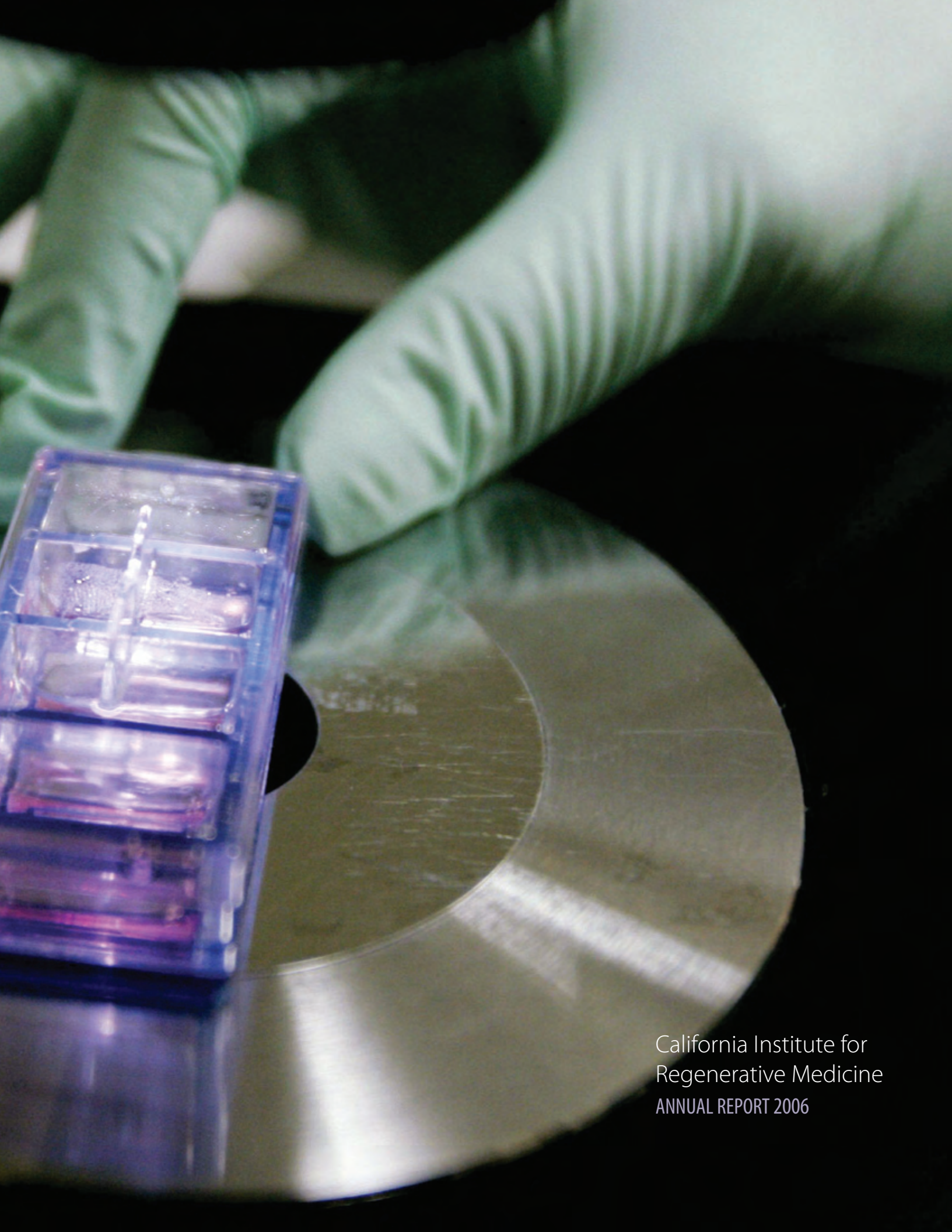


California Institute for Regenerative Medicine

ANNUAL REPORT 2006

Independent Citizens Oversight Committee of the California Institute for Regenerative Medicine

NAME	AFFILIATION	ICOC POSITION
Ricardo Azziz, MD, MPH, MBA	Chairman, Department of Obstetrics and Gynecology, Cedars-Sinai	An executive officer from a California Research Institute (1 of 4)
David Baltimore, PhD	Robert A. Millikan Professor of Biology at the California Institute of Technology	An executive officer from a California University (1 of 4)
Robert Birgeneau, PhD	Chancellor, University of California, Berkeley	An executive officer from a California University (2 of 4)
Susan V. Bryant, PhD	Dean, School of Biological Sciences University of California, Irvine	An executive officer from a UC with a medical school (1 of 5)
Marcy Feit, RN, MSN	President and CEO, ValleyCare Health Systems	Patient pdvocate (1 of 10), Type II Diabetes
Michael A. Friedman, MD	President and CEO, City of Hope	An executive officer from a California Research Institute (2 of 4)
Michael Goldberg	General Partner, Mohr, Davidow Ventures	An executive officer of a Commercial Life Science Entity (1 of 4)
Brian E. Henderson, MD	Dean, Keck School of Medicine University of Southern California	An executive officer from a California University (3 of 4)
Edward W. Holmes, MD	Vice Chancellor for Health Sciences and Dean, School of Medicine University of California, San Diego	An executive officer from a UC with a medical school (2 of 5)
David A. Kessler, MD, JD	Dean, School of Medicine and Vice Chancellor for Medical Affairs University of California, San Francisco	An executive officer from a UC with a medical school (3 of 5)
Robert Klein	Klein Financial Corporation	Chairman of the ICOC, patient advocate with expertise in legal affairs, financial affairs and governmental funding
Sherry Lansing	Founder and Chair, Sherry Lansing Foundation	Patient advocate (2 of 10), Cancer
Gerald S. Levey, MD	Vice Chancellor, Medical Sciences and Dean, School of Medicine University of California, Los Angeles	An executive officer from a UC with a medical school (4 of 5)
Ted W. Love, MD	President, CEO and Director, Nuvelo	An executive officer of a Commercial Life Science Entity (2 of 4)
Richard A. Murphy, PhD	President and CEO, Salk Institute	An executive officer from a California Research Institute (3 of 4)
Tina S. Nova, PhD	President, CEO and Co-Founder, Genoptix, Inc.	An executive officer of a Commercial Life Science Entity (3 of 4)
Ed Penhoet, PhD	President, Gordon and Betty Moore Foundation	Vice Chairman, patient advocate with expertise in biological sciences, therapy development, public health and biotech
Philip A. Pizzo, MD	Dean of the School of Medicine, Stanford University Professor of Pediatrics and of Microbiology and Immunology	An executive officer from a California University (4 of 4)
Claire Pomeroy, MD, MBA	Vice Chancellor for Human Health Sciences and Dean of the UC Davis School of Medicine	An executive officer from a UC with a medical school (5 of 5)
Francisco J. Prieto, MD	President, Sacramento-Sierra chapter, American Diabetes Association	Patient advocate (3 of 10), Type I Diabetes
John C. Reed, MD	President and CEO, The Burnham Institute	An executive officer from a California Research Institute (4 of 4)
Duane J. Roth	Chairman and CEO, Alliance Pharmaceutical Corporation	An executive officer of a Commercial Life Science Entity (4 of 4)
Joan Samuelson, JD	Founder, Parkinson's Action Network	Patient advocate (4 of 10), Parkinson's Disease
David Serrano Sewell, JD	Amyotrophic Lateral Sclerosis Association National Multiple Sclerosis Society	Patient advocate (5 of 10), MS/ALS
Jeff Sheehy	Deputy Director for Communications, UCSF AIDS Research Institute	Patient advocate (6 of 10), HIV/AIDS
Jonathan Shestack	Founder and Vice President, Cure Autism Now	Patient advocate (7 of 10), Mental Health
Oswald Steward, PhD	Chair and Director, Reeve, Irvine Research Center University of California, Irvine	Patient advocate (8 of 10), Spinal Cord Injury
Leon J. Thal, MD	Chair and Professor, Department of Neurosciences University of California, San Diego	Patient advocate (9 of 10), Alzheimer's Disease
Janet S. Wright, MD, FACC	American College of Cardiology	Patient advocate (10 of 10), Heart Disease

Former ICOC Members

NAME	AFFILIATION	ICOC POSITION
Keith L. Black, MD	Director of Neurosurgery Cedars-Sinai Medical Center	An executive officer from a California Research Institute
Phyllis Preciado, MD	Diabetes Resource Network	Patient advocate, Type II Diabetes
Gayle Wilson	Board of Directors Gilead Sciences	Representative of a Commercial Life Science Entity

The new frontier of stem cell research has generated scientific excitement and medical hope throughout the world.

California Institute for Regenerative Medicine

ANNUAL REPORT 2006

Researcher Rudy Gonzalez handles human embryonic stem cell cultures at the Burnham Institute in La Jolla, California.

Letter to the People of California

Seven million Californians voted for Proposition 71 — the California Stem Cell Research and Cures Initiative — in November of 2004. The measure establishes the California Institute for Regenerative Medicine ("CIRM" or the "Institute"), a new state agency, and authorizes the allocation of $3 billion in public bond funds for scientific and medical research in California. The Institute has a clear and simple mission: to support stem cell research and other vital medical technologies to develop therapies and potentially cures for patients suffering with chronic disease and injury.

Californians believe that stem cell biology has the potential to prevent, diagnose, treat, and cure disease and disability, backing that belief with a multi-year commitment matched by no other state or country. Since its first meeting in December 2004, the CIRM governing board — the Independent Citizens Oversight Committee ("ICOC") — and staff have been working tirelessly to fulfill the voters' mandate.

The ICOC, a distinguished 29-member body appointed by a group of California's elected officials and public university chancellors, includes patient advocates, members of the private sector, and the leadership of some of the state's top research institutions. The ICOC members, must approve all grants and loans, regulations, standards, and policies in public session conducted under the Bagley-Keene Open Meeting Act. The ICOC elected its Chairman, Robert N. Klein, and Vice Chairman, Edward E. Penhoet, Ph.D.; appointed Zach W. Hall, Ph.D., President and Chief Scientific Officer of CIRM; and named key scientific and administrative personnel.

Following the blueprint provided by the California Stem Cell Research and Cures Act (the "Act"), the ICOC appointed working groups and subcommittees that developed medical and ethical standards for research with the assistance of the National Academies, along with critical governance, administrative, and regulatory policies to ensure that CIRM's efforts meet the highest standards of public integrity and accountability. These policies are crafted in public under the ultimate auspices of the ICOC—but it is the collaboration among the working groups, CIRM staff, elected officials, patients, and members of the public that has laid the foundation for a large-scale, vigorous stem cell research program. The challenge for the Institute's first eighteen months was daunting: 1) initiate a bold, new

scientific venture at the frontier of biomedical research; 2) establish the regulatory and administrative framework to support hundreds of research grants; and 3) build a new state agency to carry out these functions. Our achievements for the year are substantial in each of these areas. They are summarized on the following pages and in the body of the annual report.

CIRM Initiatives Laid the Foundation for Strong Science

CIRM has worked hard in this first eighteen months of existence to ensure that the foundation for its stem cell research funding program is in place. Among our key accomplishments:

- CIRM solicited and received Research Fellowship applications for the CIRM Training Program in Stem Cell Research to train pre-doctoral, post-doctoral and clinical fellows, and to build collaborations across research areas to create a new generation of interdisciplinary stem cell scientists in California. The Scientific and Medical Research Funding Working Group reviewed the proposals and rated them based upon scientific merit, and the ICOC completed a final review and approval of grants to 16 outstanding California research institutions to train 169 brilliant young stem cell scientists and clinicians. The awards for the first year grants were made possible on April 6, 2006 through the leadership of six philanthropic individuals and foundations who purchased Bond Anticipation Notes of the State of California, despite the ongoing litigation challenging the state's ability to repay those notes.

- The ICOC appointed the members of the Scientific and Medical Accountability Standards Working Group, composed of five ICOC patient advocates, nine nationally-recognized scientists, and four biomedical ethicists, to develop ethical standards governing CIRM-funded research. (Membership of the Working Group, including the ICOC Members, is on page 28.)

- The ICOC appointed members of the Scientific and Medical Research Funding Working Group, including fifteen nationally prominent stem cell scientists from outside of California, as well as seven patient advocates from the ICOC, to develop criteria for reviewing scientific applications and to evaluate research proposals. (Membership of the Working Group, including the ICOC Members, is on page 27.)

- The ICOC appointed a Scientific and Medical Research Facilities Working Group that is responsible for overseeing the development of research facilities by the Institute. (Membership of the Working Group, including the ICOC Members, is on page 26.)

- CIRM appointed a nationally prominent scientific administrator, Arlene Chiu, Ph.D., as Director of Scientific Activities.

- CIRM organized a major scientific conference, *Stem Cell Research: Charting New Directions for California*, which brought biomedical experts from all over the world to advise CIRM on scientific priorities for funding.

- CIRM accepted an invitation to join the Interna-

tional Stem Cell Forum, a prestigious multinational organization of scientific funding agencies representing 19 countries that facilitates worldwide collaboration in stem cell research

Regulatory and Administrative Infrastructure Protects Science

CIRM has been a national leader in setting the highest medical and ethical guidelines and in developing grant administration and intellectual property policies. Among our top achievements:

- Many ICOC appointees participated in a public meeting in December 2004, organized by the Board on Life Sciences of the National Research Council of the National Academies, where national experts in scientific administration contributed to a broad platform of information on "best practice" policy alternatives for key ethical, regulatory and administrative policies.

- The ICOC approved draft regulations for medical and ethical standards modeled after the National Academies' *Guidelines for Human Embryonic Stem Cell Research*. The interim CIRM standards are the first comprehensive state regulations in the country for stem cell research.

- The ICOC approved an Intellectual Property Policy for Non-Profit Institutions that surpasses national standards and Federal statutes. The policy requires the prompt sharing of research results, provides a financial return to the State for intellectual property (beyond the most important potential return: new therapies), and ensures accessibility to treatments for low-income and uninsured Californians.

- CIRM developed, and the ICOC approved a grants administration policy that establishes processes and procedures for all CIRM-funded research at non-profit California institutions.

Building a State Agency from the Ground Up

Immediately after passage in November, 2004, CIRM began building itself into California's newest government agency.

- After a vigorous competition between 10 California cities, the ICOC selected San Francisco for its headquarters, based on the city's proposal that provided $18 million in donated benefits and services to CIRM, including:

  — 20,000 square feet of office space, rent free for a decade;

  — 16,000 hotel rooms over 10 years (2,000 free rooms with the balance discounted);

  — Seven conference venues of 300-50,000 seats free for 10 years.

- The San Francisco proposal saves taxpayers money and allows the Institute to devote more funds to scientific research. This represents the first time in the history of the state that a public/private partnership group has come together to financially underwrite a main headquarters facility and incentive package for a California government agency.

- The ICOC established conflict-of-interest policies for the ICOC, CIRM employees, and working group members that go beyond state law.

- The ICOC established open meeting policies and held more than 70 public meetings (as of June 2006) at sites throughout California.

- CIRM and the ICOC developed an organizational structure for CIRM and established personnel compensation policies.

Funding the Agency Grants: Financial Innovation and Civic Support

Although groups opposed to stem cell research sought to prove, through litigation, that they could stop the State of California from implementing the grant program, the CIRM successfully funded its first 169 research fellows grants in April, 2006. This represented the beginning step in authorizing an innovative interim financing progam to carry the CIRM grant program through the litigation period. The steps to that process are outlined below.

CIRM received authorization from the State's independent Finance Committee to sell up to $200 million in bond anticipation notes (BANs), as interim funding for CIRM operations and grants. The first $14 million in BANs were sold on April 4, 2006, to the following California philanthropic foundations:

Beneficus Foundation	$2 million
Blum Capital Partners LP	$1 million
William K. Bowes Foundation	$2 million
The Broad Foundation	$2 million
Jacobs Family Trust	$5 million
The Moores Foundation	$2 million

The second $31 million in second round BANs, closed in November of 2006 are as follows:

Mr. J. Taylor Crandall	$1 million
Gordon and Betty Moore Foundation	$10 million
Dr. Gordon E. Moore	$5 million
Jewish Community Endowment Fund	$1 million
H&S Investments I, LP	$2 million
Seventh Street Warehouse Partnership	$1 million
Steven L. Swig and Mary Green Swig	$1 million
The David and Lucile Packard Foundation	$5 million
The Sandler Family Supporting Foundation	$5 million

Several key donors whose charitable contributions have empowered a substantial portion of our work should also be acknowledged. The agency's efforts to lead the country in developing medical, ethical, and conflict of interest standards, and to process its first grants were largely funded by a generous contribution from Ray and Dagmar Dolby and their family foundation. An important supporting contribution for scientific meetings and strategic planning activities was made possible by a gift from the Richard and Rhoda Goldman Fund.

Pursuing the Voters' Mandate

Litigation challenging the constitutionality of the California Stem Cell Research and Cures Act (Proposition 71) currently precludes the State from issuing the authorized general obligation bonds to fund stem cell research at acceptable interest rates. The Attorney General, Bill Lockyer, has strongly and successfully defended

the constitutional merit of Proposition 71. On April 21, 2006, Judge Bonnie Lewman Sabraw of the Alameda County Superior Court delivered a ruling that found the California Stem Cell Research and Cures Act constitutional in its entirety.

Judge Sabraw found that the CIRM was firmly under the management and control of the state, stating in part:

> *The evidence at trial establishes that the application of the Act has been in compliance with its statutory framework, and that CIRM and the ICOC are operating in the same fashion as other state agencies. Each ICOC member, and each alternate, has taken the oath of office and publicly filed Form 700, the standard form California public officials file to disclose financial holdings. The ICOC developed and adopted incompatible activities statements, the conflict of interest code required by the Political Reform Act, and conflict of interest policies for ICOC members, CIRM staff, and members of each of the ICOC advisory groups. Between January 2005 and the date of the trial, the ICOC and its subcommittees, and its working groups held over 40 noticed, public meetings, in cities across the state, held pursuant to the Bagley-Keene Open Meeting Act. CIRM has responded to numerous Public Records Act requests.*

Judge Sabraw also found that the Institute has been accountable to the public and has conformed to all state oversight requirements in carrying out its operations. The court's decision is a significant step forward toward the point in time when General Obligation bonds can be issued at reasonable interest rates to fund voter-mandated stem cell research. It is therefore a major victory for the CIRM to have assembled its substantial interim grant funding program for the next fiscal year.

The Superior Court decision has since been appealed, and a final conclusion is not expected until 2007, when we believe the voters' intentions will be upheld. Fifteen

AMICUS PARTIES

The following research institutions, hospitals, universities, and patient advocacy organizations filed an amicus brief in support of CIRM on October 12, 2005.

Patient Advocacy Groups

- Alliance for Aging Research
- Alliance for Stem Cell Research
- ALS Association
- Alzheimer's Association, CA Council
- Cancer Research and Prevention Foundation
- Christopher Reeve Foundation
- Cystic Fibrosis Research, Inc.
- Elizabeth Glaser Pediatric AIDS Foundation
- Juvenile Diabetes Research Foundation (JDRF)
- The Leukemia and Lymphoma Society
- Michael J. Fox Foundation for Parkinson's Research
- National Brain Tumor Foundation
- National Multiple Sclerosis Society
- Parkinson's Action Network
- San Francisco AIDS Foundation

Universities

- California Institute of Technology
- Keck Graduate Institute
- Stanford University
- University of Southern California

Hospitals & Institutes

- Cedars-Sinai Medical Center
- Children's Hospital & Research Center at Oakland
- Childrens Hospital Los Angeles
- City of Hope
- Salk Institute of Biological Studies
- The Burnham Institute

Others

- Paul Berg, Nobel Laureate
- Southern California Biomedical Council

INNOVATION GRANTS

The ICOC approved three research initiatives that rely on $31 million of bond anticipation notes and a $150 million loan from the California Department of Finance.

