saghatelian**, the Izpisua Belmonte team performed extensive characterization of the new cells and found rsPSCs showed distinct molecular and metabolic characteristics as well as novel epigenetic signatures—patterns of chemical modifications to DNA that control which genes are turned on or off without changing the DNA sequence.

"The region-selective state of these stem cells is entirely novel for laboratory-cultured stem cells and offers important insight into how human stem cells might be differentiated into derivatives that give rise to a wide range of tissues and organs," says **Jun Wu**, a postdoctoral researcher in Izpisua Belmonte's lab and first author of the *Nature* paper. "Not only do we need to consider the timing, but also the spatial characteristics of the stem cells. Understanding both aspects of a stem cell's identity could be crucial to generating functional and mature cell types for regenerative medicine."



Jun Wu and Juan Carlos Izpisua Belmonte

From left: Tushar Menon, Inder Verma and Amy Firth

Immune system-in-a-dish offers hope for "bubble boy" disease

Salk researchers have been able to grow patient-derived, healthy cells in the lab, coming a step closer to treating fatal blood disorders

FOR INFANTS WITH SEVERE COMBINED immunodeficiency (SCID), something as simple as a common cold or ear infection can be fatal. Born with an incomplete immune system, kids who have SCID—also known as "bubble boy" or "bubble baby" disease—can't fight off even the mildest of germs. They often have to live in sterile, isolated environments to avoid infections and, even then, most patients don't live past a year or two. This happens because stem cells in SCID patients' bone marrow have a genetic mutation that prevents them from developing critical immune cells, called T and Natural Killer (NK) cells.

Now, Salk researchers have found a way to, for the first time, convert cells from X-linked SCID patients to a stem cell-like state, fix the genetic mutation and prompt the corrected cells to successfully generate NK cells in the laboratory.

The success of the new technique suggests the possibility of implanting these tweaked cells back into a patient so they can generate an immune system. Though the new work, published March 12, 2015 in *Cell Stem Cell*, is preliminary, it could offer a potentially less invasive and more effective approach than current options.

"This work demonstrates a new method that could lead to a more effective and less invasive treatment for this devastating disease," says senior author **Inder Verma**, Salk professor and American Cancer Society Professor of Molecular Biology. "It also has the potential to lay the foundation to cure other deadly and rare blood disorders."

Previous attempts to treat SCID involved bone marrow transplants or gene therapy, with mixed results. In what began as promising clinical trials in the 1990s, researchers hijacked virus machinery to go in and deliver the needed genes to newly growing cells in the patient's bone marrow. While this gene therapy did cure the disease at first, the artificial addition of genes ended up causing leukemia in a few of the patients. Since then, other gene therapy methods have been developed, but these are generally suited for less mild forms of the disease and require bone marrow transplants, a difficult procedure to perform on critically sick infants.

To achieve the new method, the Salk team secured a sample of bone marrow from a deceased patient in Australia. Using that small sample, the team developed the new method in three steps. First, they reverted the patient cells into induced pluripotent stem cells (iPSCs)—cells that, like embryonic stem cells, have the ability to turn into any type of tissue and hold vast promise for regenerative medicine. "Once we had patient-derived stem cells, we could remove the genetic mutation, essentially fixing the cells," explains one of the first authors and Salk postdoctoral researcher **Amy Firth**.

» **View video:**
www.salk.edu/insidesalk/0815/verma

The second innovation was to use new gene editing technology to correct the SCID-related genetic deficiency in these iPSCs. To remove the mutation, the researchers used a technology called TALEN (similar to the better known CRISPR method). This set of enzymes act as molecular scissors on genes, letting researchers snip away at a gene and replace the base pairs that make up DNA with other base pairs.

"Unlike traditional gene therapy methods, "we aren't putting a whole new gene into a patient, which can cause unwanted side effects," says **Tushar Menon**, another first author and Salk postdoctoral researcher. "We use TALEN-based genome editing to change just one nucleotide in one gene to correct the deficiency. The technique is literally that precise."

The third step of the work was to prompt the cells to proliferate into the vital immune system cells—not an easy task, but one that could offer a potentially unlimited supply that can be transplanted back into patients at intervals. To do this, the researchers collaborated with scientists at the University of California, Los Angeles, to use a concoction of nutrients and other factors that would encourage the iPSCs to generate NK cells.

And they succeeded. These corrected cells-in-a-dish did indeed develop mature NK cells.

Next, the team is working on reproducing the other vital immune components, T cells. So far, they have prompted the iPSCs to turn into the precursors of T cells, but have not yet been able to coax them to maturity.

"Ultimately, we hope these efforts will help lead to the 'holy grail' in the field: the ability to create stem cells from iPSCs capable of generating all types of blood and immune cells," says Verma, who also holds the Irwin and Joan Jacobs Chair in Exemplary Life Science. The ability to generate the corrected blood stem cells themselves could yield a one-time treatment that would ultimately replenish functioning cells throughout a patient's whole life.

Food for thought: Master protein enhances learning and memory

Salk scientists discover a single protein that energizes both muscles and the brain

JUST AS SOME PEOPLE SEEM BUILT TO RUN MARATHONS AND HAVE an easier time going for miles without tiring, others are born with a knack for memorizing things, from times tables to trivia facts. These two skills—running and memorizing—are not so different as it turns out.

Salk scientists and collaborators have discovered that physical and mental activities rely on a single metabolic protein that controls the flow of blood and nutrients throughout the body, as reported in the journal *Cell Metabolism*. The new study could point to potential treatments in regenerative and developmental medicine as well as ways to address defects in learning and memory.

"This is all about getting energy where it's needed to 'the power plants' in the body," says **Ronald Evans**, director of Salk's Gene Expression Laboratory and senior author of the new paper, published April 7, 2015. "The heart and muscles need a surge of energy to carry out **ex**ercise and neurons need a surge of energy to form new memories."

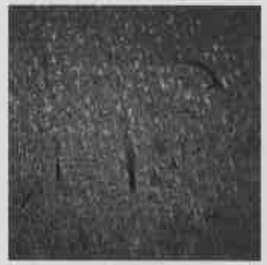
Energy for muscles and brains, the scientists discovered, is controlled by a single protein called estrogen-related receptor gamma (ERR*γ*). Evans' research group has previously studied the role of ERR*γ* in the heart and skeletal muscles. In 2011, they discovered that promoting ERR*γ* activity in the muscles of sedentary mice increased blood supply to their muscles and doubled their running capacity. ERR*γ*, they went on to show, turns on a whole host of muscle genes that convert fat to energy.

Thus, ERR*γ* became known as a master metabolic switch that energized muscle to enhance performance. Although studies had also shown that ERR*γ* was active in the brain, researchers didn't understand why—the brain burns sugar and ERR*γ* was previously shown to only burn fat. So the team decided to look more closely at what the protein was doing in brain cells.

By first looking at isolated neurons, **Liming Pei**, lead and co-corresponding author of the paper, found that, as in muscle, ERR*γ* activates dozens of metabolic genes in brain cells. Unexpectedly, this activation related to sugar instead of fat. Neurons that lacked ERR*γ* could not ramp up energy production and thus had a compromised performance.

"We assumed that ERR*γ* did the same thing throughout the body," says Evans. "But we learned that it's different in the brain." ERR*γ*, they now conclude, turns on fat-burning pathways in muscles and sugar-burning pathways in the brain.

