

s pioneers in cancer research, scientists at
Fred Hutchinson Cancer Research Center push
the boundaries of medical science to find new ways
to prevent, detect and treat cancer and related

ADVANCING SCIENCE FOR LIFE

diseases. Our culture of innovative thinking and collaboration has led to critical lifesaving breakthroughs that have saved thousands upon thousands of lives. We are advancing science for life.

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MESSAGE FROM DR. LARRY COREY, PRESIDENT AND DIRECTOR

Investing in scientific innovation: You make progress against cancer possible

As I complete my first year as director of Fred Hutchinson Cancer Research Center, I am pleased to give you positive news in our battle against cancer. The National Institutes of Health reported that cancer deaths and new diagnoses are declining, proof we are making significant progress against these devastating diseases.

The Hutchinson Center has directly contributed to this progress with scientific innovations that have improved methods for detecting, treating and preventing cancer. Here are a few examples you will read about in this annual report:

- The Hutchinson Center's research teams have had a clear impact on breast cancer prevention. Our scientists who lead the Women's Health Initiative—the largest study of women's health ever undertaken—continue to make breakthroughs that reduce cancer risk and improve women's health. This year, teams led by Dr. Andrea LaCroix made two prevention discoveries that will further reduce breast cancer incidence.
- Building upon our pioneering development of bone marrow transplantation, our scientist-physicians have relentlessly refined the procedure to save even more lives. This year, Dr. George McDonald's analysis of these efforts showed they have led to unparalleled improvements in blood cancer survival rates at our transplant clinic.
- A discovery by our prostate cancer researchers this year could pave the way for a simple blood test to identify patients who should receive aggressive treatment. The team, led by

Dr. Janet Stanford, identified genetic markers linked to aggressive, lethal prostate cancer. Such a screening test could reduce overtreatment of indolent prostate tumors.

- Dr. Nina Salama, who focuses her work on the bacterium that causes stomach cancer and gastric ulcers, this year found a chink in its armor that she hopes to exploit to eliminate these diseases. Nina discovered that the corkscrew shape of *Helicobacter pylori* is essential to its survival in the stomach. Creating a targeted therapy to disable the proteins that determine the bug's shape would keep it from colonizing the stomach and causing disease.
- We are also developing "Star Wars"-like technologies to correct and disable genes so we can use this genetic surgery in combination with blood stem cell transplants to cure diseases. Drs. Hans-Peter Kiem and Keith Jerome broke new ground this year by exploring its potential to cure HIV by specifically knocking out one of the receptors the HIV virus needs to infect the immune system's helper T-cells.

These are just a few examples of our recent advances, which could not have been made without your generous contributions. Many additional innovations are described in this annual report. We are extremely grateful for your ongoing investment in scientific innovation that moves our lifesaving research forward. Thank you.

Lang Cong

MESSAGE FROM DOUGLAS W. WALKER, CHAIR, BOARD OF TRUSTEES

New heights in cancer and infectious disease research

This year was exciting—one of change and success for Fred Hutchinson Cancer Research Center. We welcomed our fourth president and director, Dr. Larry Corey, whose vision and leadership will take the Hutchinson Center to new heights in cancer and infectious disease research. Center scientists continued to explore uncharted frontiers, capitalizing on the interdisciplinary, collaborative culture unique to the Center. We also celebrated a record-breaking fundraising year with more than \$44.4 million generated from committed supporters like you.

Thank you for partnering with the Center in our quest to eliminate cancer and related diseases as causes of human suffering and death. Your investment enables researchers to explore creative and novel ways to tackle complex scientific problems.

It is this "out of the box" thinking—dependent on private support like yours—that paves the way to improve the lives of countless patients and their families now and in the future. We are honored by your trust and support.





MOVING CANCER TREATMENT FORWARD

Leading the way in immunotherapy: Harnessing the immune system to treat cancer

The human immune system has a remarkable ability to seek out, recognize and eliminate abnormal cells in the body. Immune system components such as T-cells and antibodies can selectively kill cancer cells or cells infected with a virus while leaving normal cells intact.