Comprehensive Research Grants
(up to $80 million over 4 years)

- Record of accomplishment in hESC research or closely-related field
- Opportunity to expand research or take promising new directions based on current research

  Must be related to long-term therapeutic goal
- Topics include, but are not limited to:
  - — Self-renewal and differentiation of hESCs
  - — Derivation of new hESC lines, including disease-specific lines
  - — Study of hESC-derived cells in animal models
  - — Assessing tumorigenicity of hESCs and cells derived from them
  - — Reprogramming of adult human somatic nuclei
  - — Studies related to identification, storage, maintenance, stability and storage of hESCs

Seed Grants
(up to $24 million over 2 years)

- Emphasis on new ideas, new investigators in the field
- No prior record of hESC research required
- No "preliminary data" required
- Criteria will emphasize innovation

Shared Research Laboratory Grants
(up to $47.5 million over three years)

- Dedicated laboratory for culture of hESCs, including cell lines that are outside the federal guidelines
- Will support core equipment and trained personnel
- Services available for scientists from nearby institutions without facilities
- At up to five institutions, extra funds will be provided for formal course instruction, given several times per year for California scientists and trainees.

national patient advocacy organizations and 10 of California's most prestigious research institutions and universities (shown on the previous page) joined the litigation, in support of Proposition 71, in an amicus curiae brief. The courageous backing of those support groups provided a clear message to California's courts on the urgent need to expedite this litigation. It is our hope that our litigation will finally be resolved by the middle of 2007, at the State Supreme Court.

State of California Funding Breakthroughs

For the coming year, we are actively preparing for the availability of full public funding of more than $300 million in General Obligation Bonds, so that we can quickly issue additional training, research, and facilities grants without further delay. In a bold and decisive move this past July, Governor Arnold Schwarzenegger directed the California Department of Finance to make a $150 million loan to the Institute. This loan was authorized by Section 125291.60 of Proposition 71 and will help ensure California retains its national leadership in stem cell research, while the litigation is concluded. The loan funds are expected to be available in November of 2006, and they will allow CIRM to advance a major program of research in California for the benefit of patients worldwide. The ICOC has approved three major research initiatives that rely on the $31 million of additional BAN's funds and the $150 million loan. Those programs are outlined at left..

The successes of our inaugural eighteen months, as well as those we will record going forward, are the cumulative efforts of many people, here in California, across the country, and around the globe. We are grateful to the residents and public interest groups who helped shape our scientific and governance policies; the experts who

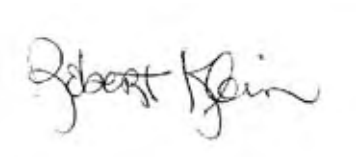
helped navigate complex ethical and intellectual issues and chart the direction of our research funding; the elected officials who contributed advice and counsel to navigate the challenges of creating a new government agency; the CIRM staff who continually exceed high expectations; and finally, to the ICOC board members — their tireless dedication to our mission and the tremendous scope of their expertise is a great gift to all Californians.

A Focus on Therapies and Cures

Our overall organizational mission is to support and advance stem cell research and regenerative medicine under the highest ethical and medical standards for the discovery and development of cures, therapies, diagnostics and research technologies to relieve human suffering from chronic disease and injury. One of the ways in which we remain connected to our primary constituency, patients, is through a presentation series called "Spotlight on Disease." In cooperation with the non-profit organization, Alliance for Stem Cell Research, we have organized presentations before most ICOC meetings so that ICOC Members, CIRM staff, and members of the public are able to learn more about the state of stem cell science and the experience of patients within a particular chronic disease or injury.

One-page summaries of these very moving Spotlight presentations appear in the following pages: immediately after this introductory letter and at the end of the Annual Report itself. We hope that in perusing these summaries, you capture a sense of the primary motivation for why we are working so hard every day to ensure that we meet our mission.

We are at a pivotal point in the history of medical research. In approving Proposition 71 on November 2, 2004, the citizens of California created the vision of a future for humanity that holds the potential for remarkable progress in the understanding and treatment of chronic disease and injury.



Robert N. Klein, II
Chairman, Independent Citizens Oversight Committee

Amyotrophic Lateral Sclerosis (ALS)

Hugh Winokur, whose youngest brother Douglas died of ALS in 1997, was diagnosed with the same disease in 2001.

What is ALS?

Commonly known as Lou Gehrig's disease, ALS is a chronic, progressive disease characterized by degeneration of the neurons that control voluntary muscle movement. ALS prevents the motor neurons in the brain and spinal cord from sending impulses to the muscles. This causes muscle atrophy, weakness and eventual paralysis. It typically begins with loss of fine motor control or weakness in the extremities, and progresses to inhibit all movement, including unconscious activities like swallowing and breathing.

30,000 Americans have ALS, and 8,000 new cases are diagnosed each year. The cause is not yet understood, but small percentages of patients have a genetic or environmental component to disease onset. ALS is always fatal, and although the time span varies somewhat among patients, the vast majority live only 2 to 5 years after symptom onset. There is no known cure.

How do we currently understand and treat ALS?

The mechanisms of ALS are not yet understood, but a number of theories are being pursued. Inflammation is widely ob-

served in ALSaffected tissues, and it may be a faulty immune response that causes the support cells around motor neurons to attack rather than help. Scientists are also exploring how excessive protein buildup inside neurons may trigger cell death.

There is one FDAapproved drug for ALS, but it has only marginal impact on patients' lifespan and quality of life. Most patients must merely try to slow the disease's progress through a closely monitored diet, exercise promoting muscle strength and flexibility, and mechanical aids to support functions like movement, balance and ultimately, breathing.

What is it like to live with ALS?

ALS strikes people without warning and in the prime of life, making diagnosis devastating for patients and families. It gradually robs persons of their mobility, control and independence, making them increasingly reliant on others for the basic functions of life. The lack of effective treatments and the certain fatality of ALS leave patients and loved ones desperate for any treatment. The potential of stem cell research provides the ALS community with much needed hope for interventions, understanding and possibly even a cure for this insidious and intractable disease.

How might stem cell research help us better understand and treat ALS?

ALS is a complex disease and stem cells offer a number of ways to help understand its mechanisms and to treat its crippling effects. There is currently no research model for the type of ALS that accounts for over 90% of all cases—the "sporadic" form. Stem cells may provide a cellular model for sporadic ALS that would allow efficient testing of the safety and effectiveness of new drugs to protect at-risk cells and slow the disease progression. Such interventions would be a major advance over current management efforts. Stem cells may also enable more dramatic therapeutic strategies involving cell transplantation and gene therapy techniques.

Stem cells secrete protective and restorative chemical factors that can help at-risk cells survive, and research in animal models of familial forms of ALS shows that transplanted stem cells do protect motor neurons and prolong life. Similar experiments prove that stem cells reduce the ALS-related scar tissue that further inhibits function and impedes therapeutic intervention. Other research in animals shows that stem cells migrate towards areas of nerve damage and stimulate re-growth of axons (the connections between nerve cells that enable muscle control.)

Research indicates that ALS affects more than motor neurons. It also appears to impair aspects of the immune system, or at least the support cells that surround neurons. Repairing or replacing such a complex system requires the integration of multiple cell types, and stem cells seem to possess the innate ability to construct—under optimal circumstances—just such an environment. Much additional research is necessary to realize this potential, but stem cells offer the hope to repair, not just slow, ALS-related damage.

Cystic Fibrosis

Tess Dunn has cystic fibrosis. In 2000, a child or young adult with a mild case of cystic fibrosis faced approximately $30,000 in annual medical care and prescription costs, creating a huge burden for their families.

What is Cystic Fibrosis?

Cystic fibrosis is a chronic, progressive and fatal disease primarily affecting the respiratory and digestive systems in children and young adults. It is one of the most common lethal genetic diseases in America, affecting an estimated 30,000 children and young adults. There is currently no cure.

How do we currently understand and treat Cystic Fibrosis?

Normal respiration exposes the lungs to many infection-causing agents, which are continuously cleared by a layer of viscous mucus on the airway surfaces. Cystic fibrosis is caused by a single gene defect that creates a mutant version of a protein called CFTR. CFTR helps regulate the lung's protective mucus, but the defective protein makes the mucus abnormally thick and less able to clear particles from the lungs. Airways become clogged and non-functional, further raising the risk of infection. The body's immune system fights the infections, but the response can also do harm. In fact, much of the lung damage associated with cystic fibrosis is caused by an exaggerated and overly aggressive inflammation reaction.

The dense mucus secretions also obstruct the pancreas, preventing digestive enzymes from reaching the intestines to help

break down and absorb food. The trapped enzymes can actually destroy the pancreas, leading to malnutrition, which is most severe in infants.

Existing therapies and drugs, including antibiotics and anti-inflammatory medications, help alleviate some of the symptoms. Improved neonatal screening and genotyping tests have increased the rate of early diagnosis and intervention. Lung transplantation is the only option for advanced disease, and can extend patients' lives. However, there are not nearly enough available donors, and transplantation does not address the disease's underlying cause.

What is it like to live with Cystic Fibrosis?

Symptoms can vary widely from person to person, but include persistent coughing, wheezing or shortness of breath, an excessive appetite but poor weight gain, and chronic fatigue. Lifethreatening infections are a constant fear, creating anxiety and behavioral changes in patients and family members. The potential for infection requires severely limited exposure to other people and the environment.

Patients have daily health regimens, including taking pancreatic enzymes and other supplements, drug injections, "percussive therapy" (banging on chest and back to break up congestion), breathing through medicated nebulizers (see photo), as well as closely monitoring diet, sleep and exercise.

In the past, most children with cystic fibrosis did not reach adulthood. Improved therapies have extended the average life expectancy, but it remains only 32 years.

How might stem cell research help us better understand and treat Cystic Fibrosis?

Early studies have shown that blood- and bone marrow-derived human stem cell transplants can integrate themselves into tissue of the airways and produce normal CFTR protein. The normal protein produces normal mucus and could help keep lungs clear. Spontaneous cell regeneration in damaged lung tissue following transplant has also been observed. Human embryonic stem cells have been used to produce new lung cells that may be implanted to repair damage associated with cystic fibrosis.

Scientists are also working to model cystic fibrosis in the laboratory with specially engineered stem cells. Studying these cells will increase understanding of the disease and lead to new treatments. Ongoing studies also indicate that stem cells could play an important role in the delivery and efficacy of potential gene therapy treatments—including strategies to correct the gene defect that causes cystic fibrosis.

Liver Disease

Without receiving a liver transplant at age seven, Amy Wang would not have lived to see her wedding day.

What is liver disease?

The liver is one of the body's most versatile and vital organs. It continually filters the blood and detoxifies everything we eat, breaking down and absorbing some chemicals while secreting others into the blood stream. It also serves important functions in the body's metabolic and immune systems.

The term "liver disease" applies to many diseases and disorders that cause the liver to function improperly or cease functioning. These include hepatitis, cancer, alcohol- and nonalcohol- related cirrhosis and certain autoimmune diseases (in which the body's immune system mistakenly attacks its own cells) among others.

How do we currently understand and treat liver disease?

Many of the diseases affecting the liver are well understood, but there is a frustrating lack of effective long-term treatments other than transplantation. Liver transplant is a common, highly successful and durable surgery—65% of transplant patients live for at least 15 years after surgery, while most of those patients would likely die within six months without transplant. The liver is believed to have the most regenerative potential of any organ, and the success of "living donor" transplantation— in

which a portion of a living person's liver is transplanted into another individual—dramatically exemplifies its regenerative capacity. Despite significant progress in recent decades, liver transplant is not a viable option for many patients. The surgery itself may be too traumatic for some patients. Even successful surgery usually requires life-long immune suppression therapy, which has major complications, including heightened risk of serious infections and cancer. Furthermore, there are not nearly enough available donor livers for all the patients in need. Almost all patients endure long waiting periods and far too many die while on the waiting list.

What is it like to live with liver disease?

The many diseases of the liver affect a large and diverse population—from newborns to the elderly, and everyone in between. They inflict a wide variety of symptoms, ranging from uncomfortable to debilitating to life threatening. Patients must rely on family members, and often machines, to manage their day-to-day life and health. Diagnosis often comes as a shock and can result in confusion, major life alterations or even depression.

Transplant recipients can live long and productive lives, but they also live with lingering side effects, the loss of some function or freedoms, and the constant fear of major complications or relapse. And far too many people suffering with liver disease never get the chance for transplantation. Stem cell research offers hope to patients and families living with liver disease.

How might stem cell research help us better understand and treat liver disease?

Stem cells can provide new and unique human cellular models for studying liver diseases. They can also be used to create large-scale screens to efficiently identify safe and effective new drugs.

Researchers are working to induce stem cells to become the liver's three main cell types. These cells could be transplanted (or infused) directly into the diseased liver to replace dead or damaged cells and restore healthy function. Stem cells may also enable scientists to grow healthy liver tissues in the laboratory for use in transplantation. Researchers hope to use a process called somatic cell nuclear transfer to embed an individual patient's DNA in the stem cells from which new liver tissue is grown. Since the transplanted tissue will have the same DNA as the patient, their body will accept it without hazardous immune suppression therapy.

These techniques promise healthy transplants to many more patients, without the need to wait in line, endure major surgery or risk their future health with a compromised immune system.

Spinal Cord Injury

Improved technologies, including stem cells, promise both the small and big advances that keep people with spinal cord injuries and their families hopeful that improved quality of life, and even a cure, is within reach.

What is spinal cord injury?

A spinal cord injury refers to any damage to the spinal cord that results in a loss of function such as mobility or feeling. Injuries typically occur through trauma or disease, and can involve cellular damage, sustained compression, or complete or partial severing of the nerves encased within the spinal column.

Approximately 11,000 Americans sustain a spinal cord injury each year. More than half of those injured are 15 to 29 years of age. Motor vehicle crashes are the leading cause of spinal cord injuries among persons under age 65. The vast majority of spinal cord injuries are currently irreversible. Annual U.S. costs related to spinal cord injuries are estimated at $9.7 billion.

How do we currently understand and treat spinal cord injuries?

Spinal cord injuries damage the cells that enable communication between the brain and motor neurons throughout the body. The effects of injuries vary depending upon their type, severity and location along the spinal column. In general, the higher the injury the more bodily function is at risk. For example, a lower back injury may paralyze the legs, while injury to the thoracic region of the neck may immobilize the entire body and impair breathing, requiring use of a respirator.

There are limited therapeutic options for most people with spinal cord injuries. Physical therapy benefits some patients, and a few are even able to regain some of their lost motor function or reduce the time they must use a respirator. Even small improvements usually require long periods of retraining and hard work. Lacking adequate treatments, the injured person's environment is altered to help them adopt new methods of mobility and functionality.

What is it like to live with spinal cord injuries?

People with spinal cord injuries can lose a great deal of independence, often needing to rely on machines or other people to perform the basic tasks of daily life. Seemingly simple things, like getting out of bed or eating a meal can be enormously difficult and time-consuming. Spinal cord injuries also increase one's risk for other conditions, from painful and dangerous pressure sores to life-threatening infections and metabolic crises. Depression and other psychological issues can also be concerns.

Hope persists despite the challenges. While total function remains the ultimate goal, small improvements make huge differences in people's lives. Restoring the muscle control needed for one to lift themselves between their bed and wheelchair greatly increases their independence, and also reduces the cost of care. Improved technologies, including stem cells, promise both the small and big advances that keep people with spinal cord injuries and their families hopeful that improved quality of life, and even a cure, is within reach.

How might stem cell research help us better understand and treat spinal cord injuries?

Some researchers believe that people suffering spinal cord injuries may be the first beneficiaries of therapies derived from human embryonic stem cells. This is because most spinal cord injuries are small and localized, so the area of treatment is easily identified. Also, much is already understood about the function(s) required from implanted cells. There are three leading strategies for stem cell treatments: increase cell survival after injury by using stem cells to deliver protective and nourishing chemical factors; transplant new cells to replace those lost to injury or disease; and restore function to nerve cells that are intact but unable to conduct electrical impulses because they lost their protective layer of insulation.

This last approach may offer the most immediate promise because it is comparatively simple, requiring transplantation of a single type of cell (called an oligodendrocyte) specifically programmed to wrap around neuron cells and form the protective sleeve known as myelin. Studies show that oligodendrocytes derived from embryonic stem cells will replace the myelin insulation on "naked" nerve cells and lead to restored function of paralyzed rodents. Though not yet viable for chronic injuries, this treatment will soon be tested in newly injured persons.

Multiple Sclerosis

Mary Hill has been living with Multiple Sclerosis for over twenty years. Although it has forced her to slow down in many ways, she has become a tireless patient advocate. In fact, in 2001, she participated in an international open-water relay swim from Catalina Island to the Santa Monica Pier, representing the USA in an event called "Turning the Tides on MS."

What is Multiple Sclerosis?

Meaning "many scars," multiple sclerosis is a chronic, degenerative disorder of the central nervous system. Nerve cells communicate by sending electrical signals through their branch-like projections, known as axons. A fatty layer of tissue (called myelin) surrounds axons and acts as insulation to protect the cells and enable electrical conduction. MS strips nerve cells of their myelin, prompting scars to form and the cells to cease functioning properly or die. MS is thought to be an autoimmune disease, where the body's immune system assaults its own tissues, beginning with the nerves regulating vision, sensation and muscle control in the extremities. MS affects about 500,000 Americans; most diagnosed between the ages of 15 and 50. Patients experience a variety of progressively worsening symptoms, with extreme fatigue, muscle weakness, motor instability and cognitive dysfunction being the primary causes of disability. The cause and exact mechanisms of MS are not yet understood, although genetic and environmental factors seem to contribute in some cases. There is no cure for MS at this time.

How do we currently understand and treat Multiple Sclerosis?

The most common form of MS is called "relapsingremitting." Patients experience fairly mild symptoms, but suffer occasional severe attacks, marked by headaches, impaired vision, and loss of balance, sensation and motor function. Medications help

reduce the frequency and intensity of the attacks. The more severe "progressive" form of MS features constant and steadily worsening symptoms, leading to profound motor disability and cognitive loss. MS can begin in either form, and can advance from relapsing-remitting to progressive without warning and for unknown reasons.

Current treatments rely on drugs to reduce the brain inflammation that accompanies MS, and can effectively lessen the symptoms and attacks by as much as one-third. However, these medications require regular injections, often cause unpleasant side affects and are very expensive. Most importantly, current therapies do not protect at-risk neurons, slow disease progression or reduce brain damage.

What is it like to live with Multiple Sclerosis?

Though usually not life threatening, MS afflicts people in the prime of life and can cause disability, cognitive decline and depression. Symptoms can be unpredictable, varying from day to day and person to person. Patients must cope with weakened immune systems, crippling fatigue, stress and temperature sensitivity, mobility and balance impairment and the constant threat of a severe attack. MS patients often list the loss of independence and control over their lives as the most debilitating aspects of living with this disease. These same patients can now look to embryonic stem cell research with the renewed hope of regaining what has been taken from them by MS.

How might stem cell research help us better understand and treat Multiple Sclerosis?

Human embryonic stem cells promise to provide new cellular models of MS that will help researchers identify the disease mechanisms and test new interventions. They may also lead to new understanding of the cause, or causes, of MS.

The brain has normal protection and repair mechanisms, but even early stage MS can cause injury too significant for the brain to repair itself. Stem cells offer the best opportunities to develop the protective and restorative therapies needed to arrest the disease and heal damage.

Researchers are testing a number of strategies, including transplanting stem cells to correct or boost the normal immune and repair systems. This could reduce inflammation without drugs and prevent the loss of myelin that causes nerve damage. Studies in animal models of MS show that stem cells deliver chemical factors that protect neurons and delay scarring when myelin has been lost. Myelin-producing cells, called oligodendrocytes, can be derived from embryonic stem cells and implanted into affected areas of the central nervous system. Experiments with animals show that transplanted oligodendrocytes can restore myelin insulation to damaged nerve cells. Effectively replacing lost myelin is a step closer to curing MS.