Evans and his collaborators noticed that ERR*γ* in live mice was most active in the hippocampus—an area of the brain that is active in producing new brain cells, is involved in learning and memory and is known to require lots of energy. They wondered whether ERR*γ* had a direct role in learning and memory. By studying mice lacking ERR*γ* in the brain, they found a link.



Salk researchers and collaborators discovered that physical and mental activities rely on a single metabolic protein, ERR*γ*, which controls the flow of blood and nutrients throughout the body. In this image, ERR*γ* is shown (stained red) in the hippocampus, the area of the brain largely responsible for memory. The new work could point to a way to enhance learning.

While mice without the protein had normal vision, movement and balance, they were slower at learning how to swim through a water maze—and poor at remembering the maze on subsequent trials—compared to mice with normal levels of ERR*γ*.

"What we found is that mice that are missing ERR*γ* are basically very slow learners," says Pei. Varying levels of ERR*γ* could also be at the root of differences between how individual humans learn, he hypothesizes. "Everyone can learn, but some people learn and memorize more efficiently than others, and we now think this could be linked to changes in brain metabolism."

A better understanding of the metabolism of neurons could help point the way to improved treatments for learning and attention disorders. And possibly, revving up levels of ERR*γ* could even enhance learning, just as it enhances muscle function.

Salk scientists reveal epigenome maps of the human body's major organs

This new atlas of human organ epigenomes provides a starting place to understand the role of chemical markers in development, health and disease

FOR MORE THAN A DECADE, SCIENTISTS HAVE HAD A WORKING map of the human genome, a complete picture of the DNA sequence that encodes human life. But new pages are still being added to that atlas: maps of chemical markers called methyl groups that stud strands of DNA and influence which genes are repressed and when.

Now, Salk scientists have constructed the most comprehensive maps yet of these chemical patterns—collectively called the epigenome—in more than a dozen different human organs from individual donors (including a woman, man and child). While the methylation does not change an individual's inherited genetic sequence, research has increasingly shown it has a profound effect on development and health.

"What we found is that not all organs we surveyed are equal in terms of their methylation patterns," says senior author **Joseph Ecker**, professor and director of Salk's Genomic Analysis Laboratory and codirector of The Center of Excellence for Stem Cell Genomics. "The signatures of methylation are distinct enough between organs that we can look at the methylation patterns of a tissue and know whether the tissue is muscle or thymus or pancreas." The new data was published June 1, 2015 in *Nature*.

While the genome of an individual is the same in every cell, epigenomes vary since they are closely related to the genes a cell is actually using at any given time. Methylation marks help blood cells ignore the genes required to be a brain or liver cell, for instance. And they can vary over time—a change in a person's age, diet or environment, for instance, has been shown to affect methylation.

"We wanted to make a baseline assessment of what the epigenome, in particular DNA methylation, looks like in normal human organs," says Ecker, who is also a Howard Hughes Medical Institute and Gordon and Betty Moore Foundation investigator. To do that, the scientists collected cells from 18 organs in 4 individuals and mapped out their methylation profiles.

As expected, the patterns aligned somewhat with genes known to be important for a cell's function—there was less methylation close to muscle genes in cells collected from muscle, for instance. But other aspects of the new maps were surprising. The researchers detected an unusual form of methylation, called non-CG methylation, which was thought to be widespread only in the brain and stem cells. Researchers don't yet know the function of that non-CG methylation in adults, but hypothesize that it may suggest the presence of stem cell groups in adult populations. Another surprise was how extensively organs differed from each other in the degree of genome-wide methylation.

The new results just scratch the surface of completely understanding DNA methylation patterns—there are dozens more organs to profile, numerous unknowns about what shapes and changes the epigenome, and questions about whether different cells—even within a single organ—vary in their methylation patterns.

"You could imagine that eventually, if someone is having a problem, a biopsy might not only look at characterizing the cells or genes, but the epigenome as well," says Ecker.

From left: Matthew Schultz, Yupeng He and Joseph Ecker

"You could imagine that eventually, if someone is having a problem, a biopsy might not only look at characterizing the cells or genes, but the epigenome as well."
— Joseph Ecker

» **View video:** www.salk.edu/insidesalk/0815/ecker

Kathy Jones and Conchi Estarás

Vital step in stem cell growth revealed

Salk scientists' finding could aid regenerative and cancer therapies

STEM CELLS, WHICH HAVE THE POTENTIAL to turn into any kind of cell, offer the tantalizing possibility of generating new tissues for organ replacements, stroke victims and patients of many other diseases. Now, scientists at the Salk Institute have uncovered details about stem cell growth that could help improve regenerative therapies.

While it was known that two key cellular processes—called Wnt and Activin—were needed for stem cells to grow into specific mature cells, no one knew exactly how these pathways worked together. The details of how Wnt and Activin influence each other, published April 30, 2015 in *Molecular Cell*, offer guidance for improving stem cell therapies. The new work also reveals more about certain cancers that arise when these processes go astray, for example, when the Wnt signaling step becomes inappropriately reactivated, as happens in most colon cancers.

"We found that the mechanisms of these two pathways are complementary and activate the transcription, or turning on, of about 200 genes essential for stem cells to differentiate," says **Kathy Jones**, senior author of the paper and Salk professor in the Regulatory Biology Laboratory. These genes are among the first steps that prompt stem cells to begin to change, or differentiate, into specific tissues, particularly ones that will eventually form the digestive and respiratory tracts, including intestines, lung, pancreas, thyroid and liver.

The researchers found that Wnt loads up the cellular machinery needed to begin the copying and activation of genes. Activin, meanwhile, boosts the process further. It increases the speed and efficiency by which the cellular machinery moves to copy the gene. Whereas Wnt treatment alone enhances the expression of developmental genes by a factor of 20-fold, further treatment with Activin boosts the signal to 150-fold or higher, says Jones. The team also found that the order of the signaling is equally important, because Activin could not turn on these genes unless the cells were first exposed to the Wnt signal.

"Wnt gets the ball rolling and Activin amplifies the signal," says **Conchi Estarás**, first author of the paper. "This is a particularly clear example of how two different pathways, working through two different mechanisms, can cooperate to activate the same genes." The new finding adds to a growing picture that the transcription process is much more dynamic than previous thought.

"Now we understand stem cell differentiation at a much finer level by seeing how these cellular signals transmit their effects in the cells," adds Jones. "Understanding these details is important for developing more robust stem cell protocols and optimizing the efficiency of stem cell therapies."

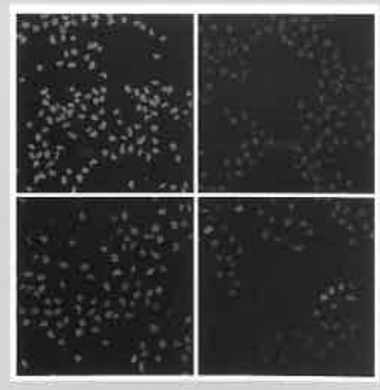
When they looked closer at the genes that both pathways activated, researchers were surprised to find that the pathways were further connected to a third process, which is known to control tissue growth and organ size. The central protein in this new pathway, called Yap, acted specifically at these genes to counteract the effects of the Activin.