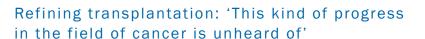
Fred Hutchinson Cancer Research Center scientists were the first to demonstrate the power of the immune system to cure cancer when they developed bone marrow transplantation to treat leukemia and other cancers of the blood. Over the past three decades, we have built a deep understanding of this therapeutic effect and have led the way in developing more techniques to harness the immune system to treat cancers—a field called immunotherapy.

Our leadership in the field was recognized this year by the National Cancer Institute when it selected the Hutchinson Center to direct the new Cancer Immunotherapy Trials Network.

The network—led by Dr. Mac Cheever, head of the Hutchinson Center's Solid Tumor Research Program—brings together the collective expertise of 27 research institutions across the country to accelerate clinical trials of the most promising immunotherapies for solid tumor cancers.

As a widely recognized center of excellence in immunotherapy research, the Hutchinson Center is increasingly relied upon to participate in and lead such national and international collaborations. Our ability to seize these opportunities has been significantly strengthened by the financial support of our donors.

A high point was reached this year when many supporters made contributions to complete the Bezos family challenge gift for immunotherapy research. Their extraordinary gift and leadership united the community in funding this potentially transformative cancer treatment.



"How is medical progress made? With transplantation, we are talking about a series of little steps, one on top of another on top of another."

That's how Dr. George McDonald characterizes his recent study that showed how a decade of steady refinements by Hutchinson Center researchers to bone marrow and stem cell transplantation led to unparalleled improvements in blood cancer survival rates. Our researchers pioneered transplantation

more than 40 years ago—and they remain the world's leaders in the field. McDonald's study underscores that fact. Comparing survival rates of patients treated by Center physicians in the

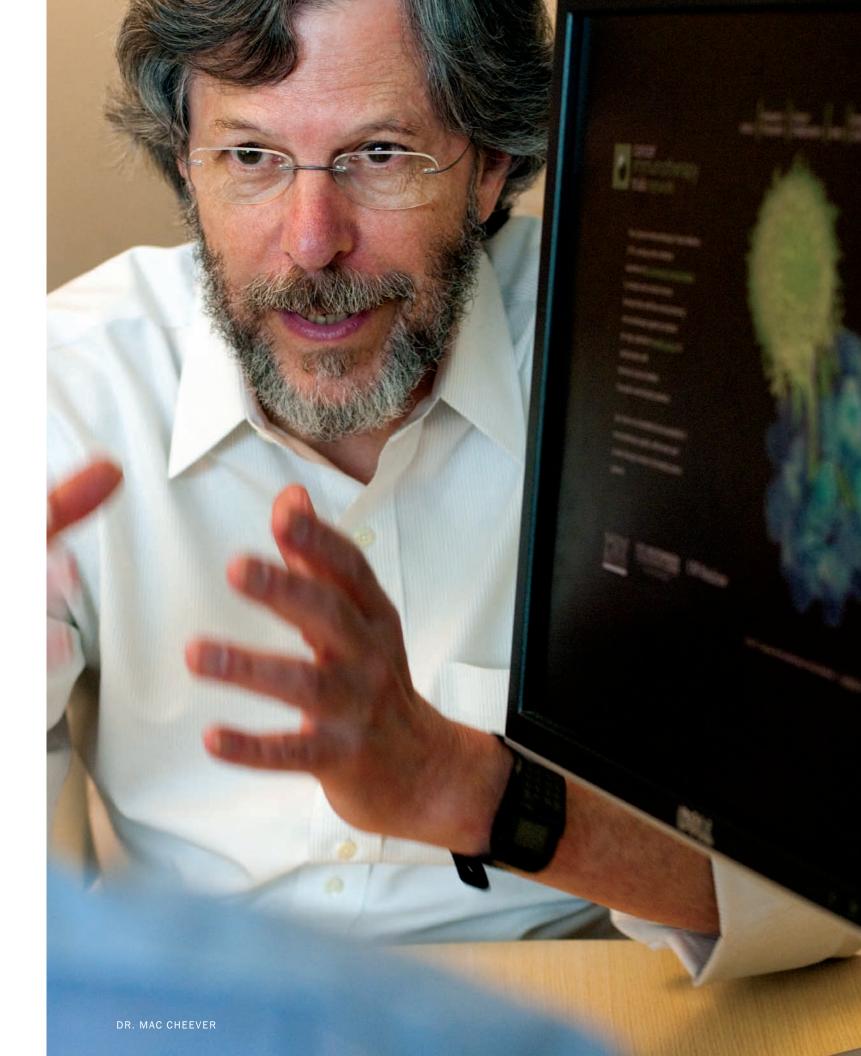
mid-1990s to those in the mid-2000s, he and his colleagues reported a 60 percent drop in the risk of death within 200 days of transplant and a 41 percent reduction at any time after transplant.