Introduction — The Annual Report

Rarely has a field of biomedical research caught the public imagination as dramatically as stem cell research. The concept of transplanting human cells grown in vitro (in the laboratory) into tissues to replace damaged or diseased cells is easy to understand and appealing in its concept. Moreover, cell replacement therapy has a potentially wide application for scores of diseases ranging from diabetes to cancer to arthritis. Beyond cell replacement, stem cell research offers the potential of scientific tools, like tissue-specific cell lines, to test toxicity of new therapies and to study the biological development of individual diseases. Stem cell research also offers the possibility of expanding the breadth of patient applications of adult stem cell therapies by broadening immune tolerance or enhancing the opportunity for immune system matching. As a result, the new frontier of stem cell research has generated scientific excitement and medical hope throughout the world.

In spite of its potential, stem cell research has been handicapped in the United States — the global leader in biomedical research — by severe restrictions on federal funding. Californians stepped into the funding gap with the passage of Proposition 71, the California Stem Cell Research and Cures Act ("the Act"), by an overwhelming majority on November 2, 2004. The Act authorized the investment of $3 billion in public bond funds for stem cell research through California non-profit and for-profit research entities. No other state has ever made such a significant commitment to basic and applied scientific research and clinical research medicine. Following California's bold lead, several other states have now allocated monies for stem cell research.

The Act created a new state agency, the California Institute for Regenerative Medicine (CIRM or "the Institute"), and its governing board, the Independent Citizens Oversight Committee (ICOC). The ICOC and CIRM have a clear and simple mission: use stem cell research and other vital technologies to develop therapies for patients suffering with chronic disease and disability.

This first CIRM annual report primarily covers the first 18 months of the Institute's life, from January 2005 through June 2006. In this first phase of implementation, the Institute has begun to fulfill the mandate of the California voters. Despite challenges in court on con-

stitutional grounds by opponents of stem cell research, the Institute funded its first grants: an ambitious, statewide training program for young stem cell scientists, held an international scientific conference, and laid the necessary ethical, administrative and regulatory foundations for a comprehensive, large-scale program of scientific research.

Meeting the Funding Challenges

CIRM has also devised several innovative and unprecedented solutions to funding challenges. Faced with litigation designed to deprive the Institute of voter-approved bond funding, the Institute designed and implemented bridge funding solutions never before used in California or in any other state. Second, a competition was held among California's leading cities to provide an administrative headquarters and conference facilities at no cost for 10 years. The winning bid was a unique public-private collaboration in the City and County of San Francisco, and CIRM is now installed in world-class headquarters at no cost to the taxpayers of California.

The Dolby family, with the assistance of San Francisco Mayor Newsom's office, then elevated the Institute's staffing capacity with a dramatic contribution of $5 million. With the initial staff in place, the Institute designed an unprecedented private placement of $45 million in Bond Anticipation Notes (BANs), in cooperation and with the strong support of State Treasurer Phil Angelides' office and with the approval of the California Stem Cell Research and Cures Finance Committee, in order to provide critically needed bridge funding for grant programs. On July 20, 2006, California's Governor Schwarzenegger authorized a loan of $150 million from the state's general fund to CIRM. When combined with the BAN program, CIRM will have access to $195 million in grant funding before the anticipated resolution of the legal challenge next summer ensures our ability to issue voter-approved bonds, at low, cost-effective interest rates.

Initial Steps

Even before State Controller Westly and State Treasurer Angelides convened the first meeting to seat the governing board in December, 2004, Proposition 71's author, Robert Klein, requested the President of the National Academies of Science to convene an extraordinary public working group, representing many of the nation's leading scientific researchers and medical ethicists to examine critical challenges the

ICOC would face during the initial organizational phase. The Board on Life Sciences of the National Research Council of the National Academies organized and convened the meeting just five weeks after the 2004 election. The meeting covered the following the topics:

- Conflicts of interest
- Medical and ethical standards for research
- Grant program strategies
- Policies for public transparency and accountability

The ICOC is grateful for this leadership of the National Academies in providing an invaluable contribution to the formulation of the ICOC's early policies and standards. Immediately following the certification of the election results, the state's elected officials and the chancellors of its public universities appointed 29 members to the ICOC. Its members were drawn from the state's leading research institutions, from the private sector, and from the patient advocate community. The distinguished list of appointees included a Nobel Prize winner, two former commissioners of the U.S. Food and Drug Administration, seven medical school Deans, and a former First Lady of California.

At its first meeting, the ICOC elected Robert N. Klein as Chairman and Edward E. Penhoet, Ph.D. as Vice-Chairman. Through its quality and diversity the board gives strong leadership and oversight to CIRM. During its second meeting, Robert Klein was also authorized to act as interim President in order to organize the agency and to hire preliminary staff. By March 2005, the ICOC was in a position to hire an interim president, Zach W. Hall, Ph.D., with scientific and administrative credentials. In September 2005, after a presidential search, Dr. Hall was named permanent President and Chief Scientific Officer of CIRM.

ICOC Search Subcommittees and Working Groups

To aid CIRM in its work and to provide recommendations to the ICOC, the Act provides for three advisory Working Groups, each composed of patient advocates from the ICOC board and outstanding scientific and medical experts from around the world. The focus of the three working groups is: 1) to review and provide recommendations for funding research grant applications, 2) to review and provide recommendations for funding facility grant applications, and 3) to establish and provide oversight of medical and ethical standards. The board formed the following search subcommittees to populate these working groups:

1) Scientific and Medical Research Funding Working Group ("Grants Working Group") Search Subcommittee — Chaired by Dr. Ed Holmes and Joan Samuelson
2) Scientific and Medical Accountability Standards Working Group ("Standards Working Group") Search Subcommittee — Chaired by Dr. David Kessler and Jeff Sheehy
3) Scientific and Medical Research Facilities Working

Group ("Facilities Working Group") Search Subcommittee — Chaired by Dr. Michael Friedman

The subcommittees worked under intense time pressure and faced monumental tasks — including, for example, choosing 15 scientific and medical experts for the Grants Working Group from approximately 800 nominations. Members were appointed by the ICOC in early 2005 after an extensive search and selection process. The ICOC drew upon nationally prominent scientists, ethicists, and distinguished California real estate experts.

SEARCH SUBCOMMITTEES

STANDARDS SEARCH SUBCOMMITTEE
David Kessler (Chair)
Joan Samuelson
David Serrano Sewell
Jeff Sheehy
Jon Shestack
Os Steward

GRANTS SEARCH SUBCOMMITTEE
Brian Henderson
Ed Holmes (Chair)
Sherry Lansing
Gerald Levey
Ted Love
Phil Pizzo
John Reed
Jeff Sheehy
Jon Shestack
Leon Thal
Janet Wright

FACILITIES SEARCH SUBCOMMITTEE
Michael Friedman (Chair)
Bob Klein
Ted Love
Claire Pomeroy
Francisco Prieto

SCIENTIFIC AND MEDICAL FACILITIES WORKING GROUP

PATIENT ADVOCATES
Marcy Feit, *ICOC Patient Advocate for Type II Diabetes*
Robert Klein, *Chairman of the ICOC*
Sherry Lansing, *ICOC Patient Advocate for Cancer*
Joan Samuelson, *ICOC Patient Advocate for Parkinson's Disease*
David Serrano Sewell (Vice Chair), *ICOC Patient Advocate for MS/ALS*
Jeff Sheehy, *ICOC Patient Advocate for HIV/AIDS*
Janet Wright, *ICOC Patient Advocate for Heart Disease*

ALTERNATE REAL-ESTATE SPECIALISTS
Stuart Laff, First Alternate, *DMJM Consulting/AECOM*
James Frager, *Taylor Frager*
Joe Mock, *ZORO LLC; Signature Fruit Company LLC*
Warren "Ned" Spieker, *Spieker Partners*

REAL-ESTATE SPECIALIST MEMBERS
Albert "Rusty" Doms (Chair), *Redmond Doms Company, President*
Deborah Hysen, *The California Performance Review*
Edward Kashian, *Lance-Kashian & Company*
David Lichtenger, *Integrity Office Solutions*

AD HOC REAL-ESTATE SPECIALISTS
John Archibald, *Grubb & Ellis*
Stuart Shiff, *Divco West Properties*

SCIENTIFIC AND MEDICAL RESEARCH FUNDING WORKING GROUP

PATIENT ADVOCATES

Robert Klein (ex-officio), *ICOC Chairman*
Marcy Feit, *ICOC Patient Advocate for Type II Diabetes*
Sherry Lansing, *ICOC Patient Advocate for Cancer*
Joan Samuelson (Vice Chair), *ICOC Patient Advocate for Parkinson's Disease*
David Serrano Sewell, *ICOC Patient Advocate for MS/ALS*
Jeff Sheehy, *ICOC Patient Advocate for HIV/AIDS*
Jonathan Shestack, *ICOC Patient Advocate for Mental Health*
Janet Wright, *ICOC Patient Advocate for Heart Disease*

SCIENTISTS	AFFILIATION	EXPERTISE
Susan Bonner-Weir	Harvard Joslin Institute	Diabetes
Ali Brivanlou	Rockefeller University	Developmental Biology
Patricia Donahoe	Massachusetts General Hospital	Cancer
Andrew Feinberg	Johns Hopkins University	Cancer
Alexandra Joyner	New York University Medical Center	Developmental Biology
Judith Kimble	University of Wisconsin	Stem Cell Generalist, Organogenesis
Jeffrey Macklis	Massachusetts General Hospital	Neurodegenerative Diseases (ALS, SCI)
Stuart Orkin (Chair)	Dana Farber Cancer Institute	Hematopoiesis
Jeffrey Rothstein	Johns Hopkins University	Neurodegenerative Diseases (ALS)
Pablo Rubinstein	New York Blood Center	Hematopoiesis
Dennis Steindler	University of Florida McKnight Brain Institute	Neurodegenerative Diseases
Rainer Storb	Fred Hutchinson Cancer Research Center	Hematopoiesis, Bone Marrow Transplant
Clive Svendsen	University of Wisconsin	Neural Stem Cells
George Yancopoulos	Regeneron Pharmaceuticals	Neural and Autoimmune Disorders
Wise Young	Rutgers University	Neurodegenerative Diseases (SCI)

ALTERNATES	AFFILIATION	EXPERTISE
Marie Csete	Emory University	Transplantation
Ian D. Duncan	University of Wisconsin	Neurodegenerative Diseases (MS)
Ihor Lemishka	Princeton University	Hematopoiesis
Olle Lindvall	Lund University	Hematopoiesis
Ray MacDonald	University of Texas Southwestern Medical Center	Developmental Biology, Organogenesis
Arthur Nienhuis	St. Jude Medical Center	Hematopoiesis
Jon Odorico	University of Wisconsin	Diabetes
Frank Rauscher	The Wistar Institute Cancer Center	Cancer
Yair Reisner	Weizmann Institute of Science	Immunology
James Roberts	Fred Hutchinson Cancer Research Center	Developmental Biology
R. Paul Robertson	Pacific Northwest Research Institute	Diabetes
Raymond Roos	University of Chicago	Neurodegenerative Diseases (ALS, MS, AD)
Robert Rosen	Columbia University	Cardiovascular Disease
David Scadden	Massachusetts General Hospital	Hematopoiesis
Catherine Verfaillie	University of Minnesota	Hematopoiesis, Mesenchymal Stem Cells
Fiona Watt	London Research Institute	Epidermal Stem Cells

AD HOC MEMBERS	AFFILIATION	EXPERTISE
George Daley	Boston Children's Hospital & Harvard Stem Cell Institute	Biological Chemistry, Molecular Pharmacology
John Trojanowski	University of Pennsylvania	Neurodegenerative Diseases (AD)
Joshua Sanes	Harvard University	Molecular and Cellular Biology
Allan Spradling	Carnegie Institution & Johns Hopkins University	Cellular Biology

SCIENTIFIC AND MEDICAL ACCOUNTABILITY STANDARDS WORKING GROUP

PATIENT ADVOCATES

Robert Klein, *ICOC Chairman*
Marcy Feit, *ICOC Patient Advocate for Type II Diabetes*
Sherry Lansing (Co-Chair), *ICOC Patient Advocate for Cancer*
Francesco Prieto, *ICOC Patient Advocate for Type 1 Diabetes*
Jeff Sheehy, *ICOC Patient Advocate for HIV/AIDS*
Jonathan Shestack, *ICOC Patient Advocate for Mental Health*

ETHICISTS	AFFILIATION	EXPERTISE
Alta Charo	University of Wisconsin	Health Law, Bioethics and Biotechnology Law, Medical Ethics, Reproductive Rights
Bernard Lo (Co-Chair)	University of California San Francisco	Biomedical Ethics related to Oocyte, Embryo and Stem Cell Research
Patricia King	Georgetown University	Biomedical Ethics Related to Stem Cell Research and Therapy; Reproductive Technology, Minority Populations
Ted Peters	Pacific Lutheran Theological Seminary, Graduate Theological Union	Biomedical Ethics of Stem Cell Research, Genetics

SCIENTISTS/ CLINICIANS	AFFILIATION	EXPERTISE
Jose Cibelli**	Michigan State University	SCNT & Primate Embryonic Stem Cells
Kevin Eggan	Harvard University	Epigenetics, SCNT
Ann Kiessling	Harvard University	SCNT & Oocyte Derivation, IVF and Egg Donation
Jeffrey Kordower	Rush Presbyterian-St. Luke's Medical Center	Neurodegenerative Diseases
Kenneth Olden	National Institute of Environmental Health Sciences	Cellular Biology/Biochemistry, Hematopoietic Stem Cells
Janet Rowley	University of Chicago School of Medicine	Oncology, Molecular Genetics, Cell Biology, Hematopoietic Stem Cells
Robert Taylor	Emory University	Reproductive biology; IVF and egg donation
John Wagner	University of Minnesota	Stem Cell Transplant Biology, Clinical Trials
James Willerson	University of Texas Health Sciences Center Texas Heart Institute	Stem Cell Biology, Cardiac Tissue, Clinical Trials

Public Meeting Policy and Programs

The ICOC has led an agency formation process with the highest standards for public transparency. The ICOC is required by law to hold at least two public meetings each year, yet in 2005, it held twelve board meetings and four additional board meetings through June 2006, with an additional five public board meetings scheduled before the end of the calendar year.

The Chairman's Office instituted a series of disease-focused "Spotlight" presentations to begin most ICOC meetings, with a briefing from scientists, physicians, and patient advocates on diseases with the potential to benefit from stem cell research. (Summaries of these Spotlight presentations precede and follow this section of this Annual Report). Additional public meetings and public hearings were held by the ICOC's Working Groups and committees, as listed at right.

This commitment to public participation started with the more than 1,100,000 California voters who signed petitions to place Proposition 71 on the ballot in 2004. The ICOC's far reaching commitment to public transparency was further amplified, in a cooperative relationship with the State Legislature, that expanded the public meetings to the impressive totals shown above.

COMMITTEE	NUMBER OF MEETINGS
Standards Working Group	8
Facilities Working Group	1
Grants Working Group	3
Intellectual Property Task Force	5
Finance Committee	1
Governance Subcommittee	6
Legislative Subcommittee	2
Site Search Subcommittee	9

The ICOC's public meeting model was again heavily influenced by advice from the National Research Council of the National Academies of Science, requested and received by Robert Klein, the Chairman of the Board, in February of 2005. Special thanks are owed to the past President of the National Academies, Bruce Alberts, and past Chief Counsel, Jim Wright.

ICOC PRESIDENTIAL SEARCH SUBCOMMITTEE
Bob Birgeneau
Susan Bryant
Michael Goldberg
Brian Henderson
David Kessler
Bob Klein (Chair)
Sherry Lansing
Richard Murphy
Tina Nova
Phil Pizzo
Joan Samuelson
Janet Wright

ICOC LEGISLATIVE SUBCOMMITTEE
Susan Bryant
Michael Goldberg
Bob Klein (Chair)
Richard Murphy
Sherry Lansing
Tina Nova (Vice-Chair)
Claire Pomeroy
Francisco Prieto (Vice-Chair)
John Reed
Joan Samuelson
David Serrano Sewell
Jeff Sheehy
Janet Wright

ICOC GOVERNANCE SUBCOMMITTEE
Brian Henderson
Bob Klein
Sherry Lansing (Chair)
Richard Murphy
Tina Nova (Vice-Chair)
Phil Pizzo
Claire Pomeroy
John Reed
David Serrano Sewell
Os Steward

Legislative Efforts

Institute representatives were also invited to testify at public hearings in the State Legislature in 2005 and 2006:

- A joint informational hearing by the State Senate Health Committee and the Assembly Health Committee to review the implementation of the Act (March 9, 2005);
- A hearing before the Assembly Budget Subcommittee on Education to consider the establishment of the CIRM and the ICOC (May 4, 2005);
- A joint hearing before the Senate Health Committee and Subcommittee on Stem Cell Research Oversight and Assembly Health and Judiciary Committees to examine options for handling intellectual property associated with stem cell research grants (October 31, 2005); and
- A hearing of the Assembly Select Committee on Biotechnology to examine the life sciences industry in California (January 12, 2006).

ICOC members, CIRM staff, and other representatives also briefed legislators regularly on the Institute's progress throughout the year, and offered public comment on various legislative proposals.

Investing In The Future: CIRM's Stem Cell Research Training Program

In early 2005, CIRM identified a compelling need for highly advanced scientific and medical education and laboratory training for researchers to carry out California's ambitious stem cell research program. One unfortunate consequence of the federal restrictions of stem cell research has been to discourage promising young scientists from entering the field. With the approval of the ICOC, CIRM's first grant funds were used for the establishment of a program to place young Ph.D. and M.D. scientists in stem cell research laboratories and provide them with cutting edge knowledge of the scientific, medical and ethical theories and techniques to advance this new frontier of science.

The ICOC approved a Request for Application in May of 2005. In just three months, the Scientific and Medical Research Funding Working Group peer reviewed 26 institutional applications, representing proposals for training over 300 research fellows. In September 2005, the ICOC approved research fellowship programs for 16 institutions. Supporting funds were secured on April 6, 2006, from proceeds from the first sale of Bond Anticipation Notes (BANs) to six philanthropic organizations. The grants total $12.1 million in the first year and will support an outstanding scientific and laboratory research program for 169 scientists per year at institutions throughout California.

The grant award required that each institution establish a training program that includes one or more courses in stem cell biology and its application to disease, as well as a course in the ethical, legal, and social implications of stem cell research. Each institution is also required to demonstrate a commitment to training a racially and ethnically diverse group of scientists. The training programs will not only reach the 169 young scientists supported directly, but also a much wider audience of interested students and fellows.

At a meeting on June 16, 2006, the training program directors described the progress and plans at each of their institutions. Three impressions were paramount. First, even though they share a common core goal, the training programs show a remarkable spread of expertise, ranging from developmental biology to computation to chemistry to engineering to highly focused clinical problems. This spectrum takes advantage of the range of training environments in the state. Second, the quality of the trainees is exceptional. The training programs have been successful in attracting outstanding young scientists from across the country (and the world, in some cases) to participate in the new frontier of stem cell research in California. Third, more candidates applied than were trainee positions available, demonstrating that the program met a critical and pent-up need for young students and graduate fellows to advance in the field of stem cell research.

In the future, we expect to expand the training program to include additional institutions and technical, as well as professional training.