» **View video:** www.salk.edu/insidesalk/0815/jones

"The opposing effects of Activin and Yap are exerted at a late step in transcription, the elongation phase," says Jones. "We don't know very much about how the signaling networks in normal or cancer cells specifically affect the elongation stage of transcription, so it was a real bonus to find that it is targeted by two pathways in stem cells."

Both the Wnt and Activin signaling processes operate differently in cancer, compared to stem cells. Wnt, in particular, is turned on very early in human colon cancer in nearly 90 percent of cases. The aberrant behavior of the Activin process, meanwhile, is tied to the metastasis of many cancers.

"There is great interest in developing transcription-based inhibitors of the Wnt pathway, because these would have strong anticancer activity for many tumor types," says Estarás. "Because the environments of stem cells and cancer cells are quite distinct, and different target genes are involved, it will be interesting to see how the synergy and regulation that we have defined in stem cells operates in the cells of a tumor."



In early-stage cell nuclei (blue), developmental genes (green) must be turned on for the cell to develop. When the two cellular processes, Wnt and Activin, work together (upper left), genes are activated to a much greater degree than when either process is active (upper right). When just a single pathway is active (blue, lower left, Activin; lower right), only a few genes are turned on.

Walking on ice takes more than brains

Salk scientists discover how a "mini-brain" in the spinal cord aids in balance

WALKING ACROSS AN ICY PARKING LOT IN winter–and remaining upright–takes intense concentration. But a new discovery suggests that much of the balancing act that our bodies perform when faced with such a task happens unconsciously, thanks to a cluster of neurons in our spinal cord that function as a "mini-brain" to integrate sensory information and make the necessary adjustments to our muscles so that we don't slip and fall.

In a paper published January 29, 2015 in the journal *Cell*, Salk Institute scientists map the neural circuitry of the spinal cord that processes the sense of light touch. This circuit allows the body to reflexively make small adjustments to foot position and balance using light touch sensors in the feet.

The study, conducted in mice, provides the first detailed blueprint for a spinal circuit that serves as a control center for integrating motor commands from the brain with sensory information from the limbs. A better understanding of these circuits should eventually aid in developing therapies for spinal cord injury and diseases that affect motor skills and balance, as well as the means to prevent falls for the elderly.

"When we stand and walk, touch sensors on the soles of our feet detect subtle changes in pressure and movement. These sensors send signals to our spinal cord and then to the brain," says **Martyn Goulding**, senior author and Salk professor. "Our study opens what was essentially a black box, as up until now we didn't know how these signals are encoded or processed in the spinal cord. Moreover, it was unclear how this touch information was merged with other sensory information to control movement and posture."

Every millisecond, multiple streams of information, including signals from the light touch transmission pathway that Goulding's team has identified, flow into the brain. One way the brain handles this data is by preprocessing it in sensory way stations such as the eye or spinal cord. In the case of touch, scientists have long thought that the neurological choreography of movement relies on data-crunching circuits in the spinal cord. But until now, it has been exceedingly difficult to precisely identify the types of neurons involved and chart how they are wired together.

In their study, the Salk scientists demystified this fine-tuned, sensory-motor control system. Using cutting-edge imaging techniques that rely on a reengineered rabies virus, they traced nerve fibers that carry signals from the touch sensors in the feet to their connections in the spinal cord. They found that these sensory fibers connect in the spinal cord with a group of neurons known as RORα neurons, named for a specific type of molecular receptor found in the nucleus of these cells. The RORα neurons in turn are connected by neurons in the motor region of the brain, suggesting they might serve as a critical link between the brain and the feet.

When Goulding's team disabled the RORα neurons in the spinal cord using genetically modified mice developed at Salk, they found that these mice were substantially less sensitive to movement across the surface of the skin or to a sticky piece of tape placed on their feet. Despite this, the animals were still able to walk and stand normally on flat ground.

However, when the researchers had the animals walk across a narrow, elevated beam, a task that required more effort and skill, the animals struggled, performing more clumsily than animals with intact RORα neurons.

The scientists attribute this to the animals' reduced ability to sense skin deformation when a foot was slipping off the edge and respond accordingly with small adjustments in foot position and balance–motor skills similar to those necessary for balancing on ice or other slippery surfaces.

Another important characteristic of the RORα neurons is that they don't just receive signals from the brain and the light touch sensors, but also directly connect with neurons in the ventral spinal cord that control movement. Thus, they are at the center of a "mini-brain" in the spinal cord that integrates signals from the brain with sensory signals to make sure the limbs move correctly.

The team's study represents the beginning of a new wave of research that promises to provide precise and comprehensive explanations for how the nervous system encodes and integrates sensory information to generate both conscious and unconscious movement.

Salk researchers mapped neural circuits in the mouse spinal cord that process light touch signals from the feet, a critical function for fine motor tasks, such as walking on ice. The red cells are motor neurons, which merge signals from neural fibers coming from the brain and cells (both colored blue).

Brain cells capable of "early-career" switch

Salk scientists find a single molecule that controls the fate of mature sensory neurons

SCIENTISTS AT THE SALK INSTITUTE HAVE DISCOVERED THAT the role of neurons—which are responsible for specific tasks in the brain—is much more flexible than previously believed.

By studying sensory neurons in mice, the Salk team found that the malfunction of a single molecule could prompt the neuron to make an "early-career" switch, changing a neuron originally destined to process sound or touch, for example, to instead process vision.

The finding, reported May 11, 2015 in *PNAS*, will help neuroscientists better understand how brain architecture is molecularly encoded and how it can become miswired. It may also point to ways to prevent or treat human disorders (such as autism) that feature substantial brain structure abnormalities.

"We found an unexpected mechanism that provides surprising brain plasticity in maturing sensory neurons," says the study's first author, **Andreas Zembrzycki**, a senior research associate at the Salk Institute.

The mechanism, a transcription factor called Lhx2 that was inactivated in neurons, can be used to switch genes on or off to change the function of a sensory neuron in mice. It has been known that Lhx2 is present in many cell types other than in the brain and is needed by a developing fetus to build body parts. Without Lhx2, animals typically die in utero. However, it was not well known that Lhx2 also affects cells after birth.

"This process happens while the neuron matures and no longer divides. We did not understand before this study that relatively mature neurons could be reprogrammed in this way," says senior author **Dennis O'Leary**, Salk professor and holder of the Vincent J. Coates Chair in Molecular Neurobiology. "This finding opens up a new understanding about how brain architecture is established and a potential therapeutic approach to altering that blueprint."

Scientists had believed that programming neurons was a one-step process. They thought that the stem cells that generate the neurons also programmed their functions once they matured. While this is true, the Salk team found that another step is needed: the Lhx2 transcription factor in mature neurons then ultimately controls the fate of the neuron.

In the mouse study, the scientists manipulated Lhx2 to make the switch in neuronal fate shortly after birth (when the mouse neurons are fully formed and considered mature). The team observed that controlling Lhx2 let them instruct neurons situated in one sensory area to process a different sense, thus enlarging one region at the expense of the other. The scientists don't know yet if targeting Lhx2 would allow neurons to change their function throughout an organism's life.

"This study provides proof that the brain is very plastic and that it responds to both genetic and epigenetic influences well after birth," says O'Leary. "Clinical applications for brain disorders are a long way away, but we now have a new way to think about them."