"This kind of progress in the field of cancer, in cancer studies, is unheard of," McDonald said.

The study also revealed the one-year survival rate jumped from 55 percent to 70 percent.

They also found significant declines after transplantation in the risks of severe graft-vs.-host disease, infections, and complications from damage to the lungs, kidneys and liver.

As the world approaches 1 million transplants, we celebrate these remarkable advances that have improved survivorship for people with lifealtering blood cancers.



DR. GEORGE MCDONALD

Prostate cancer: Genetic discovery holds promise for better screening

A new kind of prostate cancer screening could one day determine which patients need aggressive treatment and which would benefit from a more conservative "active surveillance" approach.

Led by the Hutchinson Center's Dr. Janet Stanford, an international team of researchers this year identified five inherited genetic variants strongly associated with aggressive, lethal prostate cancer.

If the biomarkers prove valid in further studies, a resulting simple blood test could decrease the personal toll and economic burden of prostate cancer overtreatment.

"Tests that can distinguish between patients

with indolent tumors versus more-aggressive tumors are urgently needed," Stanford said. "The panel of biomarkers we've identified provides the first validated evidence that inherited genetic variants play a role in prostate cancer progression and mortality."

The researchers analyzed DNA in blood samples taken from a group of more than 4,000 prostate cancer patients. They looked for variants within the DNA alphabet to identify those that appeared to play a role in the development or progression of the disease. Patients who carried four or five of the genetic markers had a 50 percent higher risk of dying from their prostate cancer than patients who had two or fewer.

DRS. ALAN KRISTAL AND JANET STANFORD



Muscular dystrophy: Biggest discoveries in decades could improve diagnosis and treatment

This year brought two historical leaps forward in our understanding of a common form of muscular dystrophy—the biggest steps in two decades—paving the way for better diagnosis and treatment.

Facioscapulohumeral muscular dystrophy (FSHD), characterized by progressive weakening and loss of skeletal muscle, is the most prevalent type of the condition. FSHD is a genetic disease, caused by a flaw in the DNA instructions near the end of chromosome 4. In those with FSHD, the DNA sequence is cut short. But here's the puzzle: not everyone with this so-called "contraction" gets FSHD.

The Hutchinson Center's Dr. Stephen Tapscott, working with a multinational team, discovered that people with FSHD have both the DNA sequence contraction and a molecular signal that tells cells not to destroy a rogue protein, allowing

it to cause chaos in the form of FSHD.

They also found that the disease is caused by a faulty "off" switch for a particular retrogene, normally expressed only in early development and then tamped down in all other cells of the body. When the retrogene isn't suppressed, it bursts in the muscle cells and leads to cell death and muscular dystrophy. It is the first time in genetic research history that a retrogene has been found to "wake up" and cause disease.

The basic biology of a disease must be understood before treatment targets are clear. These landmark findings will make it easier to diagnose FSHD and better predict who will get the disease, even before symptoms appear, as well as provide critical focus for future development of FSHD therapies.

Improving women's health and saving lives with scientific evidence

For 20 years, research from the Hutchinson Center-based Women's Health Initiative has saved thousands of lives by debunking conventional wisdom and allowing millions of women and their doctors to make key health decisions based on scientific evidence.

The WHI's biggest landmark was the finding that combined hormone replacement therapy (estrogen plus progestin) to manage the symptoms of menopause increases a woman's risk of breast cancer and heart disease. Use of the once-widespread therapy immediately dropped, followed by a consequent decline in breast cancer in the U.S.

Hutchinson Center researchers with the WHI continue to make important discoveries, including a new study this year by Dr. Andrea LaCroix showing certain women who used only estrogen

hormone therapy had markedly reduced risk for breast cancer and heart attacks.