APPROVED TRAINEE SLOTS

INSTITUTION	PRE-DOCTORAL	POST-DOCTORAL	CLINICAL	1ST YEAR BUDGET
Burnham Institute	0	6	0	$ 445,500
California Institute of Technology	0	10	0	690,608
Children's Hospital Los Angeles	0	7	3	784,006
Scripps Research Institute	3	3	0	347,160
Stanford University	6	5	5	1,221,694
The J. Gladstone Institutes	0	7	3	799,080
The Salk Institute for Biological Studies	0	6	0	481,010
University of California, Berkeley	6	4	2	815,990
University of California, Davis	4	4	4	896,082
University of California, Irvine	8	4	0	674,482
University of California, Los Angeles	5	5	6	1,231,802
University of California, San Diego	6	4	6	1,203,207
University of California, San Francisco	6	6	4	1,152,431
University of California, Santa Barbara	2	4	0	393,091
University of California, Santa Cruz	3	3	0	374,730
University of Southern California	5	2	2	601,379
TOTAL	**54**	**80**	**35**	**$12,112,252**

Turning California's Investment To The Common Good: A Scientific Strategic Plan

Although CIRM was able to identify certain compelling early priorities for funding, a research project of the size, scope and duration as mandated by the Act requires careful planning to achieve the maximum scientific and medical benefit of stem cell research for Californians and others. An important early step has been to develop a scientific strategic plan that will guide the disbursement of funds over a ten year period.

The Institute began this process by sponsoring an international scientific conference, Stem Cell Research: Charting New Directions for California, in San Francisco in October 2005. The purpose of the meeting was to assess current scientific challenges and opportunities in the field of stem cell research and to identify scientific priorities for CIRM. To do this, 30 of the world's leading stem cell researchers and clinicians, including those from the United States, Australia, Canada, Israel, Sweden

and the United Kingdom were invited to participate. After two days of presentations, the participants presented a set of recommendations to CIRM. These recommendations (available at www.cirm.ca.gov/meetings/pdf/2005/10/100105_ConfRpt.pdf) have served as the starting point for the strategic plan.

More than 200 scientists, patient advocates and public citizens attended the conference in person; thousands more participated through a live web cast available around the globe. (The archived web cast is available at www.tsntv.org/Events/CIRM_meeting_10.1-2.05)

Scientific strategic planning is expected to conclude by February 2007 with the adoption of the plan by the ICOC, as required by the Act. This will prepare the Institute for its first large-scale funding efforts, when public funds become available in mid-2007, as expected.

The development of the strategic plan, which CIRM is undertaking with the assistance of the consulting firm, PricewaterhouseCoopers, involved interviews with more than 70 prominent scientists, clinicians, scientific leaders, patient advocates, ethicists, and representatives of the public interest and private sector. Three public meetings and parts of three ICOC meetings were also being devoted to gathering information and developing the plan. Finally, focus groups on patient advocates and diversity issues will also contribute to our plan.

Ensuring Scientific Integrity Through Strong Public Policy

In addition to completing the scientific strategic plan and devising the governance infrastructure to support the research funding program, the Institute began developing major policies in three areas in 2005: medical and ethical standards, intellectual property, and grants administration. Together, these policies form the foundation for the stem cell research grants programs that CIRM will administer. The policies are innovative, inter-related, and mutually reinforcing. They are structured to meet three objectives: 1) to protect the public interest, 2) to promote ethical, collaborative science, and 3) to ensure scientific integrity.

As the official regulations of a state government agency, they will carry the full force and effect of law. They will guide the grants awarded and define expectations for the research funded. Individually, the policies go well-beyond guidelines and regulations established by other scientific grant-making agencies, both in the United States and abroad. They are essential to our mandate, as they assure that stem cell research in California will be performed according to the highest scientific, ethical, and fiscal standards.

The Standards Working Group, composed of ICOC

members and internationally recognized experts from around the country, formulated the Medical and Ethical Standards, while the Intellectual Property Policy for Non-Profit Organizations has been the product of a separate ICOC task force. The Grants Working Group, which is composed of out-of-state stem cell research experts and patient advocate members of the ICOC, recommended the staff-developed Grants Administration Policy for Academic and Non-profit Institutions. For each effort, public meetings and public hearings were held around the state over many months.

Thoughtful and constructive advice came from outside experts, legislators, patient advocates, public interest groups, the ICOC, and private citizens. Their collective counsel shaped the final policy recommendations that were submitted to the ICOC. Both the Medical and Ethical Standards and Intellectual Property Policy for Non-Profit Organizations were approved by the ICOC on February 10, 2006, and the Grants Administration Policy for Academic and Non-profit Institutions was approved on June 2, 2006.

Scientific and Medical Accountability Standards

Before CIRM developed its own policies, the ICOC adopted the National Academies' Guidelines for Human Embryonic Stem Cell Research as interim regulations for grant awards. The National Academies' Guidelines were considered the "gold standard" for ethical and medical standards in the conduct of scientific stem cell research when they were announced in April 2005. When they were adopted by the ICOC in May 2005, California became the first state to employ them as interim regulations.

The ICOC has now approved standards that have been submitted to the California Office of Administrative Law as regulations and have undergone a period of formal public hearings. After final approval by the ICOC, the standards will become state regulations. The recommended regulations address medical, scientific, and ethical issues associated with stem cell research funded by CIRM. They represent the first comprehensive set of state regulations to implement and build on the National Academies' Guidelines ensuring that research is conducted safely and in an ethically sound manner.

In just over a year, the 19-member Standards Working Group held eight public meetings to develop its final recommendations. Between March and July 2006 four formal comment periods were held pursuant to the Administrative Procedures Act (APA). Each of the more than 80 formal written comments during in the APA process received a response. The text of the regulations, a summary and the response to public comments are available at www.cirm.ca.gov/laws/default.asp.

The standards adopted by the ICOC go beyond the National Academies' Guidelines in several ways. First, they include all potential sources of stem cells, including

cord blood, fetal tissue and mature tissue. Second, they provide medical care for complications that women may have after egg donation. Third, they require that donors not only give informed consent but show evidence of understanding the scope and meaning of their approvals.

Protections for egg donors were paramount in the formulation of this policy. For example, the Institute's regulations place a woman's reproductive interests before the needs of researchers. Potential donors who are undergoing fertility treatment cannot donate eggs for research unless their reproductive goals are attained first. The CIRM regulations require that donors be informed fully of all risks associated with egg retrieval and of all possible aspects of research using their eggs.

Furthermore, the recipient institution's Stem Cell Research Oversight Committee must approve a process for determining whether prospective donors understand the essential aspects of the research, including, but not limited to, how eggs will be used and the medical risks associated with participation. The Institute's regulations ensure that donor consent is voluntary and truly informed.

Medical and Ethical Standards Oversight Structures and Controls

The availability of health care for women who suffer complications after donating eggs is another significant innovation of the Medical and Ethical Standards (MES) Regulations. The CIRM regulations directly address the issue by requiring research institutions to provide any necessary medical care needed to treat illness sustained as a direct result of egg donation, and this care must be available at no cost to the donor.

Each institution that receives funding through the Institute must establish and maintain a Stem Cell Research Oversight Committee, with expertise in the unique scientific and ethical issues related to stem cell research. Institutions traditionally rely on an Institutional Review Board (IRB) to evaluate protocols for all scientific research carried on in their facilities. California is the first state to mandate a separate body with defined expertise to monitor stem cell research, as an addition to the overall institutional review process. This new model fulfills directive language of the National Academies' Guidelines.

The MES Regulations reaffirm Proposition 71's prohibition on both human reproductive cloning and payments to egg donors in California. The standards permit reimbursement only for donors' out-of-pocket expenses – including lost wages – but prohibit all other payments, regardless of the source of funds used for donor compensation. Furthermore, to ensure that the highest ethical standards are followed for all stem cell lines used

in CIRM-funded research, the policy prohibits the use of new embryonic stem cell lines acquired from sources that compensate donors beyond incurred expenses.

Consistent with the CIRM Grants Administration Policy, the MES regulations require prompt reporting and contain numerous enforcement actions for non-compliance. The grants administration team has built into its tracking system protocols for documenting compliance with required approvals and notification. These efforts illustrate the inter-related and mutually reinforcing nature of CIRM's policies.

An international consensus on informed consent and donor compensation is clearly desirable, and CIRM continues to work with state, national, and international bodies that are developing research guidelines and regulations. We sponsored an international scientific conference organized by the Institute of Medicine on September 28, 2006, on the medical risks to egg donors and how they can be minimized, to advance this debate and to inform future deliberations within the Standards Working Group regarding protection of egg donors. Because of our strong policies, Californians can be confident that CIRM-funded stem cell research will be conducted according to the highest scientific and ethical standards so that this new biomedical research field is advanced for the benefit of all.

Intellectual Property: Innovation Serving California

CIRM's Intellectual Property (IP) Policy for Non-Profit Organizations defines obligations researchers must accept to receive CIRM grants. It applies specifically to non-profit research institutions and it was developed by a subcommittee of the ICOC chaired by Ed Penhoet, Ph.D. A separate policy for for-profit entities is under development and will be initially approved in December 2006.

The IP policy allows any intellectual property generated by CIRM-sponsored grantees to be owned by the grantee institution. In the event that CIRM-funded researchers discover patentable inventions, grantee organizations are responsible for costs associated with filing patent applications, maintaining patents and licensing patented inventions to third parties. In this respect, the policy is consistent with the Bayh-Dole Act which grants ownership of intellectual property generated as a consequence of federally-funded research to the grantee

The CIRM IP policy surpasses the scope and substance of similar requirements at other scientific funding agencies, including those at the federal level, and breaks new ground in several areas. The CIRM IP policy describes revenue sharing requirements intended to enable the State to benefit from revenues created as a consequence of licensing rights to CIRM-funded patented inventions. The IP policy establishes a 25 percent financial return (minus inventors' share) to the State when a

grantee institution's net revenues from a CIRM-funded patented invention exceed $500,000.

Another novel feature of the policy is a commitment to the provision of scientific results to the public. Grant recipients must provide 500-word abstracts that describe in layperson's terms discoveries published in scientific journals. CIRM will make all abstracts publicly accessible.

A commitment to the sharing of biomedical materials is also a significant element of the IP policy. CIRM-funded researchers must make publication-related biomedical materials available to other scientists within 60 days of a request. This provision encourages wide, rapid distribution of new advances and tools in stem cell research to the scientific community. It is intended to foster an environment that encourages the scientific community to replicate significant breakthroughs more quickly than prevailing practices allow.

Public testimony highlighted significant concern for the potential cost of stem cell therapies and the inability of many Californians to pay for needed treatments. While shortcomings in the healthcare delivery system are beyond the reach of the Institute, the IP policy addresses access to stem cell treatments that result from CIRM funding. For example, exclusive licenses for CIRM-funded patents will be granted only to third parties with a plan that specifies how the therapy can be made available to uninsured Californians. The policy also states that publicly subsidized healthcare programs (including MediCal, Healthy Families, the AIDS Drug Assistance Program, and other qualifying state, county, and community health programs) can benefit from CIRM-funded research. The IP policy stipulates "march-in" rights for the State to be exercised not only if a grantee organization or licensee fails to develop CIRM-funded inventions, but also if they fail to follow their access plans.

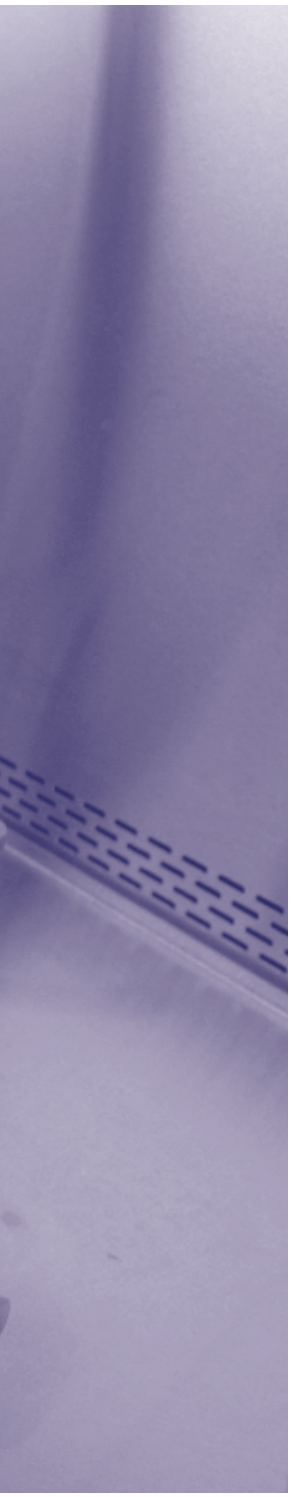
INTELLECTUAL PROPERTY TASK FORCE

Susan Bryant	Francisco Prieto
Michael Goldberg	John Reed
Sherry Lansing	Duane Roth
Ted Love	Jeff Sheehy
Ed Penhoet (Chair)	Os Steward
Phil Pizzo	Janet Wright

Ballot materials for Proposition 71 described royalty revenue from the program as unknown since the actual financial returns to State government from the royalty and licensing of stem cell research are uncertain. Nevertheless, CIRM policy covers how taxpayers share in revenue-generating advances that emerge from CIRM-funded research. The CIRM IP Policy establishes a 25 percent financial return (minus inventors' share) to the State when a grantee institution's net revenues from a CIRM-funded patented invention exceed $500,000.

The IP subcommittee began meeting in October 2005, and held three public meetings before approving its recommended proposal on January 23, 2006. The recommendation was modified and approved by the ICOC on February 10, 2006, and submitted to the California Office of Administrative Law for additional public review and final approval. A policy for For-Profit Organizations is expected to be completed in 2007.

Graduate student Michelle Wedemeyer works with stem cell cultures at the Reeve-Irvine Research Center at the University of Californiaa, Irvine.



Grants Administration Policy for Academic and Non-Profit Institutions

CIRM's Grants Administration Policy (GAP) is a comprehensive policy that describes the terms and conditions (including public policy requirements) that apply to all CIRM grants awarded to public and private colleges and universities, as well as non-profit research organizations. After interim regulations were adopted by the ICOC to govern the CIRM Training Grants, a revised, comprehensive policy for all Institute grants was developed and endorsed by the Grants Working Group and approved by the ICOC at its June 2006 meeting. The policy defines specific requirements for the submission of funding applications from academic and non-profit institutions and from individuals at these institutions; the process for reviewing and awarding grants; financial accounting procedures and reporting requirements; and the penalties for violations of CIRM regulations, standards, and policies. The GAP describes allowable costs and activities for research projects and allowable charges for indirect administrative costs.

These three sets of regulations – Intellectual Property, Scientific and Medical Standards, and Grants Administration – are comprehensive, integrated, and mutually reinforcing. The California Attorney General has the power to enforce these regulations, but principal responsibility for regulatory enforcement rests with both the CIRM and the institutions that receive CIRM awards. The Institute will closely monitor grant recipients to ensure their research complies with all provisions of the CIRM regulations. Grant recipients must be fully compliant with all regulations, actively engaged in compliance monitoring, and must immediately disclose to CIRM any regulatory violations committed by their employees and associates. Any researcher or institution found in violation of a CIRM regulation faces severe penalties, ranging from postponement or a return of funding to cancellation of the grant to a prohibition on any future grant application.

Given that each of these policies breaks new ground, they will be studied and debated, widely accepted as a model by some, and refined by others. In each case, the Institute has gone beyond accepted national standards to achieve new levels of accountability and to provide strong stewardship of public funds. The CIRM is committed to remaining at the leading edge of sound scientific regulation, and it is prepared to modify its regulations over time, when new developments warrant new standards.

Protecting The Public Interest: Conflicts of Interest and Disclosure Policies and Regulations

As a public agency, CIRM, along with the ICOC, is committed to responsible stewardship of the funds with which it has been entrusted. CIRM must disburse funds in a manner that is open, fair and free of bias, and based on scientific and medical merit. To ensure that this occurs, CIRM has adopted strong conflict of interest policies for ICOC members, for CIRM employees and for the members of the working groups that aid CIRM in its work. CIRM and the ICOC have also adopted policies and best practices that promote transparency and accountability.

All ICOC members and all CIRM employees are required to disclose their financial assets and investments on the form used by all State Constitutional Officers and government appointees and employees (Statement of Economic Interests [Form 700] of the California Fair Political Practices Commission). The financial disclosure statements of ICOC members and CIRM staff are available through the Institute's offices. In addition to following state regulations for prohibited activities, CIRM members follow specific policies dealing with commercial interests in stem cell companies. These policies are available for review on the Institute's website (www.cirm.ca.gov/policies).

The members of the three working groups who are not ICOC members also must file statements listing financial, professional and personal interests that might yield a conflict of interest. For the working groups, conflict of interest issues are most relevant when grant applications are being evaluated.

The Grants Working Group for example, which is composed of stem cell researchers and the ICOC patient advocate members, follows a number of procedures to identify and manage conflicts of interest. First, the scientific and medical peer review experts must come from outside California; thus they are precluded from receiving funding from CIRM which awards grants only to California researchers and institutions. Second, they are required to submit a statement, before each review session under penalty of perjury, that lists relevant financial, professional and personal information and that identifies any applications for which they might have a conflict of interest. After gathering other relevant information, CIRM staff identifies those working group members who have a conflict of interest for each application.

Working group members who have a conflict with an application are recused from the review of the application in question; they do not see the body/content of the application, do not participate in the discussion of the application, and do not vote on its evaluation. Reviews are held in closed session to protect the confidentiality of the applicants, the intellectual property of the applicants (i.e., the unpublished data and novel concepts and ideas presented in the application), and to elicit critical candid evaluations by the reviewers. For

each application reviewed, confidential records of those who voted and those who were recused (because they have a conflict of interest) are kept on file and are available for audit.

The Grants Working Group then recommends applications for funding to the ICOC, which is responsible for making all final funding decisions in open session. ICOC members who have a conflict of interest with respect to a particular application are identified; they do not participate in the discussion of the application and do not vote. The CIRM and the ICOC has set standards of conflict of interest that significantly go beyond those of other government and private agencies that disburse research funding.

Serving a Broad Constituency: Patients and Diversity

Few government agencies come into existence through the direct, expressed desires of citizens. CIRM was created by more than seven million Californians, who voted for state government to provide significant financial support for stem cell research therapy development and the potential for cures. It is a tremendous mandate and a great vote of confidence in the capabilities of scientists and biomedical research. CIRM is entrusted with one of the largest public scientific research projects in recent history, and we owe all Californians our very best efforts to capture the promise of stem cell research.

There are two groups, however, with whom we have a special relationship and for whom we have a special responsibility: patient advocates and those representing the diverse population of California.

Patient advocacy organizations were essential to the creation of CIRM. More than 70 were actively involved in the campaign for the initiative, and leading patient advocacy organizations rose to help defend Proposition 71 as it faced legal challenge. Patient advocates are intimately involved with the governance, operations, and plans for the Institute, serving on the ICOC, the working groups, and other committees. They actively participated in the development of our scientific strategic plan. Several are featured in the disease spotlights described in the middle section of this report.

The rich diversity of California's population is a source of the state's strength, and we want to see that diversity expressed throughout the Institute's activities. Research institutions were encouraged to promote diversity in their training programs for CIRM Fellows, and we are pleased that so many of those named as research fellows are from minority communities. We will be looking for similar rates of participation in future training grants for clinicians, researchers, and technicians.

Disease and disability are color blind. For scientific and medical reasons, it is critically important that diversity is reflected in the stem cell lines used to understand disease and develop tools and therapies. Diversity is

one of the core values adopted by the ICOC to guide CIRM's scientific strategic plan. Early on, a distinguished group of Californians agreed to serve on an advisory committee to help the Institute understand and address diversity in our plans and grants. They have been thoughtful, constructive, and imaginative, and their continued guidance will help fulfill the promise of stem cells. The Diversity Advisory Committee membership is presented below.