View the photo gallery at: www.salk.edu/insidesalk/0815/oleary

How the brain balances risk-taking and learning

Salk scientists discover a learning circuit in worms that gives clues to human behavior

IF YOU HAD 10 CHANCES TO ROLL A DIE, would you rather be guaranteed to receive $5 for every roll ($50 total) or take the risk of winning $100 if you only roll a six?

Most animals, from roundworms to humans, prefer the more predictable situation when it comes to securing resources for survival, such as food. Now, Salk scientists have discovered the basis for how animals balance learning and risk-taking behavior to get to a more predictable environment. The research reveals new details on the function of two chemical signals critical to human behavior: dopamine—responsible for reward and risk-taking—and CREB—needed for learning.

"Previous research has shown that certain neurons respond to changes in light to determine variability in their environment, but that's not the only mechanism," says senior author **Sreekanth Chalasani**, an assistant professor in Salk's Molecular Neurobiology Laboratory. "We discovered a new mechanism that evaluates environmental variability, a skill crucial to animals' survival."

By studying roundworms (*Caenorhabditis elegans*), Salk researchers charted how this new circuit uses information from the animal's senses to predict the environment and prompt the worm to move to a new location if needed. The work was detailed April 9, 2015 in *Neuron*.

The circuit, made up of 16 of the 302 neurons in the worm's brain, likely has parallels in more complex animal brains, researchers say, and could be a starting point to understanding—and fixing—certain psychiatric or behavioral disorders.

"What was surprising is the degree to which variability in animal behavior can be explained by variability in their past sensory experience and not just noise," says **Tatyana Sharpee**, associate professor and co-senior author of the paper. "We can now predict future animal behaviors based on past sensory experience, independent of the influence of genetic factors."

The team discovered that two pairs of neurons in this learning circuit act as gatekeepers. One pair responds to large increases of the presence of food and the other pair responds to large decreases of the presence of food. When either of these high-threshold neurons detects a large change in an environment (for example, the smell of a lot of food to no food) they induce other neurons to release the neurotransmitter dopamine.

Dumping dopamine onto a brain—human or otherwise—makes one more willing to take risks. It's no different in the roundworm: stimulated by large varieties in its environment, dopamine surges in the worm's system and activates four other neurons in the learning circuit, giving them a greater response range. This prompts the worm to search more actively in a wider area (risk-taking) until it hits a more consistent environment. The amount of dopamine in its system serves as its memory of the past experience, about 30 minutes or so and it forgets information gathered in the time before that.

While it's been known that the presence of dopamine is tied to risk-taking behavior, how exactly dopamine does this hasn't been well understood. With this new work, scientists now have a fundamental model of how dopamine signaling leads the worm to take more risks and explore new environments.

"The connection between dopamine and risk is conserved across animals and is already known, but we showed mechanistically how it works," says Chalasani, who is also holder of the Helen McLoraine Developmental Chair in Neurobiology. "We hope this work will lead to better therapies for neurodegenerative and behavioral diseases and other disorders where dopamine signaling is irregular."

Interestingly, the scientists found that the high-threshold neurons also lead to increased signaling from a protein called CREB, known in humans and other animals to be essential to learning and retaining new memories. The researchers showed that not only is the presence of CREB important to learning, but the amount of CREB protein determines how quickly an animal learns. This surprising connection could lead to new avenues of research for brain enhancements, adds Chalasani.

How did researchers test all of this in worms exactly? They began by placing worms in dishes that contained either a large or a small patch of edible bacteria. Worms in the smaller patches tended to reach the edges more frequently, experiencing large changes in variability (edges have large amounts of food compared to the center). Worms on the large patch, however, reached the edge less frequently, thereby experiencing a generally stable environment (mainly an area with constant food).

Using genetics, imaging, behavioral analysis and other techniques, researchers found that when worms are on small patches, the two pairs of high-threshold neurons respond to the greater variation and give a signal leading to increased dopamine. When worms in these smaller patches (and higher dopamine) were taken out and put into a new dish, they explored a larger area, taking more of a risk. Worms from the larger patches, however, produced less dopamine and were more cautious, exploring just a small space when placed in a new area.

Additionally, when the protein CREB was present in larger amounts, the team found that the worms took far less time to learn about their food variability. "Normally the worms took about 30 minutes or so to explore and learn about food, but as you keep increasing the CREB protein they learn it faster," says Chalasani. "So dopamine stores the memory of what these worms learn while CREB regulates how quickly they learn."

C. elegans

» **View video:** www.salk.edu/insidesalk/0815/chalasani

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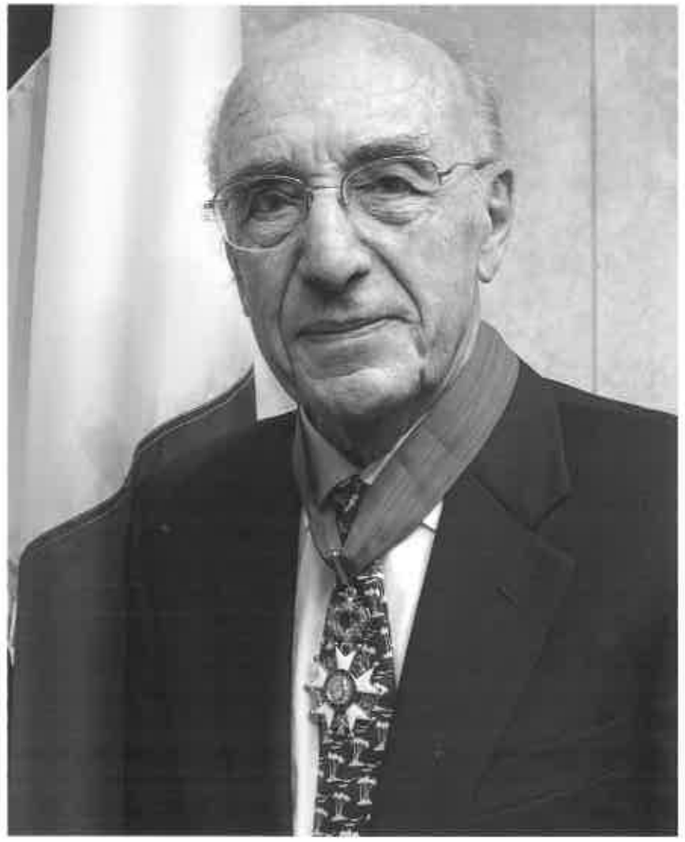


"You have been, Roger Guillemin, one of these distinguished 'soldiers of science' that Bonaparte wished to recognize when he established the Legion of Honour."

— Jean-Pierre Changeux

A commanding presence

ROGER GUILLEMIN, A SALK PROFESSOR AND NOBEL LAUREATE WHO pioneered the study of brain chemistry, was presented with France's highest accolade—the rank of Commander in the Legion of Honour—during a ceremony this spring at the Salk Institute. In bestowing the medal created by Napoleon Bonaparte in 1802 to recognize civilians and soldiers, neuroscientist Jean-Pierre Changeux of the College de France and Pasteur Institute in Paris praised Guillemin, 91, before an assemblage of dozens of Guillemin's family members—including his wife, Lucienne—and friends and colleagues.

"You have been, Roger Guillemin, one of these distinguished 'soldiers of science' that Bonaparte wished to recognize when he established the Legion of Honour," Changeux said. "Through your scientific achievements and your many discoveries, you have played a key role in illustrating the excellence of scientific research, but most of all, as a French scientist working abroad, in fostering scientific collaboration and friendship between the United States and France."