Her estrogen-only hormone study

followed nearly 11,000 women for an average of 11 years, the most extensive look at the topic. Women DR. ST in their 50s taking estrogen had a lower risk of heart attack, but the risk was increased for those in their 70s. The risk of breast cancer was reduced for all ages. LaCroix and colleagues also found that strokes and other health problems linked with estrogen pills appeared to fade after the medication was stopped.

From this and numerous other findings, the Women's Health Initiative continues to contribute a greater understanding of the role of hormones, diet and calcium on midlife female health.



DR. STEPHEN TAPSCOTT

SAVING LIVES THROUGH SCIENTIFIC INNOVATION

Traffic patterns of brain cells: Clues to cancer spread?

A study on the "traffic patterns" of cells and how they travel has shed new light on how cells migrate in the developing brain, which may also reveal how other types of cells, including cancerous ones, travel within the body.

This groundbreaking research by the Hutchinson Center's Drs. Jonathan Cooper and Yves Jossin could lead to a better understanding of neurological development and how cancer spreads.

In the developing brain, the cerebral cortex—
the command and control center—grows from the
inside out, adding new neurons to the outermost
layer. The researchers solved the mystery of how

this migration is regulated, finding that a signaling protein called Reelin guides the new neurons into place by triggering changes in the membranes of the migrating neurons that allow the cells to respond to direction signals.

The scientists observed that a membrane protein called N-cadherin increases on the surface of the neurons when the neurons encounter Reelin, which helps the cells choose the appropriate direction for the next stage of migration. Elsewhere in the body, N-cadherin holds cells in place, so this unexpected role may help explain how normal and cancerous cells move around.



Among the 100 trillion bacteria living in the human body, Helicobacter pylori has managed to infect half the world's bellies. For tens of thousands of years, H. pylori has for the most part caused us no harm. But in some people, H. pylori becomes a destructive guest, leading to painful ulcers, and sometimes, deadly stomach cancer. H. pylori, like any other living organism, has many tools at its disposal for survival, and it has adapted successfully to its environment. Because it's capable of causing disease, researchers have been trying to figure out its strengths and weaknesses and the sort of tools that enable it to thrive in the stomach's caustic surroundings.

This year, Hutchinson Center researcher Dr. Nina Salama and colleagues unlocked one of its main secrets: *H. pylori's* corkscrew shape is essential to its survival because it allows it to burrow deeply into the moist lining of the stomach, where it is safe from highly corrosive hydrochloric acid that aids digestion.

H. pylori has four key proteins that turn it into a corkscrew. But if you remove these proteins, the bacterium has trouble colonizing the stomach.

Now, Salama and her team are working to apply their discovery to create a vaccine that selectively targets only these proteins. If the bacteria can't colonize, they won't be able to cause disease, eliminating gastric ulcers and gastric cancers.



DR. MARK ROTH

Suspended animation could lengthen storage time of human organs and extend transplantation to more people

In Dr. Mark Roth's Hutchinson Center lab, organisms such as roundworms and yeast have been subjected to lethally cold temperatures and survived unharmed—after he first put them into a state of suspended animation.

But this is no mere lab exercise for Roth and his scientific team. He wants to save lives.

His technique of inducing suspended animation via oxygen deprivation and induced hypothermia may soon extend the shelf life of human organs for transplants, a development that could make transplantation an option for more people in need of replacement organs.

For several years, Roth has focused his research on finding lifesaving applications for suspended animation. Once the sole province of science fiction, it is now reality at the Hutchinson Center. In addition to aiding organ transplants, it also could buy time for patients in trauma situations, such as victims of heart attack or blood-loss injury, by reducing the need for oxygen

until definitive medical care can be given.

Depriving yeast and worms of oxygen before putting them into a deep freeze helped answer several questions. Under normal conditions, 99 percent of these species die when exposed to temperatures just above freezing for 24 hours.

But if they're first deprived of oxygen and thus enter a state of anoxia-induced suspended animation, 66 percent of the yeast cells and 97 percent of roundworm (nematode) embryos will survive. Once normal growth conditions are resumed—through rewarming and reintroduction of oxygen—the organisms will reanimate and go on to have normal lifespans.