DIVERSITY ADVISORY COMMITTEE

NAME	ASSOCIATION	LOCATION
Malik Baz, M.D.	Board of Directors of American Lung Association of Central California President, Baz Allergy, Asthma and Sinus Center	Fresno
Ed Chow, M.D.	Physician; Executive Director, Chinese Community Health Care Association; Network of Ethnic Physicians Organization	San Francisco
Arthur Flemming, M.D.	Chair, Network of Ethnic Physicians Organizations Chair, Region VI, National Medical Association	Los Angeles
Pamela Freeman Fobbs, J.D.	Past President, Auxiliary to the National Medical Association	Fresno
Diane Harris-Wilson, Ph.D.	Professor of Psychology, San Francisco State University Fellow - Center for Health Disparities Research and Training	San Francisco
Margaret Juarez, M.D.	Physician, Chair, California Latino Medical Association	Los Angeles
Keda Obledo	Co-Founder Mexican American Legal Defense and Education Fund	Sacramento
Mario Obledo	Co-Founder Mexican American Legal Defense and Education Fund	Sacramento
Randal Pham, M.D.	Chair, Ethnic Medical Organization Section, California Medical Association	San Jose
Scott Syphax	Affordable Housing Executive CEO & President, Nehemiah Corporation of America	Sacramento

Financial Accountability and Oversight of Public Funds

To oversee the operations of the CIRM, the ICOC established a Governance Subcommittee to review and make recommendations to the ICOC regarding the Institute's budget, bylaws, employment practices and policies, and significant contracts with outside vendors. CIRM complies with State regulations

and laws for contracting and hiring that apply to other government units.

CIRM is required by the Act to conduct an annual audit. After soliciting and reviewing competitive bids, the Institute retained Sacramento-based Gilbert and Associates to conduct an independent financial audit of the Institute's activities from November 2, 2004 through June 30, 2005 (to coincide with the close of the State's fiscal year). Gilbert gave CIRM an "unqualified opinion" on its financial statements, i.e., the firm found no deficiencies in our accounting practices or internal controls. A separate management letter from Gilbert recommended a technical change to procedures for closing our books and a requirement that each ICOC member sign a copy of the CIRM conflict of interest statement that they had previously adopted, acknowledging that they understand and will comply with the statement. Both recommendations were adopted.

The audit was completed in May 2006, and it is included in this annual report. Separately, it is available on the CIRM website (www.cirm.ca.gov). It was reviewed by the Office of the State Controller. An independent audit of the Institute for the 2005-06 fiscal year should be completed in the first half of 2007.

As established by Proposition 71, CIRM is the only agency in the history of California State government with an independent financial oversight committee. As required by Proposition 71, the Citizens' Financial Accountability Oversight Committee (CFAOC), chaired by Steve Westly (an early champion of Proposition 71), was appointed to review the agency's independent audit, as well as the State Controller's separate review of the Institute's financial practices (also mandated by Proposition 71). After reviewing the ICOC and CIRM financial practices, policies, and audit for the fiscal year ending June 30, 2005, the oversight committee verified the sound financial practices of the state's newest government agency in September 2006.

CITIZENS' FINANCIAL ACCOUNTABILITY OVERSIGHT COMMITTEE

The CFAOC is chaired by the State Controller. Its members are appointed by State officeholders and are listed at right (with the appointing officer in parentheses).

Steve Westly, Chair	State Controller
Richard D. Siegal *(State Controller)*	President and CEO, Palace Exploration Co.
Daniel S. Brunner *(State Treasurer)*	Executive Vice President (Retired), FirstHealth
John Hein *(Speaker of the Assembly)*	Executive Director, Communities for Quality Education
Jim Lott *(Senate President Pro Tem)*	Executive Vice President, Policy Development and Communications, Hospital Association of Southern California
Myrtle Potter *(ICOC Chairman)*	Principal, Myrtle Potter Consulting, LLC

Undergraduate student Jason Romero works with stem cell cultures in a lab at the Reeve-Irvine Research Center at the University of California, Irvine.

Public Trust and Confidence

In the agency's first 18 months, the ICOC and CIRM staff worked to build trust and understanding with the public, press, and Legislature. The early months of 2005 were marked by criticism of the CIRM and ICOC by state legislators, newspaper editorials, and public interest groups concerned about the potential policies, practices, and regulations that would govern the agency and its board. The Institute demonstrated its ability to listen, to respond, and to seek the counsel of all parties affected by its decisions, and to build cooperative working relationships with a wide range of interested parties. In response to concerns from state legislators, for example, the ICOC:

- broadened its conflict of interest policies for working group members;
- made working group recommendations publicly available earlier;
- provided comprehensive reports to the Legislature summarizing grant awards and recipients;
- ensured that the Grants, Standards, and Facilities working groups each held public meetings when covering policy decisions; and
- established an Intellectual Property Task Force to develop a policy regarding financial returns to the state from CIRM grants and accessibility to CIRM-funded therapies for all Californians.

To provide assurance to the Legislature of its commitment to these enhanced policies, the ICOC adopted supplemental governance procedures that require it to notice the Legislature before modifying these enhanced provisions and to amend these provisions only when approved by a 70% or greater vote by the ICOC board.

Public confidence is essential to the success of the CIRM. The Institute is dedicated to fulfilling the mandate entrusted to it by California voters, by acting responsibly, by following the highest standards for ethical conduct and scientific integrity, and by demonstrating an unwavering commitment to protecting and promoting the public interest. The surest path to public trust is marked by strong, steady progress on the many tasks required to achieve our scientific mission. They will remain the focus of our attention and efforts.

National and International Cooperation: Strategic Alliances In The Race Against Disease

CIRM is eager to establish cooperative relationships and partnerships with stem cell researchers in other states and other countries, in order to leverage the research done in California. Representatives of other states and countries across the globe have visited the Institute to learn of developments and to explore ways to foster collaboration. To date, scientists and government officials from 15 countries, including the United Kingdom, Israel, Sweden, Australia, China, and Singapore have sent delegations to and/or held meetings with the leadership of the ICOC and CIRM. As an example of this collaboration, a joint meeting with the Medical Research Council (MRC) and the Biotechnology and Biological Sciences Research Council (BBRC) of the United Kingdom was held in November 2006.

CIRM also has a strong interest in promoting common scientific and ethical standards that will allow the exchange of cell lines and biological materials across state and national boundaries. In January 2006, we were pleased to be invited to join the International Stem Cell Forum, a 19-member international organization that promotes good practices in research on human stem cells. Most members of the Forum represent national research organizations; CIRM, which was invited to join along with the Chinese Academy of Sciences and the University of Milan, is the only American state organization that is currently a member.

Conserving and Leveraging Funds For Science

CIRM will never be a large agency. Under Proposition 71, the costs for administrative overhead and grants administration cannot exceed 6 percent of the bond proceeds, e.g., if California issues $300 million in stem cell bonds in a given year, $18 million would be available to cover the agency's operating expenses. By contrast, the average cost for administrative and overhead expenses for non-profit organizations with budgets comparable to CIRM is 11.1 percent of the total budget. Proposition 71 also limits the size of the Institute's staff to 50 full-time employees. As of June 30, 2006, CIRM had 20 full-time employees on staff.

Thus, even with the availability of full funding, CIRM will remain a lean organization, and it must manage its resources prudently to fulfill its public mission. Despite these limitations, our confidence in the staff's commitment to the ambitious agenda defined for 2006 and

beyond remains high.

Litigation challenging the constitutionality of California Stem Cell Research and Cures Act currently impedes the State's ability to issue the voter-approved bonds (see below/above), and therefore the resources available to launch a new agency are severely constrained. The Institute's funding through June 30, 2006, has been limited to a $3 million advance from the State's General Fund (which must be repaid from the proceeds of the first bond offering), a gift of $5 million from the Ray and Dagmar Dolby family foundation, $14 million from the sale of Bond Anticipation Notes (BANs) to private philanthropic entities, and a number of smaller gifts from generous donors totaling more than $400,000. These sources have provided the vital cash-flow to move the Institute's programs forward.

Early in 2005, the Institute began operations in temporary quarters in Emeryville after the ICOC Chairman's office mandated soliciting no-cost bids for interim space. The California Department of General Services (DGS) managed the competitive bid process, and Wareham Development, Inc. and the City of Emeryville generously provided $250,000 of office space, tenant improvements, furniture, and facilities operating costs free of charge. We very much appreciated the hospitality of Wareham Development, Inc., the Emeryville Chamber of Commerce and the City of Emeryville during our stay there.

To find permanent facilities, Chairman Robert Klein again asked DGS to collaborate on a unique request for proposals, and more than 10 bids were received from around the state. After careful consideration, including visits to the potential sites, the ICOC selected San

Private Donors Step In

While California's commitment of $3 billion to stem cell research is extraordinarily significant, the generosity of individuals to this emerging field of biomedical science is often breathtaking.

The University of California, Berkeley, for example, received a $40 million gift from the Li Ka Shing Foundation to establish a research center focused on new scientific fields, including stem cell biology, in June 2005.

The New Year began with the Kozmetsky family donating $1 million to San Diego's Burnham Institute for Medical Research to support ALS studies involving stem cells. In February, New York Mayor Michael Bloomberg made a $100 million personal gift to Johns Hopkins University for stem cell research, and Eli Broad gave the University of Southern California $25 million for new research facilities.

In May, Dagmar and Ray Dolby contributed $16 million to begin the UCSF Institute for Regeneration Medicine. Californians Tashia and John Morgridge gave $50 million towards a public/private interdisciplinary research center affiliated with the University of Wisconsin that will conduct stem cell research.

UC Irvine received a $10 million gift for its stem cell research center from Sue and Bill Gross.

CIRM is another beneficiary of generous individuals: 15 California philanthropists committed $46 million in loans to support our scientific mission in 2006.

Francisco's bid, which offered office space with 10-years of free rent and utilities; $1.6 million for tenant improvements; the free services of one of the nation's premier architects; 2,600 free hotel-room nights; another 14,000 room nights at reduced rates; and seven separate conference facilities (including the 50,000-seat Moscone Convention Center) at no charge, as available, over 10 years. All told, San Francisco's package was worth an estimated $18 million, saving taxpayers' money and making more funds available to advance stem cell research. The CIRM moved into its permanent headquarters on November 14, 2005.

We are also enormously grateful to a group of individuals and organizations who offered their assistance either through pro bono services or specific advice and counsel. Among those we wish especially to thank: Dale Carlson (our Chief Communications Director who donated 4 months of his time and expertise before coming on board full-time), Marty Carr, Steve Churchwell, Susan DeLaurentis, Dan Bedford, Ashley Fong, Lauren Gollaher, Al Halluin, Sangeetha Raghunathan, and Ken Taymor, as well as the California Council on Science and Technology, and the National Research Council of the National Academies of Science. Additionally, special thanks to the law firm of Munger Tolles and Olson for pro-bono services in connection with an amicus curiae brief.

Litigation

Opponents of stem cell research filed two lawsuits challenging the constitutional validity of the California Stem Cell Research and Cures Act in the Alameda Superior Court in 2005. The litigation precludes the State from issuing general obligation bonds to fund stem cell research (at a reasonable cost) until the matter is at least close to final resolution.

The Institute is represented in the litigation by the Attorney General for the State of and by outside counsel at Remcho, Johansen and Purcell. The Institute was supported by research institutions and national patient advocacy organizations from throughout the state that filed an amicus curiae brief, represented pro bono by the law firm of Munger, Tolles & Olson, supporting CIRM's position.

On April 21, 2006, the Alameda County Superior Court ruled in the state's favor, and, in a very strong judgment, found the Act constitutional in its entirety. **Specifically, Judge Bonnie Lewman Sabraw found that ICOC and the CIRM are clearly operating within the constitutional and statutory provisions authorized by the Proposition 71 initiative and the Institute's operations are firmly under the management and control of the state. She also ruled that the agency is accountable to the public and it is subject to a broad range of governmental oversight.**

Plaintiffs appealed the decision in June 2006 to the

state Court of Appeals and the Attorney General immediately filed a motion to expedite the appeals process. The Institute expects to prevail on appeal, but the Appellate Court decision is likely to be appealed to the State Supreme Court. We hope the lawsuits will be resolved in 2007, but until then, they inhibit the Institute's ability to issue bonds at reasonable interest rates.

The Year Ahead

Five objectives drive the ICOC and CIRM agenda for the rest of the fiscal year:

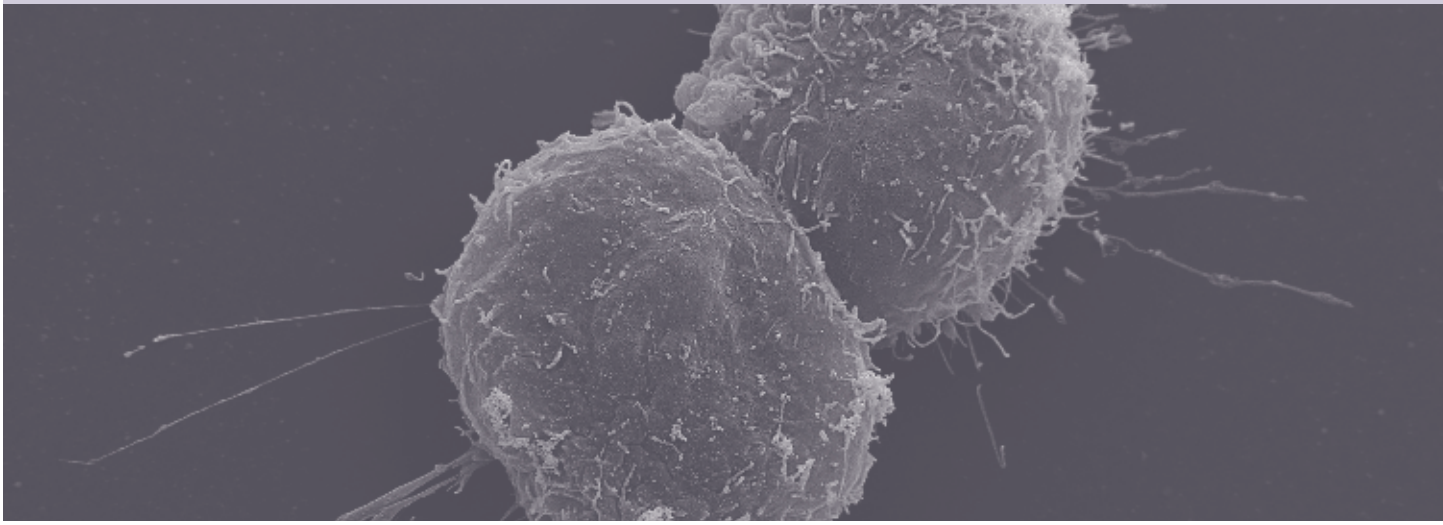
- continue to demonstrate nationally precedent setting public transparency and accountability;
- fund and extend a major expansion of the agency's scientific program;
- complete the regulatory, administrative, and information technology infrastructure essential to solicit, review, award, and manage hundreds of scientific grants;
- maintain and strengthen public trust and confidence in the Institute's integrity and competence; and,
- review and approve the Scientific Strategic Plan.

The Institute looks forward to the day when bonds can be issued to fund stem cell research at the level mandated by the voters.

As we wait, CIRM is making plans to continue its own scientific activities and to lay the administrative and scientific groundwork for the large-scale program of grants that will define our scientific program.

These plans have been accelerated by Governor Arnold Schwarzenegger's dramatic announcement that the State of California will loan $150 million to CIRM so that its research program can begin. Under the leadership of Chairman Robert Klein, a first round of BANs of $14 million was announced in April 2006, and a second round of $31 million closed in November of 2006. Thus, we will have a total of almost $200 million in funds available for disbursement. Of that amount, $12 million has already been committed to our stem cell research fellowship training program. The remainder will be committed during the coming year to a variety of new research grant and training programs, including our second major grant program: Innovation in hESC Research. Most of the grant funds will be committed, in 2007, after the completion of our Scientific Strategic Plan currently scheduled for final review in December of 2006.

We will continue our scientific activities during the coming year through several scientific meetings. In September 2006, CIRM sponsored a meeting under the auspices of the National Academies and the Institute of Medicine on "Assessment of Medical Risk for Oocyte



Asilomar and Recombinant DNA

Advances in the life sciences, particularly in biomedicine, are increasingly being scrutinized and their acceptance questioned. Novel technologies and ideas that impinge on human biology and their perceived impact on human values have renewed strains in the relationship between science and society. Thirty years ago, nations were engaged in debates about whether recombinant DNA research, also referred to as gene splicing and genetic engineering, was too dangerous to be allowed to continue. Fears of creating new kinds of plagues or of altering human evolution or of irreversibly altering the environment were only some of the concerns that were rampant. Lingering doubts and concerns still persist about the use of that technology in the development of genetically modified plants and animals used as food. Notably, some nations have enacted legislation that prohibits genetically-modified plants and animals from entering into their food supply. Paradoxically, no such embargo exists for the drugs and therapies that have revolutionized the treatment of serious diseases although many of them were created with the same technologies.

Today, it is research with human embryonic stem cells and attempts to prepare cloned stem cells for research and medical therapies that are being disavowed as being ethically unacceptable….

…the use of the recombinant DNA technology [now] dominates research in biology. It has altered both the way questions are formulated and the way solutions are sought. The isolation of genes from any organism on our planet, alive or dead, is now routine. Furthermore, the construction of new variants of genes, chromosomes and viruses is standard practice in

research laboratories as is the introduction of genes into microbes, plants and experimental animals. Without the tools of recombinant DNA there would be no human or any other genome sequence. Equally profound is the influence it has had in many related fields. Even a brief look at journals in such diverse fields as chemistry, evolutionary biology, paleontology, anthropology, linguistics, psychology, medicine, plant science, and, surprisingly, forensics, information theory and computer science shows the pervasive influence of this new paradigm….

The emergence of a new paradigm in any field of science generates, along with the excitement of a new frontier and perspective, an uncertainty about its full implications. This was especially true for the geneticists that fueled the emergence of the recombinant DNA technology during the 1970s.

At [that] time…scientists optimistically predicted that the recombinant DNA methods would soon yield important drugs, industrial products and improved agricultural varieties. In fact, such developments took longer than anticipated. Some have never been realized because learning how to manipulate genes for useful purposes presented unexpected difficulties. Since the mid-1980s, however, the number of products has increased continually. Hormones, vaccines, therapeutic agents and diagnostic tools are enhancing medical practice. The production and consumption of genetically engineered food plants are realities although their dissemination has been limited. A thriving biotechnology industry has created products, interesting jobs and wealth for scientists and others. In retrospect, very few...foresaw the pervasive, complex, robust, and rich ramifications of recombinant DNA technology. Nor could most have predicted the pace at which fundamental understanding of biology has deepened.

Frequently heard in the 1970s were criticisms of scientists for assuming leadership in formulating policies that were matters of public concern. This led some scientists to believe that the public debate itself was a great threat and that the fallout of claim and counterclaim would bring debilitating restrictions or even prohibitions on molecular biological research. In truth, many scientists grew impatient with the time-consuming, contentious debates. Yet the effort to inform the public also encouraged responsible public discussion that succeeded in developing a consensus for the measured approach that many scientists supported. Restrictive national legislation was avoided, and in the long run, scientists benefited from their forthrightness and prudent actions in the face of uncertainty….

By contrast, there is little prospect for consensus in our society on the ethical issues concerning fetal tissue and embryonic stem cell research, genetic testing, somatic and germ-line gene therapy, and engineered plant and animal species and hence little incentive to seek a compromise. Compromise in those instances may only be achievable by political means, where majority rule prevails.

by Paul Berg, 1980 Nobel Laureate in Chemistry

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Donors," held in San Francisco. In November, the Institute hosted a joint meeting with the Medical Research Council (MRC) and the Biotechnology and Biological Sciences Research Council (BBRC) of the United Kingdom on "The Control of Stem Cell Self-Renewal and Commitment to Differentiation." The purpose of the meeting was to bring together 32 scientists from the UK and California with the aim of sharing information and potentially developing collaborations. These activities have been funded by private sources.

Stem cell research is increasingly a global endeavor. CIRM needs to partner and collaborate with scientists and institutes in foreign countries to ensure we are staying abreast of new developments, avoid redundant efforts, maximize the value of our grants, and exploit promising opportunities. While science is a competitive enterprise, our mission will be achieved faster if we provide for the open exchange of ideas, materials, and data, regardless of geographic boundaries. We are committed to a race against disease, not a race against other nations. In a collaborative global enterprise, we can advance medical science, together, at a much faster pace than any one nation might accomplish alone.