Colleagues attending the ceremony echoed the sentiment, describing Guillemin as a "national treasure" for both countries.

Guillemin, a native of Dijon, France, earned his medical degree in 1949 from the University of Lyon. He joined Salk in 1970 and received the 1977 Nobel Prize in Physiology or Medicine for his work with hypothalamic hormones. His work introduced a new class of substances proven to be important for the regulation of growth, development, reproduction and responses to stress.

Changeux characterized Guillemin as "the founder of a new science called neuroendocrinology" and said his work led to major medicinal advances including the understanding of thyroid diseases, infertility and juvenile diabetes.

After the presentation, Guillemin expressed his gratitude in French before thanking his family and Salk colleagues, many of whom, including the late **Wylie Vale**, he had worked with for more than 45 years. He concluded his remarks, to a standing ovation, with "Let's close this unique event in the French tradition with a glass of champagne."

Vicki Lundblad elected to National Academy of Sciences

From left: Beverly Emerson, Roger Guillemin and Vicki Lundblad

PROFESSOR VICKI LUNDBLAD IS ONE OF 84 NEW MEMBERS elected to the National Academy of Sciences (NAS) this year. The election is considered one of the highest honors accorded a U.S. scientist. Lundblad's recognition brings the number of Salk faculty elected to the NAS to 14.

Lundblad, the Becky and Ralph S. O'Connor Chair and professor in the Molecular and Cell Biology Laboratory, seeks to understand how the ends of chromosomes determine how many times a cell can divide. Her early work showed that these chromosome ends, called telomeres, act as a cellular timekeeper by shortening with each cell division. Fortunately, there is a way around this countdown: an enzyme called telomerase rebuilds these eroding telomeres and allows cells to divide indefinitely.

Lundblad's group pioneered the discovery of the key subunits that make up this telomerase enzyme, using the yeast *Saccharomyces cerevisiae*—the same yeast used to make wine and bread—as their experimental system. This simple single-celled organism has also allowed Lundblad and her colleagues to subsequently uncover numerous insights about what dictates when and where telomerase acts inside the cell.

Joseph Ecker and Dennis O'Leary elected to American Academy of Arts & Sciences

Dennis O'Leary

Joseph Ecker

PROFESSORS JOSEPH ECKER AND DENNIS O'LEARY have received the prestigious honor of being elected to the American Academy of Arts and Sciences (AAAS) class of 2015. AAAS is one of the nation's most prominent honorary societies. There are 197 accomplished leaders from academia, business, public affairs, the humanities and the arts accepted to this year's class. Its members include winners of the Nobel Prize and Pulitzer Prize; MacArthur and Guggenheim Fellowships; and Grammy, Emmy, Oscar and Tony awards. Ecker and O'Leary bring the number of Salk scientists elected as members of AAAS to 16. The new class will officially be inducted during a ceremony in October.

Ecker is director of Salk's Genomic Analysis Laboratory and a Howard Hughes Medical Institute and Gordon and Betty Moore Foundation investigator. He has made many distinguished contributions to the fields of genomes/epigenomes of plant and human cells, particularly for the development of new tools that enable genome-wide analyses. He also holds the Salk International Council Chair in Genetics.

O'Leary, a professor in Salk's Molecular Neurobiology Laboratory, holds the Vincent J. Coates Chair in Molecular Neurobiology. O'Leary tackles questions about brain development in order to better understand the genes and molecules which not only help neurons form and find their place in a developing brain, but also play key roles in neural function and health throughout life.

Ronald Evans receives Frontiers in Science Award

RONALD EVANS, PROFESSOR AND DIRECTOR of Salk's Gene Expression Laboratory, is the recipient of the 2015 Frontiers in Science Award. The award is presented to an individual who has demonstrated exemplary contributions to their individual profession or area of expertise.

A Howard Hughes Medical Institute investigator, Evans is known for his work on nuclear receptors and the mechanism of hormone signaling, which is crucial to understanding body physiology and the treatment of diseases. His work on the isolation of the genes encoding hormone receptors revealed how they help control sugar, salt, calcium and fat metabolism as well as reproductive physiology.

Pew Charitable Trusts names Nicola Allen a Pew Scholar in the Biomedical Sciences

NICOLA ALLEN, ASSISTANT PROFESSOR IN THE Molecular Neurobiology Laboratory, has received the honor of being named a Pew Scholar in the Biomedical Sciences. She is one of only 22 researchers in biomedical sciences to receive the honor this year. She joins the ranks of more than 600 outstanding scientists who have been selected as Pew scholars in the 30 years since the program's inception.

Allen's research investigates the role of astrocytes in reinforcing the brain's ability to learn new tasks and make sense of its environment. Astrocytes are the most abundant cells in the brain and play critical roles in regulating neuronal function. During her postdoctoral fellowship, Allen identified molecules that astrocytes use to guide the formation of neuronal connections in the developing mammalian brain. She has extended this work to analyzing the critical period of development when newborns rewire their brains in response to the stream of visual input.

Joanne Chory elected to American Philosophical Society

Joanne Chory with her husband, Stephen Worland, and children Joe and Katie

JOANNE CHORY, PROFESSOR AND DIRECTOR OF THE PLANT MOLECULAR and Cellular Biology Laboratory, has received the prestigious honor of being elected to the American Philosophical Society (APS). The APS is an eminent scholarly organization of international reputation, which promotes useful knowledge in the sciences and humanities. This country's first learned society, the APS has played an important role in American cultural and intellectual life for over 250 years.

For more than 25 years, Chory has used *Arabidopsis thaliana*, a small flowering mustard plant, as a model for plant growth. She has pioneered the use of molecular genetics to study how plants respond to their environment and has made major discoveries surrounding how plants sense light and make growth hormones.

Esteemed neuroscientist and entrepreneurial leader elected to the Salk institute Board of Trustees

IN APRIL, THE SALK INSTITUTE BOARD OF Trustees elected two new members to the Board: neuroscientist Thomas Jessell and Daniel Tierney, co-founder of GETCO (now KCG), a technology-enabled market making firm.

"Tom and Dan bring outstanding records of scientific expertise and entrepreneurial success to Salk," said **Irwin M. Jacobs**, chairman of the Salk Institute Board of Trustees. "We are greatly pleased to have them join our Board of Trustees."

Jessell has been a Howard Hughes Medical Institute (HHMI) investigator since 1985, and a Salk Institute Non-Resident Fellow since 2001. He is also the Claire Tow Professor in the Department of Neuroscience and the Department of Biochemistry and Molecular Biophysics at Columbia University. His research explores the link between the assembly and organization of neural networks and the behaviors they encode. He is examining these issues through an analysis of circuits that control movement.

Tierney currently serves as a board member and advisor at KCG Holdings, Inc. After stepping down from the co-CEO role at GETCO in 2012, Tierney became the founder and president of his family office, Wicklow Capital. He now spends most of his time investing in other entrepreneurs and helping them turn their visions into reality.

> "Tom and Dan bring outstanding records of scientific expertise and entrepreneurial success to Salk."
> — Irwin M. Jacobs

Salk recruits human geneticist Graham McVicker

EXPANDING ON ITS LEADERSHIP IN genetics, the Salk Institute is pleased to announce the appointment of **Graham McVicker** as an assistant professor in the Integrative Biology Laboratory and in the Laboratory of Genetics.