"We have found that extension of survival limits in the cold is possible if oxygen consumption is first diminished," Roth said. "Our experiments in yeast and nematodes suggest that organs may last longer outside the body if their oxygen consumption is first reduced before they are made cold."

DR. NINA SALAMA

Better breast cancer treatment, fewer side effects from targeted therapy

Cancer research takes teamwork, and few institutions know teamwork as well as the Hutchinson Center. That's why the National Cancer Institute recently chose the Center to lead a five-year, Seattle-based breast cancer research consortium.

The consortium's goal: to improve breast cancer prevention, detection, treatment and care for women who have or are at risk for the disease.

Led by the Hutchinson Center's

Drs. Peggy Porter and Mac Cheever, the Seattle Cancer Consortium Breast SPORE (Specialized Program in Research Excellence) involves 25 researchers from the Center and University of Washington as well as project consultants from institutions across the U.S.

and abroad.

"The collaborations that have been formed among basic, clinical and translational scientists at the Hutchinson Center and University of Washington were key to landing the consortium," Porter said.

Developing targeted breast cancer treatments is the unifying mission behind the consortium's four scientific projects. Because targeted therapies zero in on specific molecules involved in tumor growth, they often have less severe side effects than standard chemotherapy and radiation.

"Our mission is to provide better breast cancer treatment options that are developed from the science at the Center and the UW," Cheever said.

DR. PEGGY PORTER

Breast cancer researchers make progress on several fronts

The Hutchinson Center's unique approach to breast cancer research unites scientists from a spectrum of disciplines: basic science, genetics, clinical medicine, cancer prevention and epidemiology. This year, our researchers made several discoveries to further our mission of reducing breast cancer incidence and deaths.

The osteoporosis drug lasofoxifene reduced breast cancer risk by 79 percent in postmenopausal women with low bone density, according to a study by Dr. Andrea LaCroix. The drug also substantially reduced risk of stroke, heart events and fractures. Lasofoxifene poses fewer safety concerns and provides more benefits than similar drugs, making it an "attractive option" for postmenopausal women with osteoporosis, LaCroix said.

Young women with breast cancer who carry an inherited mutation in the breast cancer susceptibility genes BRCA1 or BRCA2 are four times more likely to develop cancer in the other breast than those without a mutation, according

to a study by Dr. Kathi Malone and colleagues. These findings "underscore the need for women diagnosed with a first breast cancer at a young age—regardless of family history—to consider genetic testing and to discuss it with their health care providers," Malone said.

Full-term pregnancy has long been associated with a reduced risk of breast cancer, but a study led by Dr. Amanda Phipps found that the more times a woman gives birth, the higher her risk of "triple-negative" breast cancer, a relatively uncommon but particularly aggressive form of the disease. Conversely, women who never give birth have a 40 percent lower risk of such breast cancer, which has a poorer prognosis than other types of breast cancer.

"We were surprised by these findings because researchers have known for quite some time that women who have children, especially those who have them at an early age and have multiple full-term pregnancies, have a lower risk of breast cancer overall," Phipps said.

Tackling the problem of cancer in the developing world

It's well known that cancer has become the world's leading cause of death, killing about 8 million people annually. What may be suprising is the fact that infectious diseases cause more than 20 percent of the world's cancer cases.

Several common viral and bacterial infections can lead to cancers, such as stomach, liver, cervical, bladder, Kaposi sarcoma and lymphoma. Because these infections can be prevented or controlled, they represent an immediate opportunity to reduce the world's cancer burden —by preventing the development of cancer in the first place.

As a leader in the prevention and treatment of cancer and infectious diseases, the Hutchinson Center is uniquely suited to address this problem. By working in a country where infection-related cancers are common, our researchers and colleagues at the Uganda Cancer Institute (UCI) are accelerating new prevention and treatment breakthroughs.

The two institutions formed an innovative collaboration—the UCI/Hutchinson Center Cancer Alliance—designed to make substantial inroads against infection-related cancers. The collaborators broke ground this year on an integrated research, training and treatment

facility—the first comprehensive cancer center jointly constructed by U.S. and African cancer institutions.