Conclusion

By any measure, the Institute has created an impressive record over the first twenty months. Certainly the potential economic benefits to California — new jobs, higher tax revenues, royalty and licensing fees — encouraged support for Proposition 71. But the greater promise of stem cell research lies in the possibility of finding new research tools, knowledge, treatments and cures for debilitating diseases and injuries. Millions of Californians, tens of millions of Americans, and patients around the globe are hoping that our efforts here will save and improve lives everywhere.

Hope for breakthroughs in understanding disease progression, new therapies, and in the long run, possibly, cures and treatments motivated Californians to approve the California Stem Cell Research and Cures Act in 2004. The field is in its launching phase, however, inspiring both dreams and debate that mirror the emergence of recombinant DNA research 30 years ago. We are hopeful that the time, effort, and funds invested in stem cell research today will yield similar rewards and benefits to those of recombinant DNA in its earliest years.
Public support for stem cell research — particularly for work on human embryonic stem cells, which is the focus of sharp national debate — is strong. A growing number of states are making public funds available to their medical schools and research institutions for stem cell research, though none approach the levels of funding provided in California, with private philanthropy adding tens of millions more. The ICOC and CIRM have utilized innovative approaches to advancing medical science and reducing human suffering; it has become one of the models for the nation for a true partnership

between government and private philanthropy. Although a few states have outlawed aspects of stem cell research, others are considering legislation that would specifically permit human embryonic stem cell research within their boundaries. Many in Congress are urging the President to change current federal policy and support additional funding for stem cell research. In the international arena, interest and support is equally impressive, with some foreign governments adopting policies that strongly encourage emerging biomedical research. While such policies and support abroad are drawing some top-flight scientists away from the United States, our nation remains home to the best scientists in the world, with California becoming particularly attractive to stem cell researchers from around the globe.

In short, competition for funding and research talent is keen. It certainly poses a challenge for those wishing to see California become a global leader in stem cell research. We at the Institute are encouraged by the interests of other states and other countries. We have offered advice, support, and encouragement to all who have sought our counsel on building stem cell research programs of their own. Indeed, their interests are even greater reason for hope. With more funds supporting more scientists, our collective efforts may unlock the potential for stem cell therapies and treatments faster. Again, we are not in a race with other states or other nations. We are racing together to ease suffering and cure disease. We are at a pivotal point in the history of medical research; the vote on November 2, 2004, for Proposition 71 by the citizens of California, underwrote the vision of a future for humankind that holds the potential for remarkable progress in the understanding and treatment of chronic disease and injury.

MIGRATION OF STEM CELL RESEARCHERS TO CALIFORNIA

Established Stem Cell Investigators Who Have Moved or Are Moving To California

Martin Pera, Ph.D. *(moved from Australia to USC)*

Michael Clarke, M.D. *(moved from the University of Michigan to Stanford)*

Stefan Heller, Ph.D. *(moved from Harvard to Stanford)*

Peter Donovan, Ph.D. *(moving from Johns Hopkins to UC Irvine)*

Jan A. Nolta, Ph.D. *(moving from Washington University to UC Davis)*

Gerhard Bauer, M.D. *(moving from Washington University to UC Davis)*

David H. Rowitch, M.D. *(moved from Harvard to UCSF)*

Benoit Bruneau, Ph.D. *(moved from the Hospital for Sick Children in Toronto to accept a joint appointment at the Gladstone Institute and UCSF)*

Philip Beachy, Ph.D. *(moved from Johns Hopkins to Stanford)*

Young Investigators Who Have Trained In Top Labs Who Have Taken Jobs In California

Noburo Sato, Ph.D. *(from Rockefeller to UC Riverside)*

Qi-Long Ying, Ph.D. *(from Edinburgh to USC)*

Kara E. McCloskey, Ph.D. *(from Georgia Tech to UC Merced)*

Xianmin Zeng, Ph.D. *(from NIH to Buck Institute)*

Kathrin Plath, Ph.D. *(from MIT to UCLA)*

Robert Blelloch, M.D., Ph.D. *(from MIT to UCSF)*

Holger Willenbring, M.D. *(from Oregon to UCSF)*

Tiziano Barberi, Ph.D. *(from Memorial Sloan-Kettering to City of Hope)*

April Pyle, Ph.D. *(from Johns Hopkins to UCLA)*

Emmanuelle Passegue, Ph.D. *(from Stanford to UCSF, within California)*

Wange Lu, Ph.D. *(from Cal Tech to USC, within California)*

Amander Clark, Ph.D. *(from UCSF to UCLA, within California)*

Private Sector

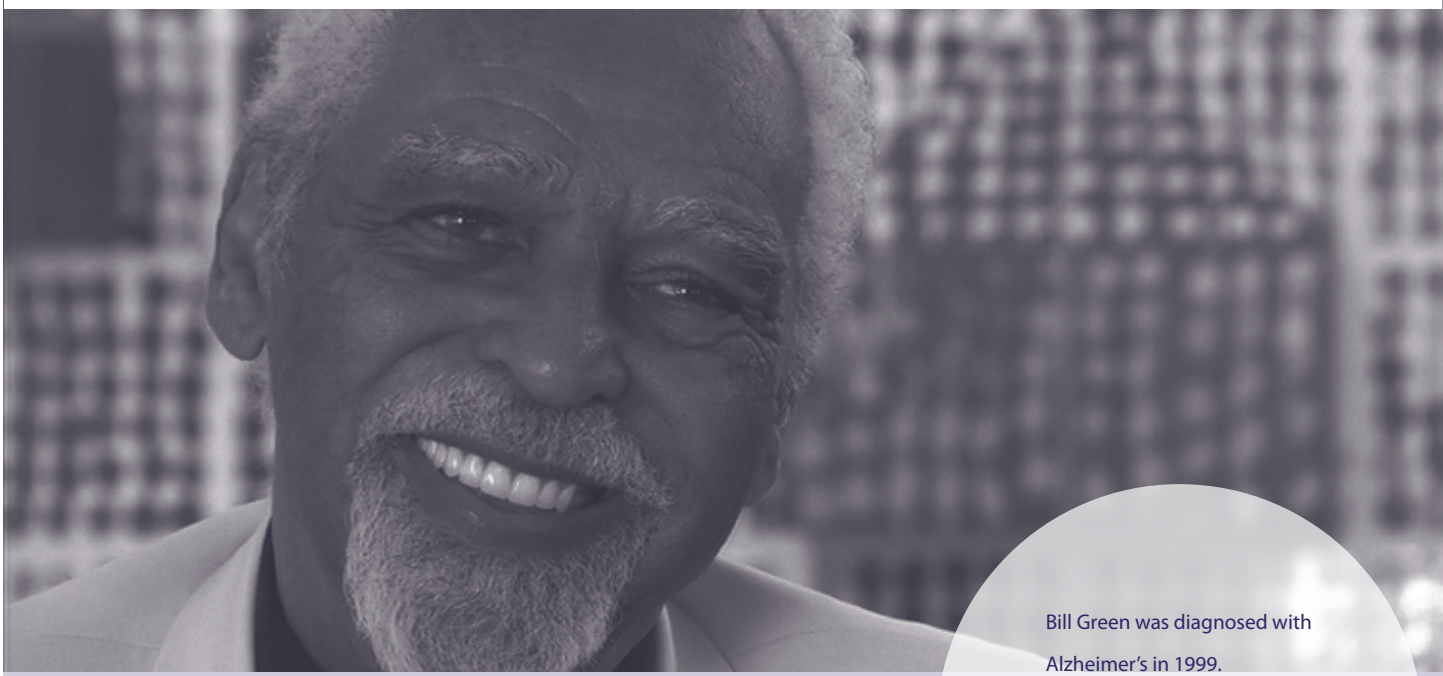
Mahendra S. Rao, M.D., Ph.D. *(leading stem cell scientist, from NIH to California-based Invitrogen)*

Advanced Cell Technologies, Michael D. West, Ph.D. *(expanded with a new facility in the East Bay Area)*

Stem Cell Sciences, Peter Mountford, President and CEO *(expanding into California from the UK)*

Melissa Carpenter, Ph.D. *(distinguished stem cell researcher, Novocell, Inc in San Diego)*

Alzheimer's Disease



Bill Green was diagnosed with Alzheimer's in 1999.

What is Alzheimer's Disease?

Alzheimer's disease is a chronic, progressive neurological disorder characterized by accelerated loss of brain cells and the connections between cells. Losing brain mass and connectivity degrades normal brain function, including reasoning and information storage and recall. The primary symptom is memory impairment greater than that expected for one's age. Other cognitive impairment, including dementia, is common and often results in difficulty managing activities of daily living. Alzheimer's also contributes to other serious psychiatric and behavioral conditions, such as anxiety, paranoia and depression.

The number of Americans with Alzheimer's has more than doubled since 1980. Over 4.5 million Americans have been diagnosed with the disease, including 500,000 Californians. Finding a treatment that could delay onset by five years could reduce the number of individuals with Alzheimer's disease by nearly 50 percent after 50 years.

How do we currently understand and treat Alzheimer's?

The cause of Alzheimer's is not yet known. Alzheimer's is uniquely human; it does not occur in any animal and no animal models have been developed with which to study the disease. Increased levels of two proteins — called amyloid and tao

— are found in the cells of an Alzheimer's brain. It is theorized that excess protein production and/or failure of the cell's normal protein breakdown and disposal process causes cells to die.

Age is the primary risk factor, though one's genetic makeup or experiencing head trauma can also increase chances of onset. Women are more likely than men to develop Alzheimer's, perhaps in part because women tend to live longer. Current treatment options are limited. There are four commonly prescribed medications to treat symptoms and slow disease progression, but nothing to address the disease itself. It is thought that people can reduce their chances of developing Alzheimer's by exercising, staying mentally active, and, in consultation with their doctor, taking anti-oxidants and non-steroidal anti-inflammatory drugs. Research shows that taking cholesterol-lowering drugs (called statins) can lessen the risk of Alzheimer's disease.

What is it like to live with Alzheimer's?

An individual is diagnosed, but a family lives with Alzheimer's disease. As the disease advances, patients lose more of their cognitive function and ability to care for themselves, and need ever-greater assistance from family, friends or professional care providers. Caregivers endure the heartbreak of "losing" the person they knew—and who knew them—and having to continually take away valued freedoms from a declining patient. Patients speak of their confusion, fear and loss of independence.

Early-stage patients stress the importance of honest self-monitoring and early diagnosis so that preventative treatment can begin as soon as possible. Patients and caregivers urge continued research, in the hopes that science will progress faster than the disease.

How might stem cell research help us better understand and treat Alzheimer's?

Stem cells could provide the first models to study Alzheimer's and its mechanisms. Human cellular models will enable exploration of the basic biology and chemistry of the healthy brain, and help understand what goes wrong in the Alzheimer's brain.

Stem cells will provide more efficient tools to search for new drug targets, as well as the first human cellular screens for testing drug safety and efficacy, enabling new drugs to get to patients much more quickly. This testing can be done even before the disease itself is fully understood.

Stem cells may be used to deliver growth factors or other compounds that protect cells or promote cell regeneration. In time, stem cells may be used to replace cells lost to Alzheimer's.

HIV/ AIDS

ICOC Board Member Jeff Sheehy (left) and his partner Bill Berry enjoy the beach with their daughter Michelle Marie. Jeff was diagnosed with HIV in 1997.

What is HIV/AIDS?

HIV is the human immunodeficiency virus that causes AIDS. HIV infects cells of the lymphoid system, including bone marrow and white blood cells, and uses their energy and nutrients to grow and reproduce. As the virus grows, it damages or kills these and other cells, weakening the immune system and leaving the infected individual vulnerable to opportunistic infections and other insults ranging from pneumonia to cancer. HIV is an unusual virus in that it is chronic, persisting for the lifespan of the infected person. There is no cure and no vaccine for HIV. AIDS (acquired immunodeficiency syndrome) is the life-threatening disease that results when the compromised immune system is unable to fight off infection or illness. Worldwide, there are over 40 million people infected with HIV — 95% are in developing countries. Every day 8,500 people die of AIDS and 14,000 new HIV infections — 10 per minute — occur.

How do we currently understand and treat HIV/AIDS?

The hallmark of HIV infection is the progressive loss of a specific type of immune cell called T-helper (or CD4) cells which are central to the immune system. These cells circulate in the blood and are primarily responsible for attacking and eliminating viruses and other infectious agents that threaten the body. The HIV virus is particularly insidious because it infects and kills

T-helper cells while successfully evading other elements of the immune system. The virus possesses a number of unique capabilities to elude discovery and elimination, which have frustrated efforts to develop a vaccine. There are 23 FDA approved drugs for treating HIV and AIDS, and in combination these drugs are saving and extending many lives. Drug therapy can suppress and maintain the virus at very low levels, but cannot completely eradicate it. HIV persists in certain cells and can revive if drug treatment is stopped. Though it is the best current option, chronic drug therapy has a number of shortcomings, including multiple side effects, difficulty with long-term adherence, resistance development as well as considerable expense and inconvenience.

What is it like to live with HIV/AIDS?

Living with HIV/AIDS encompasses a range of realities. The grimmest reality of HIV/AIDS is that the overwhelming majority of the 40 million people in the world with this deadly disease do not have access to therapy. HIV is a disease that thrives on poverty and social inequity, targeting the most vulnerable and weakest in society.

Ninety five percent of all cases of HIV/AIDS occur in the developing world, where antiretroviral therapies are scarce. Most of those who are infected will go untreated, and many will have their lives cut even shorter as a result of being co-infected with tuberculosis or malaria. In developed countries like the United States, access to quality healthcare and antiretroviral medications has dramatically improved both the length and quality of life for many individuals living with HIV/AIDS. Some who respond successfully to antiretroviral medications have even seen a complete suppression of the virus. Still, approximately 40,000 Americans with HIV/AIDS have initiated one antiretroviral regimen after another without such success. As they continue to try new drugs, their burden of side effects increases and their virus becomes even more resistant to treatment.

For most people on antiretroviral therapy, side effects are a major health concern. The metabolic disorders caused by antiretroviral drugs synergize with HIV's negative impact on the cardiovascular system to greatly increase the chances of heart attacks, strokes and cardiovascular disease. The metabolic side effects also include diabetes, the death of hip joints due to calcium malabsorption, and disfiguring body fat accumulations. Due to both HIV and the toxicity of medication, organ failure is a major cause of death. There is also an increasing risk that current therapies are not fully controlling HIV within the brain, and some studies point to the possibility of the development of Alzheimer's like conditions.

How might stem cell research help us better understand and treat HIV/AIDS?

Stem cells are believed to be able to help achieve two primary goals of HIV/AIDS treatment: permanent elimination of (or protection against) the HIV virus, and regeneration of the damaged and depleted immune system. Currently, treatments for HIV only suppress the virus; the promise of stem cell research is to eradicate it. Researchers are using adult hematopoietic cells collected from the patients, genetically altered in the laboratory to protect all blood cells from HIV and then infused back into the patients' bloodstream. However, this process yields a relatively small number of stem cells and a similar strategy utilizing human embryonic stem cells promises to be more efficient.

Blood and Lymphatic Cancers

When Anissa Ayala was diagnosed with leukemia as a teenager, doctors were unable to locate a suitable bone marrow donor for her. Facing her death, she and her parents made the brave and controversial decision to have another child in hopes that Anissa's new sibling would be a match. Her little sister was, and both are happy and healthy today.

What are blood and lymphatic cancers?

Cancer is a disease in which cells malfunction, divide without control and often invade other tissues of the body. Leukemia is a cancer that starts in blood-forming tissue, such as bone marrow, and causes large numbers of abnormal cells to enter the bloodstream. Lymphoma and myeloma are cancers that begin in the cells of the immune system. Each of these types of cancer includes a number of sub-categories, usually defined by their severity and progression rate, or the specific cell types involved.

How do we currently understand and treat blood and lymphatic cancers?

These diseases result from an acquired (not inherited) genetic injury to the DNA of a single cell, which becomes malignant and multiplies continuously. Their clinical presentations are fairly well understood and there are established therapies, including chemotherapy, radiation, immunotherapy, and bone marrow or stem cell transplantation.

Human bone marrow (also called "blood stem cell") transplant is a common and successful therapy for blood and lymphatic cancers. Bone marrow is rich in stem cells that give rise to blood cells (e.g., red cells, phagocytes and platelets) and immune

cells (lymphocytes), and transplant therapy can replenish cells ablated by radiation or chemotherapy. However, such treatments are inherently destructive and are too strenuous for many elderly, weakened or immune-compromised patients. There are also serious issues of donor availability and graft rejection that limit the viability of treatment for many patients.

What is it like to live with blood and lymphatic cancers?

Being diagnosed with blood or lymphatic cancer is devastating for individuals and their families. Though many types of blood cancers can be fatal, particularly for children and the elderly, treatment advances have greatly increased survival rates, longevity and quality of life. Some of the treatments themselves can be life threatening, however, and there still remains a lack of suitable donors for many transplant candidates. New therapies utilizing embryonic stem cells offer hope for many more patients living with diseases of the blood and immune systems.

How might stem cell research help us better understand and treat blood and lymphatic cancers?

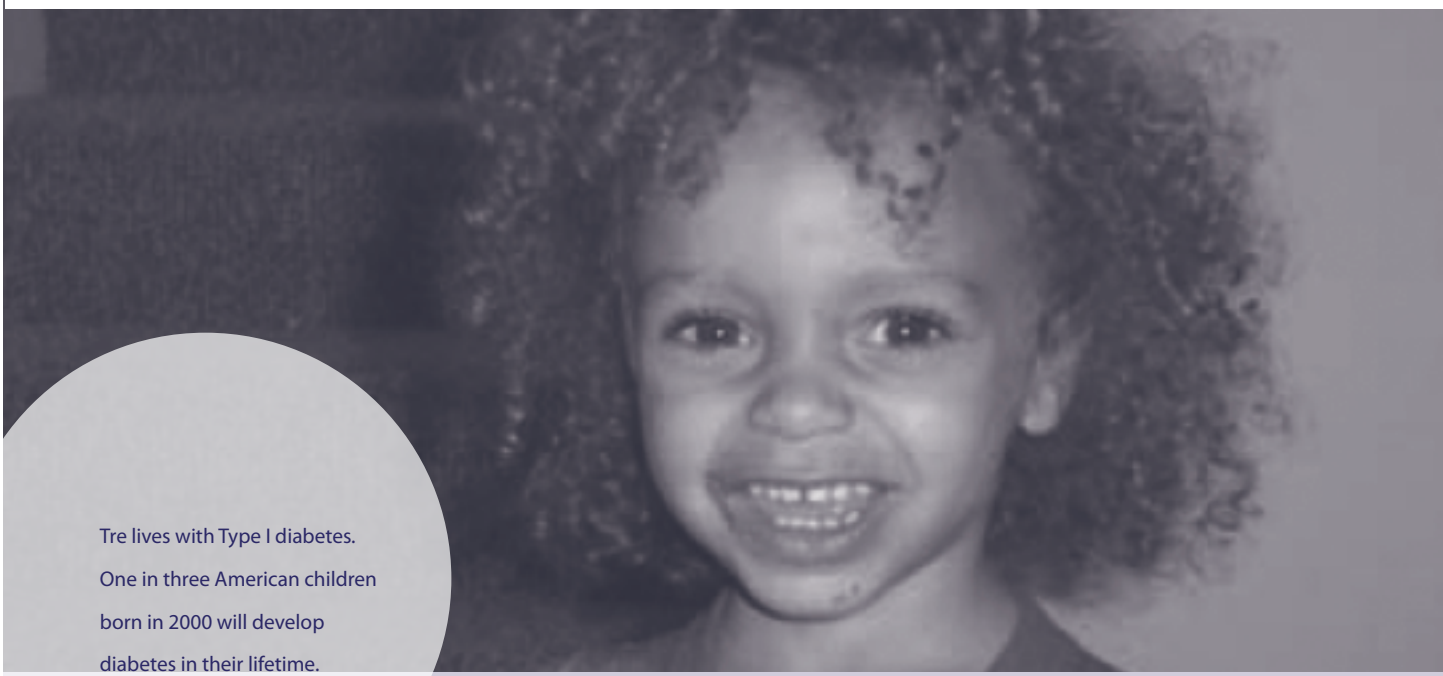
Healthy stem cells demonstrate certain characteristics of cancer cells, and it is believed that malignant stem cells are at the root of many types of cancer. Modified embryonic stem cells will enable researchers to study malignancy, learn how cells turn cancerous, and then develop strategies to inhibit malignancy and proliferation.