"Graham is a forward-thinking researcher with an impressive background in developing and harnessing innovative techniques to help unravel the human genome," says **Rusty Gage**, professor in the Laboratory of Genetics. "Understanding and analyzing human genetic diversity is crucial to both science and medicine, and Graham's breadth of expertise in computing and genetics will spur important innovations in these areas."

McVicker will join the Salk Institute in January 2016. He seeks to understand how human genetic variation affects molecular processes in the cell and contributes to disease.

Geneticists have cataloged millions of genetic differences between individuals, but it is difficult to determine which of them affect human traits such as height, blood pressure and disease risk. McVicker has begun to tackle this problem by developing powerful statistical and computational approaches to analyze the human genome and determine the molecular function of individual genetic variants.

McVicker is particularly interested in genetic variants that affect chromatin. Chromatin is the molecular packaging that organizes DNA and regulates access to the genome, which helps control which genes are turned on in specific cells. Genetic variants that affect chromatin are likely to be important for many human diseases and the McVicker laboratory will focus specifically on those that affect chromatin in immune cells. By understanding these variants and linking them to disease risk, his laboratory will illuminate why some individuals are more susceptible to autoimmune and infectious diseases.

"I plan to push the boundaries of quantitative genetics and use genetic variation as a tool to understand the molecular processes that underlie human disease," says McVicker. "I am excited to join the world-renowned faculty at the Salk Institute, where I will have the intellectual freedom, resources and collaborations to make important contributions in these areas."

McVicker earned his BS from the University of British Columbia in computer science and PhD from the University of Washington in genome sciences, where he studied how selection and mutation shape genetic variation in primate evolution. More recently, he conducted postdoctoral research at the University of Chicago, Stanford University and the Dana-Farber Cancer Institute, where he developed new methods for genetic mapping of molecular quantitative traits.

> "Graham is a forward-thinking researcher with an impressive background in developing and harnessing innovative techniques to help unravel the human genome."
>
> — Rusty Gage

Explore Salk

Tours, activities, talks

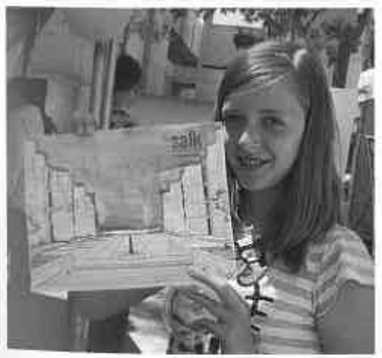
Community discovers world of science at **Explore Salk**

Eric Topol

ON APRIL 11, THE SALK INSTITUTE ONCE again opened its doors to the local community for its third annual Explore Salk event. Approximately 1,000 people—from science enthusiasts and Salk supporters to families eager to get a peek inside the world-famous laboratories—visited and spent hours exploring the campus.

Explore Salk included a number of hands-on activities for young attendees, while older participants toured labs and science booths to learn about cutting-edge research. Visitors also had the opportunity to learn about the Salk education outreach programs and were treated to a number of scientific talks. Assistant Professor **Saket Navlakha** spoke about his fascinating research on using lessons in biology to solve technology problems. Eric Topol, director of the Scripps Translational Science Institute, chief academic officer at Scripps Health and a professor of genomics at The Scripps Research Institute, presented highlights from his recent book, *The Patient Will See You Now: The Future of Medicine is in Your Hands*, to a packed auditorium.

Explore Salk is organized and staffed by Institute employees, scientists, family and friends—a volunteer effort that demonstrates their passion for scientific discovery. In praising their contribution and the event's continued success, **Rebecca Newman**, vice president of External Relations, hailed it as "a unique experience that is not replicated anywhere else in San Diego."



From left: Clodagh O'Shea, Emily Hatch and Amy Rommel

salk women & science
Where cures begin.

Women & Science: An evening of celebration and education

TWO FEMALE SALK RESEARCHERS HAVE BEEN NAMED THE FIRST grant recipients of the Salk Women & Science Special Awards Initiative. Nearly 200 people attended a celebratory event sponsored by BioMed Realty on March 24.

The event kicked off with Dress for Success San Diego, an organization committed to providing job preparation services to low-income women striving for self-sufficiency. Among the many donations Salk received for the drive were 280 dresses and suits, 31 pairs of shoes, 36 purses and more than 100 items of jewelry and accessories.

At the event, Salk researchers **Emily Hatch** and **Christina Chang** were named the 2015 inaugural Postdoctoral Fellowship Recipient and the Graduate Student Fellowship Recipient, respectively.

The awards were created to provide funding to female scientists conducting high-risk research projects. A $100,000 fundraising goal established in October 2014 was exceeded before the spring Women & Science event, thanks in part to generous initial gifts from Elizabeth Keadle, Carol and John Gallagher of the Gallagher Charitable Fund, Lyn Nelson, Hoyle Cohen Women's Practice, and Lynne Rosenthal and Patti Silver of the Leo S. Guthman Fund.

On the heels of the inaugural Initiative's success, **Joanne Chory**, director of the Salk's Plant Molecular and Cellular Biology Laboratory, pledged the first lead gift for the 2016 grant program "in honor of the 111 women in PBIO-C who enriched my life over the past 27 years." In the nearly three decades Chory has been mentoring young scientists, 44 percent of them have been women.

Before the recognition ceremony, the evening's host, Associate Professor **Clodagh O'Shea**, took the stage to thank attendees for their philanthropy and their growing ranks. Marveling at the mainly female congregation, she said, "This is the first time I've seen more women in the audience at a scientific talk than men. Let's celebrate that."

Citing double-digit statistics that illustrate the gap still existing between men and women in scientific academia, O'Shea said that is why the Salk Women & Science program is "important to preserve." She expressed gratitude for the opportunities afforded not only her, but also the young women in the field today.

Amy Rommel, a postdoctoral research associate in Professor **Inder Verma**'s Laboratory of Genetics, then proceeded to captivate the audience with a talk about her research efforts on glioblastoma, one of the most lethal forms of cancers.

Current treatment of glioblastoma combines surgical removal of the tumor, administering toxic chemicals and depriving the tumor of nutrients, Rommel explained. Unfortunately, tumor cells have mechanisms to overcome these attacks. One mechanism of adaptation, previously published in a study from the Verma lab, suggests glioblastoma has the ability to convert some of its tumor cells into functional vascular cells. Rommel's work proposes novel strategies to treat glioblastoma by reverse engineering the mechanism the tumor is already using—reprogramming the tumor-initiating cells back to their "normal" non tumor-initiating state.

Now in its third year, Salk Women & Science was created to engage the community in biological science and technology through presentations such as Rommel's. For more information on the program, visit www.salk.edu/womenandscience or contact **Betsy Reis**, director of Donor Relations, at (858) 453-4100 x1426 or breis@salk.edu.

» **View video:** www.salk.edu/insidesalk/0815/womenandscience

Hatch, Chang garner first Women & Science awards

RESEARCH ASSOCIATE EMILY HATCH, WHO WORKS IN THE MOLECULAR and Cell Biology Laboratory led by Professor **Martin Hetzer**, has been named the inaugural Postdoctoral Fellowship Recipient of the Salk Women & Science Special Awards Initiative.