"The UCI/Hutchinson Center Cancer
Alliance is a personification of the African
proverb: 'If you want to go fast, go alone; if you
want to go far, go together,'" Dr. Larry Corey,
Hutchinson Center president and director, said
at the groundbreaking ceremony. "Cancer is a
disease that requires us both scientifically and
medically to go far and,

hence, requires us to walk together."

"Through this
collaboration, we hope
to develop new, low-cost
prevention and treatment
strategies that will not
only stem the rising burden
of cancer in sub-Saharan Africa but will benefit

millions of people worldwide," he said.

The program will increase patient access to diagnostic technology and research-based treatment while furthering study on the links between infectious diseases like HIV and Epstein-Barr virus and cancers such as Kaposi sarcoma and Burkitt lymphoma.

Viral and bacterial infections are contributing factors in:

- Lymphoma
- Sarcoma
- Stomach cancer
- Cervical cancer
- Liver cancer
- Bladder cancer



The planned state-of-the-art, integrated cancer training and treatment facility

At the forefront of finding cancer at its earliest, most curable stages

The key to curing cancer is to catch it early. For many common cancers, nine of 10 patients can be saved when their cancer is detected early, before it grows out of control.

The Hutchinson Center has been at the forefront of early cancer detection for many years, and this year the National Cancer Institute tapped the Center to continue coordinating its multi-institution Early Detection Research Network.

Finding cancer when it is most treatable and curable is a remarkably daunting challenge—
to find it at this stage amounts to conducting

molecular detective work. But thankfully, even cancer can't make a move without leaving a trail of telltale signs.

This is where biomarkers come in. Much like the presence of an antibody indicates an infection, the presence of certain proteins in the blood—biomarkers—may indicate cancer. Center researchers have been among the pioneers, having made a number of landmark biomarker discoveries that have greatly accelerated progress in the field.

LEADING THE WAY IN CANCER DETECTION AND PREVENTION

Real-world science for students: Mentoring the next generation of researchers

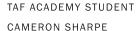
Science is the foundation for many great discoveries that benefit humankind, and science education is essential to ensuring a better quality of life for all of us. That's why the Hutchinson Center is committed to improving science education in our schools and mentoring the next generation of scientists.

This year, about 30 students from colleges across the country participated in our Summer Undergraduate
Research Program. It's a competitive nine-week internship that provides experience for students interested in careers in biological research—with a special reach into populations traditionally underrepresented in science and health care.
Students work with faculty mentors who equip them with the skills to be fully functioning members of the scientific community. By making

real-world science relevant and exciting for these promising students, we help pave the path for their careers in science.

We also established a teaching laboratory this year for two high school education programs that provide intensive training to promising students during the school year. Our unique programs with Seattle's Cleveland High School and Federal Way's Technology Access Foundation Academy focus on a spectrum of techniques and equipment used in biomedical research, which they normally wouldn't encounter until graduate school.

These programs expand upon our 21-year-old Science Education Partnership, which has trained hundreds of high school science teachers in the use of lab research tools in their classrooms, and our 13-year-old Hutch High symposium, which has brought more than 3,700 students to our campus for an introduction to lab research.



Could we correct disease-causing genetic defects before they occur?

The human body contains more than a trillion cells, and it's remarkable that the genetic information in each cell—in the form of 46 chromosomes—starts out the same. However, each time our cells divide, the potential for mistakes arises. Cancer cells, for instance, have the wrong number of chromosomes.

So how do our cells get all the right chromosomes when they divide?

For the first time, a scientific team, which included the Hutchinson Center's Dr. Sue Biggins, discovered how cells stabilize their machinery for forcing apart chromosomes. When a cell gets ready to split into new cells, this steady mechanism permits the genetic material to be separated and distributed accurately.

The researchers isolated kinetochores, a tow

truck-like mechanism for each chromosome that attaches to a structure called a spindle. They found that during cell division, kinetochores are under tremendous force as the spindle pulls the chromosome through the cell. The kinetochores manage to stay attached to the spindle by binding more tightly when force is applied, similar to a finger trap toy.

"Many cancer cells have mutations in the proteins that make up the kinetochore, so we are optimistic that we can now understand exactly what is wrong with kinetochores in cancer cells," Biggins said. "This knowledge could potentially lead to ways to correct defects before they occur, or allow us to try to target cells with the wrong number of chromosomes to prevent them from dividing again."