Embryonic stem cells can be used to improve current transplantation therapies and to make them available to many more patients. In animal studies, a process called somatic cell nuclear transfer (SCNT) enables scientists to implant an individual's DNA into a donor egg cell and develop a line of embryonic stem cells genetically identical to the individual. In time, this technique is expected to enable development of transplant tissue matched to individual cancer patients, thereby making therapies available to many more patients and reducing reliance on hazardous immunesuppression regimes.

Genetically matched donor cells could also increase use of a new treatment strategy called "Reduced Intensity Transplant." This approach transplants stem cells to strengthen a patient's blood and immune system so that it can target and eliminate cancer cells on its own, rather than using ablative treatment (like radiation) to eliminate disease and then transplanting cells to rebuild the blood and immune system. The reduced intensity treatment is safer and can be used in patients whose diminished health makes them ineligible for current transplant treatment.

Immune system cells, call "T-cells," target and eliminate harmful viruses in the body. Gene therapy techniques are now being used to modify T-cells to recognize and attack cancer cells and certain autoimmune diseases, like HIV or sickle cell anemia. It is hoped that embryonic stem cells combined with advances in SCNT techniques will enable development of modified T-cells for more patients suffering with cancer and immune related diseases.

Diabetes



Tre lives with Type I diabetes. One in three American children born in 2000 will develop diabetes in their lifetime.

What is diabetes?

Diabetes is actually a group of related diseases, commonly defined as Type 1 or Type 2, although each type contains several subcategories. All cases feature abnormally high blood sugar levels resulting from the body's inability to either produce or efficiently use its own insulin. (Insulin is a hormone produced in the pancreas that helps the body absorb and use sugar-based energy in food.) All forms of the disease are chronic, progressive and contribute to many serious side effects. There is no cure for diabetes.

How do we currently understand and treat diabetes?

Type 1 (often called juvenile or insulin-dependent diabetes) is an inherited genetic abnormality that causes the body's immune system to mistakenly destroy the insulin producing cells in the pancreas.

Type 1 accounts for 5 to 10 percent of all diabetes cases, and has no known prevention. To live, people with Type 1 require periodic doses of insulin, often many per day, delivered through multiple injections or an infusion pump. In addition to insulin therapy, proper diet and exercise are essential to managing all diabetes cases.

While genetics can contribute to the onset of Type 2, environmental and behavioral factors—particularly a poor diet and lack of exercise—cause most cases. Age used to be the primary risk factor for Type 2, but there has been a rapid increase in cases among children and young adults, particularly among African American and Latino communities. Type 2 typically begins with gradual resistance to insulin, meaning that increasing amounts are needed to extract sugar from the blood stream. This growing need for insulin can overwhelm and damage the pancreas, and over time high blood sugar levels can harm the eyes, kidneys, nerves and heart. Most Type 2 diabetics ultimately need insulin therapy to maintain health.

Hundreds of diabetics around the world have been successfully treated with transplanted cells that produce insulin (called islet cells) taken from donated pancreases. However, there are far too few donor organs available to treat the millions of needy patients, and scientists are not yet able to reliably grow or multiply islet cells in the lab.

What is it like to live with diabetes?

Diabetes demands constant monitoring of blood sugar levels and the many factors that cause blood sugar fluctuations, including diet, hydration, exertion, sleep, temperature, stress, excitement and other emotional states. This can be especially challenging for children, requiring active involvement of family members. Even with insulin therapy, diabetes can cause many secondary complications, including vision impairment and blindness, kidney disease, heart disease, stroke, increased susceptibility to infection, decreased circulation leading to amputations, as well as impaired digestion, bowel and bladder function. Despite the challenges, vigilant patients can lead long, healthy and productive lives.

"If there was no stem cell research and I was looking to the future, it would be a very bleak future."

-— Dana Lewis,

17 year-old diabetes patient

How might stem cell research help us better understand and treat diabetes?

Stem cells offer better and more plentiful sources of islet cells than donor organs. In a recent trial, 84% of patients who received concentrated infusions of their own stem cells were able to discontinue insulin therapy. Despite this success, not all diabetics are good candidates for the treatments, and most will require powerful drugs to keep their immune system from attacking the new cells. These drugs, known as immunosuppressants, cause side effects and leave patients vulnerable to infections and other serious complications.

Advances with embryonic stem cells may enable the large-scale production of islet cells required to treat millions of diabetics. Combined with genetic therapy techniques, embryonic stem cells may also be used to repair or replace the faulty immune system cells of Type 1 diabetics.

Autism

Autism is the fastest growing developmental disability in the United States, leading to one in 166 children being diagnosed with autism.

What is Autism?

Autism refers to a spectrum of related disorders that all have abnormal brain development and function. Symptoms range from mild to disabling, and include problems with verbal and nonverbal communication, and impaired social interaction. The cause is not yet known and there is no cure.

How do we currently understand and treat Autism?

Autism is not well understood. For decades it was mistakenly thought to be a psychological condition, but it is now recognized to be biological in nature. Scientists believe that autism related disorders either cause, or result from, an abnormal period of intense brain growth in the first and second years of life. However, since the cause is not known there is currently no effective means of prevention and treatments are limited.

Autism is most likely a combination of genetic, environmental, infectious, metabolic and/or immunologic factors. In fact, recent research suggests a connection between immune dysfunction and normal transmission of electronic impulses within

the brain. This seems to support observations that the connection points called synapses (through which cells communicate) in autistic brains are not as healthy in the areas that control speech, emotions and the complex processes of social interaction. These biological findings are consistent with the behavioral symptoms that define autism.

Children can be reliably diagnosed by age 3 through observation and behavioral and language tests, though many are diagnosed later or are initially misdiagnosed. Diagnosis is vital because early intervention has shown to lead to better outcomes for individuals with autism. Like the disorder itself, treatment for autism is highly individualized. Based on their symptoms, patients typically receive a combination of educational programming, behavioral and social skills training, and speech, language and sensory integration therapy. Pharmacological therapy is also prescribed for some. Given the wide range and severity of symptoms, the primary care goal is to characterize and address the individual's specific strengths and deficits.

"It's like someone sneaks into your house in the middle of the night, when your little boy or girl is two years old, and steals their mind and their personality and leaves their bewildered body behind."

— Jonathan Shestack, ICOC Board Member and parent of autistic child

What is it like to live with Autism?

Every case of autism is unique, so each patient and family faces a different set of challenges. At best, a high functioning person with autism may be recognized as eccentric or a loner. People with Asperger syndrome—a relatively mild form of autism—often pursue advanced educations, maintain full-time careers, marry and raise families. At worst, autism can result in complete disability. A severely affected person may never learn to speak or care for themselves. In some cases, aggressive and/or self-injurious behavior may be present in autistic individuals. There is hope that research will help us to understand the causes of autism and lead to better treatments or a cure for this tragic disorder.

How might stem cell research help us better understand and treat Autism?

Scientists may be able to create the first cellular models of autism, in all its varieties. Studying cell lines containing the DNA of individual patients will help us understand the genetic and molecular mechanisms that cause or contribute to autism. Comparing cell lines from patients with different symptoms will help us see the similarities and differences within the range of autistic disorders. More advanced models may be developed to study how autistic brains develop, how cells form connections and how these processes may differ from normal development. At this time, transplantation of stem cells or cells derived from stem cells is not considered a near-term option since autism affects many different cells in many areas of the brain.

Sickle Cell Disease

In the United States, 98 percent of those with sickle cell disease are African American.

What is Sickle Cell Disease?

Sickle cell disease is an inherited blood disorder that affects red blood cells. People with sickle cell disease have red blood cells that mostly contain an abnormal type of hemoglobin known as Hemoglobin S. Sometimes these red blood cells become sickle-shaped (crescent shaped) and have difficulty passing through small blood vessels. When sickle-shaped cells block small blood vessels, less blood can reach that part of the body. Tissue that does not receive a normal blood flow eventually becomes damaged. This is what causes the complications of sickle cell disease.

Inheritance

Sickle cell conditions are inherited from parents in much the same way as blood type, hair color, eye color and other physical traits. The types of hemoglobin a person makes in the red blood cells depend upon what hemoglobin genes the person inherits from his or her parents. Like most genes, hemoglobin genes are inherited in two sets, one from each parent.

How do we currently understand and treat Sickle Cell Disease?

There is currently no universal cure for sickle cell disease. A total of 50 patients have been cured of the disease via blood and

marrow transplants from HLA (Human leukocyte antigen) – compatible sibling donors. In these cases, since the patient, after the transplant, has the hemoglobin of the donors, they are disease free for life. Limitations for expanding the use of this cure treatment to larger numbers of patients include graft rejection, graft-versus-host-disease and lack of suitable donors.

While it is not yet possible to cure the majority of people with this disease, it is possible for patients with sickle cell disease to lead productive lives. Health maintenance for patients with the disease starts with early diagnosis, preferably in the newborn period and includes penicillin prophylaxis, vaccination against pneumococcus bacteria and folic acid supplementation. Treatment of complications often includes antibiotics, pain management, intravenous fluids, blood transfusion and surgery all backed by psychosocial support. Like all patients with chronic disease, patients are best managed in a comprehensive multi-disciplinary program of care. Blood transfusions help benefit sickle cell disease patients by reducing recurrent pain crises, risk of stroke and other complications.

What is it like to live with Sickle Cell Disease?

Living with sickle cell disease is painful and damaging to the body. It requires ongoing management on the part of patients and their medical care providers. Sickle cells are destroyed rapidly in the body of people with the disease causing anemia (low red blood cell count), jaundice and the formation of gallstones. Sickle cells also block the flow of blood through vessels, resulting in lung tissue damage (acute chest syndrome), pain episodes (arms, legs, chest and abdomen), stroke and priapism (painful prolonged erection). It also causes damage to most organs including the spleen, kidneys and liver. Damage to the spleen makes sickle cell disease patients, especially young children, easily overwhelmed by certain bacterial infections. This means that exposure to infections, including those viral infections that cause the common cold, is especially dangerous.

How might stem cell research help us better understand and treat Sickle Cell Disease?

Expanding the availability of hematopoietic cell transplants, making it possible to use non-HLA identical donor stem cells, would allow for the expansion of blood and marrow transplants to larger numbers of patients to cure them of sickle cell disease. Experiments are currently under way to determine whether stem cells that are genetically distinct from patients can eventually be used for transplants that could cure sickle cell disease.

Cord blood stem cells, collected after the birth of a sibling, and then stored for future use, can also be used to cure patients with sickle cell disease. Genetic screens can now be used to screen every newborn for genetic abnormalities such as sickle cell disease or thalassemia. This means that if stem cells — either cord blood stem cells from siblings or stem cells from a donors who are genetically distinct from patients — can be used for transplants to cure sickle cell disease, we could do something in the first year of life of every child born with sickle cell disease to prevent any of the consequences of the disease.

California Institute For Regenerative Medicine

FINANCIAL STATEMENTS WITH INDEPENDENT AUDITOR'S REPORT

For the Period from Inception
(November 2, 2004) to June 30, 2005

Independent Auditor's Report

To the Members of the
Independent Citizen's Oversight Committee
Sacramento, California

We have audited the accompanying financial statements of the California Institute for Regenerative Medicine (CIRM), a special revenue fund of the State of California, as of and for the period from inception (November 2, 2004) to June 30, 2005, as listed in the table of contents. These financial statements are the responsibility of CIRM's management. Our responsibility is to express an opinion on these financial statements based on our audit.

We conducted our audit in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

As discussed in Note 2, the financial statements of CIRM are intended to present the financial position and the changes in financial position of only that portion of the activities of the State of California that are attributable to the transactions of CIRM. They do not purport to, and do not, present fairly the financial position of the State of California as of June 30, 2005, and the changes in its financial position for the year then ended in conformity with accounting principles generally accepted in the United States of America.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of CIRM as of June 30, 2005, and the results of its operations for the period from inception (November 2, 2004) to June 30, 2005 in conformity with accounting principles generally accepted in the United States of America.

The Management's Discussion and Analysis on pages 2 through 6 is not a required part of the basic financial statements but is supplementary information required by accounting principles generally accepted in the Unites States of America. We have applied certain limited procedures, which consisted principally of inquiries of management regarding the methods of measurement and presentation of the required supplementary information. However, we did not audit the information and express no opinion on it.

Our audit was conducted for the purpose of forming an opinion on the financial statements that collectively comprise the basic financial statements of the CIRM. The accompanying supplementary information – combining schedule of net assets and combining schedule of activity are presented for the purpose of additional analysis and are not a required part of the basic financial statements. The combining schedule of net assets and combining schedule of activity have been subjected to the auditing procedures applied in the audit of the basic financial statements and, in our opinion, are fairly stated in all material respects in relation to the basic financial statements taken as a whole.

GILBERT ASSOCIATES, INC.
March 10, 2006

Management's Discussion and Analysis

Introduction

The following Management's Discussion and Analysis (MD&A) provides an overview to the financial statements of the California Institute of Regenerative Medicine (CIRM), a description of its activities and an analysis of the financial position of CIRM.

The audited financial report for CIRM is required under Health and Safety Code Section 125290.30(b). This audit covers the financial activities of CIRM for the state fiscal year ended June 30, 2005.

California Institute of Regenerative Medicine and Current Programs

CIRM is an agency of the State of California established under the provisions of Proposition 71 - the California Stem Cell Research and Cures Act. CIRM's responsibilities are:

- To make grants and loans for stem cell research, for research facilities and for other vital research opportunities to realize therapies, protocols, and/or medical procedures that will result in, as speedily as possible, the diagnosis, treatment and cure for, and/or substantial mitigation of, major diseases, injuries and orphan diseases.
- To support all stages of the process of developing treatments and cures, from basic research and discovery through preclinical and translational research to the conduct of successful clinical trials.
- To establish the appropriate regulatory standards and oversight bodies for research and facilities development.

Proposition 71 authorizes the State to issue, under the oversight of the Office of State Treasurer, $3 billion in state issued tax-exempt and taxable bonds to fund CIRM's operations, medical and scientific research, including therapy development through clinical trials and facilities. CIRM is authorized to receive a $3 million loan from the General Fund (Health and Safety Code Section 12290.70(b)) and to issue Bond Anticipation Notes (BANS) to fund CIRM's initial grants and operational costs until the bonds can be issued. Both will be repaid with interest from the proceeds of bonds when they are issued.

In addition, Proposition 71 established the Independent Citizens' Oversight Committee (ICOC), to govern CIRM. The ICOC may accept additional revenue and real and personal property, including, but not limited to, gifts, royalties, interest, and appropriations that may be used to supplement annual research grant funding and the CIRM operations.

During the current fiscal year litigation has delayed the issuance of bonds (see Note 9 to the Financial Statements). As a result, the funding available to CIRM has been limited to the $3 million general fund loan and a $5 million grant from the Dolby Family Foundation.

Financial Highlights

Condensed financial information as of and for the period ended June 30, 2005 is presented below:

Capital Assets	$	0
Other Assets		5,112,154
Total Assets		5,112,154
Long-term Liabilities	$	0
Other Liabilities		2,654,541
Total Liabilities		2,654,541
Restricted Net Assets	$	2,457,613
Total Net Assets		2,457,613
Grant Revenue	$	5,000,000
Other Revenue		84,660
Total Revenue		5,084,660
Salaries and Benefits	$	736,705
Operating Expenses		1,890,342
Total Expenses		2,627,047
Change in Net Assets	$	2,457,613

- Comparative analysis will be provided in future years when prior year information is available.

- CIRM relied primarily on the General Fund loan for its operations which totaled $2,627,047 as follows:

Salaries and Benefits	$	736,705
Operating Expenses		1,890,342

  See Note 5 to the Financial Statements for a discussion of the treatment of free rent received by CIRM at its temporary headquarters in Emeryville, California.

- While there was insufficient funding to issue grants, CIRM was able to develop and issue its first Request for Applications to fund a program of training grants. These grants will be used by California public colleges and universities and non-profit academic and research institutions in California to foster training in stem cell research at the level of pre-doctoral students, post-doctoral fellows and clinical fellows.

- The ICOC held 35 public meetings at which the following major actions were taken:

  — Established a Medical and Scientific Standards Working Group composed of five ICOC patient advocate

members, nine nationally recognized scientists and four biomedical ethicists to develop proposed regulations governing CIRM-funded research.

- Established a Scientific and Medical Research Funding Working Group composed of seven ICOC patient advocate members and 15 nationally prominent stem cell scientists from outside the State of California to develop recommendations for the evaluation criteria and to evaluate specific research proposals related to CIRM's first grant program – the CIRM Training Program in Stem Cell Research.
- Established a Facilities Working Group composed of five ICOC patient advocate members and four experts in the field of real estate management.
- Appointed Zach Hall, Ph.D - an eminent neuroscientist and scientific leader and administrator – as Interim President of CIRM. Also, appointed Dr. Arlene Chiu - a distinguished neuroscientist and former Grants Administrator with the National Institute of Health – as the Director of Scientific Programs and Review Activities.
- Adopted conflict of interest polices for ICOC members, CIRM staff and members of the three working groups mentioned above.

In addition, the limited staff at CIRM were able to accomplish the following:

- Secure temporary headquarters space for free in Emeryville, California.
- In partnership with the California State Department of General Services, conducted a statewide search for a permanent site. On May 5, 2005, the ICOC approved a location at the San Francisco. With free rent, free architectural services, free build-out to suit and other incentives, the value of which to CIRM over 10 years is estimated up to $18 million.
- Establish policies and procedures for travel and per diem reimbursement and contract procurements and develop and implement an accounting system that tracks operational expenditures.

Using this Annual Financial Report

The financial statements included in this annual financial report are those of CIRM and do not purport to present the financial position of any other reporting entity.

Overview of the Financial Statements

This MD&A is an introduction to the financial statements and accompanying notes. The financial statements of CIRM are presented as a special revenue fund of the State of California engaged primarily in financing activities - providing stem cell research and research facilities grants and loans to educational and private and non-profit research institutions located in the State of California. The financial statements have been prepared using two kinds of statements that generally present different views of CIRM. The *government-wide financial statements* provide both short-term and long-term information about CIRM's overall financial status using the accrual basis of accounting and the economic resources focus. The *fund financial statements* generally provide a short-term view that helps in the determination of whether there are more or fewer financial resources that can be spent in the near future to finance CIRM's programs. The fund financial statements are prepared using the modified accrual basis of accounting and focus on current financial resources. As of and for the period ending June 30, 2005, the presentation of the government-wide financial statements did not differ substantially from the presentation of the fund financial statements.

The government-wide financial statements report information about CIRM using accounting methods similar to those used by private-sector companies. They include the following two statements:

The *Statement of Net Assets* presents information on the assets and liabilities of CIRM, with the difference between the assets and the liabilities reported as net assets. Over time, increases or decreases in net assets are expected to serve as a useful indicator of whether the financial position of CIRM is improving or deteriorating.

The *Statement of Activities* presents information reflecting how the net assets of CIRM changed during the period ended June 30, 2005. All changes in the net assets are reported as soon as the underlying event giving rise to the change occurs, regardless of the timing of the cash flows. Thus, revenues and expenses are reported in the statement for some items that will only result in cash flows in future fiscal periods.