Hatch earned her bachelor's degree in biology from Williams College in 2003, and her PhD in 2011 from Stanford University, where she successfully studied various aspects of centriole duplication. She joined the Salk Institute in 2011, focusing her work on the nuclear envelope dynamics in mammalian cells. In 2013, she published a landmark paper in *Cell* in which she addressed a question centering on the mechanism of chromothripsis, a recently identified process by which chromosomes fragment and undergo massive rearrangement.

"Emily has a great personality and scientifically she is remarkably mature," Hetzer wrote in his nomination of Hatch. "She is driven by scientific passion in its purest form and also by the desire to work on cancer-related questions."

Christina Chang, a graduate student in the Nomis Foundation Laboratories for Immunobiology and Microbial Pathogenesis led by **Ye Zheng**, was named the Graduate Student Fellowship Recipient for 2015.

Currently attending the University of California, San Diego to earn her PhD, Chang joined Zheng's lab in 2011 to work on a new project that originated from collaboration between the labs of Zheng and **Ronald Evans**. Her research focuses on the molecular mechanism involved in the differentiation of T helper 17 cells, a recently identified subset of T lymphocytes.

"Christina has the genuine curiosity that propels her to constantly ask the right questions and seek answers through her own efforts," Zheng wrote in his nomination letter. "She has also presented her work at multiple meetings and conferences with very positive feedback. I can already see her on the trajectory of becoming an exceptional scientist in the future."

Christina Chang

From left: Richard Heyman, Liz Keadle and Greg Lemke

Trustee Richard Heyman addresses Salk alumni

BIOTECH ENTREPRENEUR AND RECENTLY elected Salk trustee Richard Heyman, PhD, spoke at the Institute's annual alumni mixer in June. He was well suited for the role. Heyman is also a Salk alumnus, having once worked as a postdoctoral researcher in the lab of **Ronald Evans**, professor and director of the Gene Expression Laboratory.

Salk's Alumni Program helps connect some 3,500 researchers who trained at the Institute before going on to important positions at facilities all over the world.

Five years ago, Salk established the Alumni-Faculty Fellowship Fund raising enough funds every year to grant a fellowship to a postdoctoral researcher. Both alumni and current Salk faculty contribute to the fund.

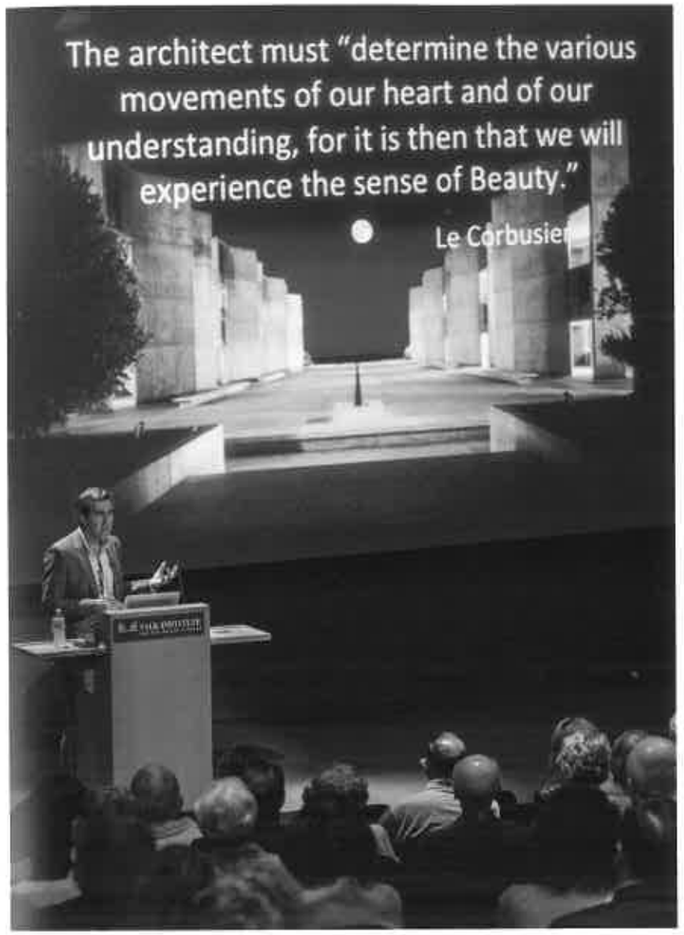
To learn more about the Salk Alumni program, visit www.salk.edu/alumni or contact **Megan Shockro** at (858) 453-4100 x1405 or mshockro@salk.edu.

Guests mingling at Salk's annual Alumni event

From left: Irwin Jacobs, Sibylle Szaggars Redford, Joan Jacobs and Robert Redford

Sibylle Szaggars Redford unveils environmental artwork at Salk

MULTIMEDIA ARTIST SIBYLLE SZAGGARS REDFORD shared selections from her series "The Shape of Color & The Way of the Rain" at an April reception at the Institute attended by Salk supporters, trustees and invited guests. Wife of renowned actor and filmmaker Robert Redford—who featured the Salk Institute in last year's *Cathedrals of Culture* documentary film project—Szaggars Redford exhibits her work throughout the world to raise awareness of humanity's impact on the environment. The pieces, which were created by exposing pigment to rain, were displayed through May, with 30 percent of all sales generously donated to the Salk Institute.



Back to Basics
LECTURE SERIES at the SALK INSTITUTE

Back to Basics
lecture links neuroscience with architecture

IN MARCH, OVER 200 PEOPLE GATHERED ON THE Salk campus to hear **Thomas Albright**, professor and director of the Vision Center Laboratory and holder of the Conrad T. Prebys Chair in Vision Research, present a Back to Basics lecture. In an engrossing talk that prompted much discussion during the reception that followed, Albright explained how what neuroscientists are learning can help architects design buildings optimally suited for the humans inside them. Informed architects can manipulate light, sound, texture and space to design, for example, hospitals that promote healing or schools that enhance learning.

Audiences continue to grow for these biannual lectures that invite the public to hear about the dynamic research performed at the Salk Institute. There is no cost to attend. For more information about the next Back to Basics event, which will be held Tuesday, September 22, 2015, please contact **Jennifer Rothrock** at (858) 500-4881 or jrothrock@salk.edu.

Samuel Pfaff shares exciting new discoveries with Salk supporters in New York City

IN APRIL, SAMUEL PFAFF, PROFESSOR in the Gene Expression Laboratory, Howard Hughes Medical Institute investigator and holder of the Benjamin H. Lewis Chair, traveled to New York to share his most recent discoveries in neurodegenerative disease. Trustee Mary Jane Salk hosted the event. Françoise Gilot, artist and widow of Jonas Salk, was among the attendees.

Pfaff's team investigates how nerve cells form and how they wire up correctly, focusing on fetal development of the spinal cord. His lab hopes to eventually harness these "embryonic pathways" to repair or augment the central nervous system. He and his team are building on their discovery that just a handful of critical genes direct the complex neuron wiring programs in early brain development, information that could lead to novel treatments for those with spinal cord injury or neurological disorders such as amyotrophic lateral sclerosis (ALS).

For more information on scientific presentations in the New York region, please contact **Megan Shockro** at mshockro@salk.edu or (858) 453-4100 x1405.

Tax Seminar attendees and representatives from the Joe W. and Dorothy Dorsett Brown Foundation at the Marine Room dinner

Representatives from the Marshall Heritage Foundation and Legacy Foundation with Senator Pfaff and Erin Dunstad

43rd Annual Tax Seminar for Private Foundations held in May

THE 43RD ANNUAL TAX SEMINAR FOR PRIVATE FOUNDATIONS, hosted by the Salk Institute, returned to La Jolla May 11-13. The event, held at the Estancia La Jolla Hotel & Spa, drew a series of nationally known lecturers and authors who provided insights on foundation tax law, management, finance and governance. The seminar covered everything from the complexity of changes in tax law to new ideas and perspectives for foundation leaders.

Edwin Hunter, chairman of the event and president of Hunter, Hunter & Sonnier, says, "No seminar in the private foundation universe offers a more distinguished or capable faculty."

Randall Munroe, the tax seminar keynote speaker and creator of the webcomic *xkcd*, offered an entertaining talk based on his nonfiction best seller, *What If?: Serious Scientific Answers to Absurd Hypothetical Questions*. Munroe, a former NASA roboticist, spoke to a nearly full house in Salk's Conrad T. Prebys Auditorium and followed up his presentation with a book signing for attendees. The seminar concluded that evening with an outdoor supper reception in the courtyard.

Inaugural meeting of Salk Institute Council offers a new way to engage with the Institute

THE INAUGURAL MEETING OF THE SALK INSTITUTE COUNCIL, HELD May 12-14, attracted a roster of more than 50 attendees who gathered to learn more about the Institute. Salk Institute Council co-chairs Rich Heyman and Diana Kalman, along with faculty liaison **Reuben Shaw**, put together an exciting and robust program focusing on the continuum of Salk science from the early visionary years to the present and beyond.

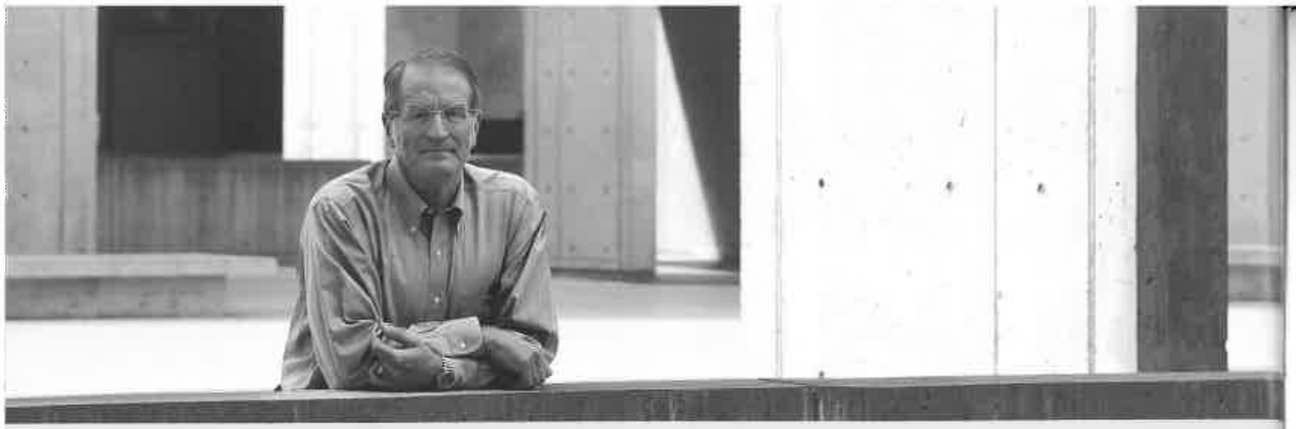
The mission of the Council is to advocate on behalf of Salk science by focusing on leadership development and fundraising through the meaningful engagement and active participation of its members.

The meeting kicked off with "Bio 101" by Salk's award-winning Education Outreach team, **Ellen Potter** and **Dona Mapston**, who focused on the basic science underlying the various research areas represented by Salk scientists. Additionally, nine Salk faculty members as well as postdoctoral researchers gave presentations on topics ranging from breakthroughs in science to creativity and the intersection of disciplines. Chief Financial Officer **Kim Witmer** and Vice President of External Relations **Rebecca Newman** also presented an insider's view of Salk's operational strategy. Finally, Salk Board of Trustees Chairman Irwin Jacobs closed the meeting with an inspiring talk about his career in innovation as well as why he was drawn to Salk.

The program offered many opportunities such as these for participants to take a behind-the-scenes peek at the inner workings of the Institute. In addition to the access attendees were granted to the Institute's scientists and Salk community, there was also an opportunity to tour Salk's Stem Cell Core and Waitt Advanced Biophotonics Center Core.

Institute Council Co-Chairs Diana Kalman and Rich Heyman

Claudia Ehrlich, senior director of External Relations and staff liaison for the Council, noted, "The meeting offered many ways for attendees to engage with the innovative work being done at Salk, from the science to the business and leadership. Our hope is they all came away invigorated and inspired to deepen their engagement with the Institute."



Insider's View

William R. Brody, MD, PhD
President, Salk Institute
Irwin M. Jacobs Presidential Chair

The Second Green Revolution

IN 1968, I REMEMBER BEING SCARED OUT OF MY wits reading the best-selling book by Stanford ecologist Paul Ehrlich, *The Population Bomb*. Professor Ehrlich's logic was impeccable: he said the global population would double by 2005 (to about 7 billion in actuality) and that the world would run out of food, causing mass starvation and deaths.

When 2005 came, Ehrlich's predictions on population growth proved remarkably accurate, but not his warnings of global-scale starvation. Where was the food shortage? As it turned out, Ehrlich's calculations hadn't factored in important developments in the growth of the food supply that would help food production keep pace with the burgeoning human population.

In fact, what happened was the Green Revolution, a period of dramatic growth in the world food supply kicked off by Norman Borlaug, an American plant biologist who developed strains of wheat that were much higher yielding and disease resistant than the status quo. In addition, the introduction of advanced agricultural practices worldwide provided a tremendous increase in productivity not thought feasible when Ehrlich made his doomsday prediction.

Borlaug launched the Green Revolution and was joined in this effort by many other scientists who introduced similar innovations in agriculture production.

Agricultural innovations allowed wheat production to increase from 800 pounds per acre in the 1950s to over 6,000 pounds per acre by the late 1960s. For his work, Borlaug received the Nobel Peace Prize and is credited with saving millions of lives from starvation.

Today, young ecologists are beginning to write books similar to *The Population Bomb*. Although the world population growth is slowing, so is the growth of agricultural productivity, and climate change is already tipping regions around the world into drought.

We need visionary plant biologists who can develop a much deeper understanding of how plants react to environmental stress and what can be done to protect existing species or create new ones that are more tolerant of heat, drought and disease.

Unfortunately, at the moment, the field of plant biology is seriously underfunded. Yes, I know that getting National Institutes of Health grants is difficult, but for plant biology the scene is even bleaker. NIH typically only funds plant biology grants where there is a link to the understanding of human diseases, while the National Science Foundation budget for plant biology has been woefully inadequate for decades.

Private philanthropy is helpful—the Gordon and Betty Moore Foundation teamed with the Howard Hughes Medical Institute to fund faculty scholars in plant biology—as was illustrated when Salk professor **Joseph Ecker** received one of these generous awards. But we need to raise awareness among the general public that funding plant science is just as important as funding cancer research.

We need to kick-start the Second Green Revolution. The well-being of our children and grandchildren will likely depend upon innovations to protect and grow our food sources.