The fund financial statements generally focus on (1) how cash and other financial assets that can be readily converted to cash flow in and out and (2) the balances left at year-end that area available for spending. The Balance Sheet and Statement of Revenues, Expenditures, and Changes in Fund Balance do not encompass the additional long-term focus of the government-wide statements, therefore additional information reconciling the fund financial statements to the government-wide statements is provided in an Adjustments column that explains the relationship (or differences) between them.

The Notes to the Financial Statements provide additional information that is essential to a full understanding of the data provided in the financial statements.

Net Assets

The CIRM net assets as of June 30, 2005, were $2,457,613 all of which were restricted. This represents a combination of $4,107,903 from the Dolby Grant and $1,650,290 that is owed to the General Fund. The remainder of the $3 million General Fund loan - $1,349,710 – the remainder of the Dolby Grant funding and the proceeds from any BANS that are issued will be used for operational expenses and grant programs in subsequent years until the bonds are issued.

Budgetary Information

All CIRM funds are continuously appropriated without regard to fiscal year to support the CIRM and its grant programs. Continuous appropriation authority means that no further appropriations are necessary to expend funds held in the State Treasury.

Economic Conditions and Outlook

In general, the State's economy and the fiscal status of its general fund did not have an impact on CIRM funds during the fiscal year. Except for the $3 million general fund loan authorized by Health and Safety Code Section 125290.70(b), CIRM does not receive any on-going State General Fund support. It is expected that when bonds are issued, the proceeds will provide sufficient revenues to support both CIRM's operational costs and grant programs.

Requests for Information

This financial report is designed to provide interested parties with a general overview of the finances of the CIRM and its funds. Questions concerning the information provided in this report or requests for additional information should be addressed to the following:

Walter Barnes, Chief Administrative Officer, CIRM, 210 King Street, Third Floor, San Francisco, CA 94107, 415.396.9100

Balance Sheet and Statement of Net Assets

June 30, 2005

	Stem Cell Fund	Adjustments (Note 3)	Statement of Net Assets
ASSETS			
Cash and equivalents	$ 5,112,154	$ —	$ 5,112,154
Total assets	$ 5,112,154		$ 5,112,154
LIABILITIES			
Accounts payable	$ 1,004,541	—	$ 1,004,541
Due to other funds	1,650,000	—	1,650,000
Total liabilities	2,654,541	—	2,654,541
FUND BALANCE / NET ASSETS			
Fund balance			
Reserved Fund Balance	2,457,613	(2,457,613)	—
Total liabilities and fund balance	$ 5,112,154		
Net assets			
Restricted		2,457,613	2,457,613
Total net assets		$ —	$ 2,457,613

The accompanying notes are an integral part of these financial statements.

Statement of Revenues, Expenditures, and Changes in Fund Balance and Statement of Activities

For the Period From Inception (November 2, 2004) to June 30, 2005

	Stem Cell Fund	Adjustments (Note 3)	Statement of Net Assets
REVENUES			
Grant Revenue (Note 6)	$ 5,000,000	$ —	$ 5,000,000
Other (Note 5)	84,660	—	84,660
Total revenues	5,084,660	—	5,084,660
EXPENDITURES / EXPENSES			
Salaries and benefits	736,705	—	736,705
Operating expenses	1,890,342	—	1,890,342
Total expenditures / expenses	2,627,047	—	2,627,047
Excess of revenues over expenditures and change in net assets	2,457,613	—	2,457,613
Fund balance / net assets, at inception	0	—	0
Fund balance / net assets, at June 30, 2005	$ 2,457,613	$ —	$ 2,457,613

The accompanying notes are an integral part of these financial statements.

Notes to the Financial Statements

For the Period From Inception (November 2, 2004) to June 30, 2005

1. THE FINANCIAL REPORTING ENTITY

The California Institute for Regenerative Medicine (CIRM) is a state agency accounted for as a special revenue fund of the State of California that was established with the passage of Proposition 71, the California Stem Cell Research and Cures Initiative. The statewide ballot measure, which provided $3 billion in funding for stem cell research at California universities and research institutions, was approved by California voters on November 2, 2004, and called for the establishment of a new state agency to make grants and provide loans for stem cell research, research facilities and other vital research opportunities.

CIRM was established for the purpose of issuing bonds to support stem cell research for the development of life-savings regenerative medical treatments and cures. CIRM is authorized under Proposition 71 to grant an average of $295 million per year in bonds over a 10-year period to fund stem cell research and dedicated facilities for scientists at California's universities and other advanced medical research facilities throughout the state.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

A. Basis of Accounting/Fund Financial Statements

Basis of accounting refers to when revenues and expenditures or expenses are recognized in the accounts and reported in the financial statements.

The government-wide financial statement (i.e. the statement of net assets and the statement of activities) reports information on all of the activities of CIRM. The government-wide financial statements are reported using the economic resources measurement focus and the accrual basis of accounting. Revenues are recorded when earned and expenses are recorded when a liability is incurred, regardless of the timing of related cash flows.

Separate financial statements are provided for CIRM's operating fund, governmental fund type. This governmental fund's financial statements are reported using the current financial resources measurement focus and the modified accrual basis of accounting. Revenues are recognized as soon as they are both measurable and available. Revenues are considered to be available when they are collected within the current period or soon enough thereafter to pay liabilities of the current period. For this purpose, revenues are considered to be available if they are collected within 12 months of the end of the current fiscal period. Expenditures generally are recorded when a liability is incurred, as under accrual accounting.

The basic financial statements of CIRM are intended to present the financial position and the changes in financial position of only that portion of the activities of the State of California that are attributable to the transactions of CIRM. They do not purport to, and do not, present fairly the financial position of the State of California as of June 30, 2005, and the changes in its financial position, for the year then ended in conformity with accounting principles generally accepted in the United States of America.

B. Accounting Principles

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America and the accounts are maintained by CIRM in accordance with the principles of fund accounting under standards issued by the Governmental Accounting Standards Board (GASB). Fund accounting is

the procedure by which resources for various purposes are classified for accounting and reporting purposes into funds established in accordance with their nature and purpose. The operations of the fund are accounted for with a separate set of self-balancing accounts that comprise its assets, liabilities, fund equity, revenues, and expenditures.

CIRM's operating fund is classified as a non-major special revenue fund of the State of California, referred to as the Stem Cell Research and Cures Fund, and is a governmental fund type.

C. Cash, Cash Equivalents and Pooled Investments

CIRM considers all short-term investments with an original maturity of three months or less to be cash equivalents. Cash and investments held in the State of California's Surplus Money Investment Fund (SMIF) are considered to be highly liquid and cash equivalents.

D. Capital Assets and Depreciation

Capital assets, when purchased, will be reported in the government-wide financial statements. In accordance with the State's capitalization policy, CIRM's capital assets are defined as assets with a useful life of at least one year and a unit acquisition cost of at least $5,000. All reported capital assets will be depreciated using the straight-line method. There were no capital assets recorded as of June 30, 2005.

E. Tax Exemption

As a component unit of the state of California, CIRM is exempt from federal and State income taxes.

E. Due to Other Funds

Due to other funds represents amounts payable to the State general fund pursuant to the loan provisions outlined in Proposition 71.

F. Classification of Net Assets and Fund Balance

Restricted net assets and reserved fund balance of CIRM represent amounts restricted due to external restrictions imposed by grantors and restrictions imposed through enabling legislation. All of CIRM's net assets and fund balance are restricted by grantors or statute for programs established by CIRM and for programs administered pursuant to Proposition 71.

G. Risk Management

CIRM is a special revenue fund of the State of California, which is primarily self-insured against loss or liability. The State generally does not maintain reserves; losses are covered by appropriations in the year in which the payment occurs or it becomes fixed and determinable. There were no accrued losses at June 30, 2005 that met these criteria.

H. Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the reporting date and revenues and expenses during the reporting period. Actual results could differ from those estimates.

3. RECONCILIATION OF GOVERNMENTAL FUND FINANCIAL STATEMENTS AND GOVERNMENT-WIDE FINANCIAL STATEMENTS

Generally, governmental fund financial statements differ from government wide financial statements due to differences in their measurement focus and basis of accounting. Accordingly, these differences are typically illustrated in reconciling schedules in the financial statements and footnotes. At June 30, 2005, no such differences existed for CIRM.

4. CASH, CASH EQUIVALENTS AND POOLED INVESTMENTS

Cash, cash equivalents and pooled investments at June 30, 2005 were as follows:

Cash in State Treasury	$ 5,112,154

CIRM has invested excess cash funds in the Surplus Money Investment Fund (SMIF). All of the resources of SMIF are invested through the Pooled Money Investment Account (PMIA). The PMIA investment program is designated by the Pooled Money Investment Board and is administered by the Office of the State Treasurer. Investments in SMIF are stated at fair value. As of June 30, 2005, the CIRM had invested funds in SMIF in the amount of $5,112,154.

Additional disclosure details required by GASB Statement No. 40, regarding cash deposits and investments risk disclosures can be found in the June 30, 2005 Comprehensive Annual Financial Report of the State of California.

5. OFFICE LEASE

From February 2005 through June 2005, CIRM's office space in Emeryville, California was provided free of charge. The fair value of the leased space during the period of occupancy was estimated to be $84,660. Accordingly, revenue and expenditures of $84,660 have been recorded in CIRM's financial statements.

CIRM continued to occupy office space in Emeryville, California until November 14, 2005, when it took occupancy of new office space in San Francisco, California for use as its headquarters. The San Francisco office space was acquired in response to a competitive bidding process. As part of the City of San Francisco's proposal, approximately 20,000 square feet of premium office space will be provided to CIRM free of charge for the next 10 years. In addition to the office space, a substantial amount of other incentives were included in the proposal. The fair value of the office space and other incentives will be evaluated on an annual basis to ascertain the economic benefit to CIRM.

6. GRANTS AND DONATIONS

Proposition 71 authorized CIRM to receive gifts that may be used for its operations. In June 2005, CIRM received a grant of $5 million from the Dolby Family Foundation. The grant letter of commitment contained specific expenditure restrictions (including the prohibition to use the funds for payment of loans, including the $3 million loan from the State General Fund) and allowances. CIRM management believes that CIRM was in compliance with these restrictions as of June 30, 2005.

7. RELATED PARTY TRANSACTIONS

As a Special Revenue Fund within the State of California, other State agencies provided CIRM with various services during the period from inception to June 30, 2005. The State Controller's Office provided administrative and accounting support, the Department of Justice provided legal support, the University of California, San Francisco provided human resources staff, and the Department of Health and Human Services and the Stephen P. Teale Data Center provided information technology support. The total amounts paid (or transferred) and payable to these agencies at June 30, 2005 were as follows:

	Amounts Paid	Amounts Payable
State Controller's Office	$ —	$ 269,197
Department of Justice	102,767	66,025
University of California, SF	—	40,000
Department of Health & Human Services	272	17,000
Stephen P. Teale Data Center	—	15,000

8. RETIREMENT SAVINGS PLAN

The State of California has established the Alternate Retirement Program (ARP), a retirement program for specified State of California employees hired on or after August 11, 2004. Under the ARP, employees do not earn retirement service credit with California Public Employees' Retirement System of the State of California (CalPERS) during their first two years of employment with the State. Rather, they are automatically enrolled in a retirement savings program, in which an ARP account is automatically set up for each employee as a 401(a) plan—a type of retirement savings account governed by federal IRS rules. During this two-year period, roughly five percent of each employee's paycheck is deducted each month (pre-tax) and deposited in the ARP account. At the end of the two-year period, the employee begins to earn retirement credit as a Tier I member.

Money in the ARP account, plus any interest, remains in that account. The employee will have a 90-day window to exercise a one-time option to (1) buy previous retirement service credit for time in ARP (the State will fund the portion of the liability not paid for the by the employee's APR account); (2) receive a lump-sum distribution; or (3) transfer all funds into a 401(k) account within the Savings Plus Program. Participant's failure to designate an option will result in automatic enrollment in option 3.

Since all CIRM employees as of June 30, 2005 were hired after the implementation of ARP, all CIRM employees participate in this program and are not eligible to participate in CalPERS.

CalPERS issues a separate comprehensive annual financial report that includes financial statements and required supplementary information. Copies of the CalPERS annual financial report may be obtained from the CalPERS Executive Office, 400 P Street, Sacramento, California 95814.

9. CONTINGENCY

CIRM and its officers are currently defendants in three separate legal actions. One of these cases was dismissed in October 2005 and is now pending appeal. Collectively, the two remaining actions seek a declaration that Proposition 71 is unconstitutional and, in general, to prevent CIRM from fulfilling the purposes for which it was created. The two remaining actions were consolidated into one action in October 2005. Trial of the consolidated action commenced on February 27, 2006 and concluded March 3, 2006. On April 21, 2006, the Superior Court issued a proposed Statement of Decision upholding the constitutionality of Proposition 71 in its entirety and rejecting each of the plaintiffs' claims. Plaintiffs have ten days to file objections to the decision, and after the court enters judgment, plaintiffs will have 30 days to file a notice of appeal. Due to the uncertain nature of these legal actions, management was unable to estimate any potential range of loss or impact on CIRM's proposed operations.

Combining Schedule of Net Assets

June 30, 2005

	Non-Grant Funds	Dolby Grant	Eliminations	Total
ASSETS				
Cash and equivalents	$ 112,154	$ 5,000,000		$ 5,112,154
Due from other fund	139,224		$ (139,224)	0
Total assets	$ 251,378	$ 5,000,000	$ (139,224)	$ 5,112,154
LIABILITIES				
Accounts payable	$ 251,668	$ 752,873		$ 1,004,541
Due to other funds	1,650,000	139,224	$ (139,224)	1,650,000
Total liabilities	1,901,668	892,097	(139,224)	2,654,541
NET ASSETS				
Restricted	$ (1,650,290)	$ 4,107,903	$ —	$ 2,457,613

Combining Schedule of Activities

For the Period From Inception (November 2, 2004) to June 30, 2005

	Non-Grant Funds	Dolby Grant	Total
REVENUES			
Grant Revenue (Note 6)		$ 5,000,000	$ 5,000,000
Other (Note 5)	$ 84,660		84,660
Total revenues	84,660	5,000,000	5,084,660
EXPENSES			
Salaries and benefits	591,627	145,078	736,705
Operating expenses	1,143,323	747,019	1,890,342
Total expenses	1,734,950	892,097	2,627,047
Change in net assets	(1,650,290)	4,107,903	2,457,613
Net assets, at inception	—	—	—
Net assets, at June 30, 2005	$ (1,650,290)	$ 4,107,903	$ 2,457,613

Current and Past CIRM Staff Members

EMPLOYEE	TITLE
Pat Becker	Senior Executive Assistant to the President
Dale Carlson	Chief Communications Officer
Tricia Chavira	Grants Technical Assistant
Arlene Chiu	Director, Scientific Activities
Meybel Cortez	Grants Technical Assistant
Marcia Davey	Finance Officer
Alexandra Campe Degg	Chief Human Resources Officer
Ed Dorrington	Chief Information Officer
Amy DuRoss	Chief of Staff to the Chair
Zach Hall	President & Chief Scientific Officer
Kumar Hari	Scientific Program Officer I
Lorraine Hoffman	Chief Finance & Administrative Officer
Melissa King	Director, ICOC Board Relations
Kirk Kleinschmidt	Director, Legislation and Research Policy
Amy Lewis	Deputy Chief of Staff
Geoff Lomax	Senior Officer for Medical & Ethical Standards
Mary Maxon	Deputy to the Vice Chair
Patricia Olson	Scientific Program Officer II
Jennifer Pryne	Executive Assistant to the Chair
Erin Robbins	Facilities & Procurement Analyst
Gil Sambrano	Scientific Review Officer I
Kate Shreve	Chair's Liaison to the Working Groups
Scott Tocher	Associate Legal Counsel

PAST EMPLOYEE	TITLE
Walter Barnes	Chief Administrative Officer
Amy Daly	Director, Patient and Medical Organization Relations
Christina Olsson	Legal Associate
Nicole Pagano	Senior Communications Specialist
Jennifer Rosaia	Administrative Coordinator
Jorge Sanchez	Senior Executive Assistant to the President

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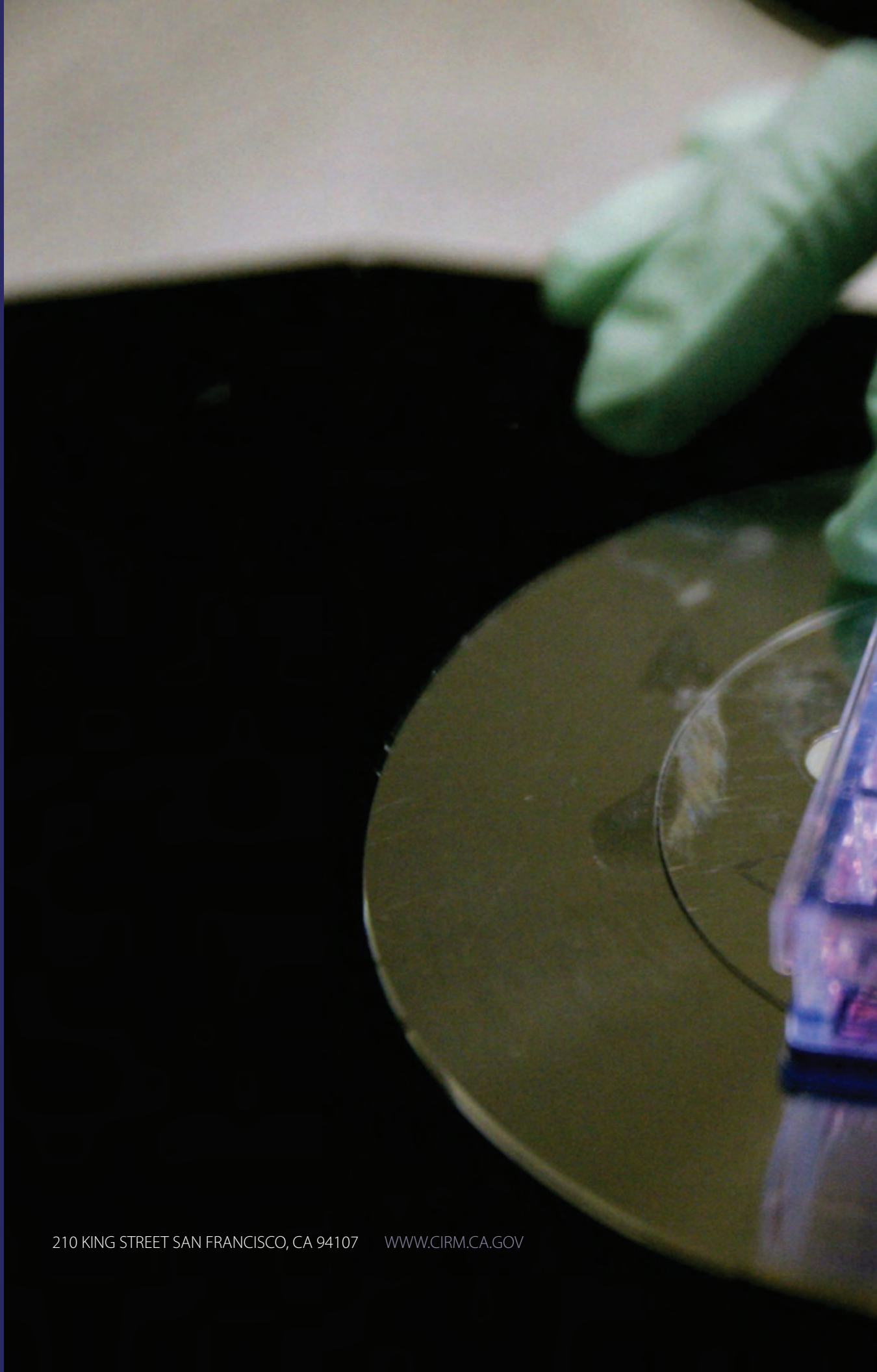

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