Gene therapy in combination with blood stem cell transplants could hold the key to curing HIV

Hutchinson Center researchers broke new ground in the treatment of HIV this year by exploring the potential of blood stem cell transplantation to cure those infected with the AIDS-causing virus.

Drs. Hans-Peter Kiem and Keith Jerome were selected by the National Institutes of Health to lead a multifaceted team of scientists and institutions to determine whether a person's own stem cells can be engineered to deny HIV entry into the body's blood cells. They also will work to develop tools to eradicate existing reservoirs of infection in the body.

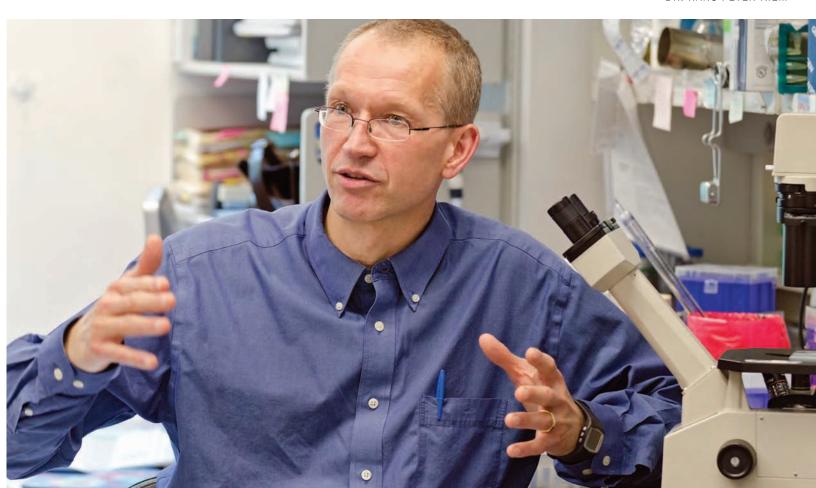
"Funding for research to find a cure for HIV-infected persons represents a paradigm shift," said Jerome, an expert in viral infections at the Hutchinson Center and the University of Washington. "HIV has been an incurable, lifelong infection that at best sentences people to a lifetime of complex drug therapies. Now the research field is shifting to address the possibility of a cure. No one would have talked about this

approach five years ago."

One approach under investigation is stem cell transplantation, in which the infected patient's own immune cells are genetically modified to be resistant to HIV by eliminating one of the receptors HIV needs to infect new cells. Led by Kiem, this method builds on the Hutchinson Center's long-standing expertise in using transplantation to treat and cure blood cancers and some autoimmune diseases.

Stem cell transplantation to eliminate HIV infection has an intriguing precursor. In 2008, a group of German physicians published results of transplanting an American man who had leukemia and HIV. The so-called "Berlin Patient" received a new immune system from donor cells that also carried a rare genetic variation that made them resistant to the virus. Today, the patient is considered cured of HIV. However, few people have this genetic variation, so a way must be found to modify the patient's own immune cells to resist HIV.

DR. HANS-PETER KIEM



MAKING RESEARCH PROGRESS POSSIBLE

Private Contributors Fiscal Year 2011

Fred Hutchinson Cancer Research Center relies on private contributions to accelerate scientific advances. This crucial support aids in the pursuit of novel ideas, sustains promising research and enables scientists to explore new directions as they emerge; all paramount in the fight against cancer and related diseases. We are grateful to each of the 23,655 donors who provided \$44.4 million in contributions and in-kind gifts between July 1, 2010, and June 30, 2011. Each of the individuals, corporations, foundations and organizations listed below contributed \$1,000 or more within fiscal year 2011.

Nobel Laureates Circle

The Nobel Laureates Circle recognizes contributors who have made cumulative gifts of \$1 million or more. These key contributors are permanent members of the Circle which was established in 2001 to honor the Hutchinson Center's Nobel Prize recipients, Drs. F. Donnall Thomas (1990). Lee Hartwell. (2001) and Linda Buck (2004). By giving at this level, members of the Nobel Laureates Circle are at the forefront of philanthropic leadership and make a significant impact on the Center's mission to eliminate cancer and related diseases as causes of human suffering and death.

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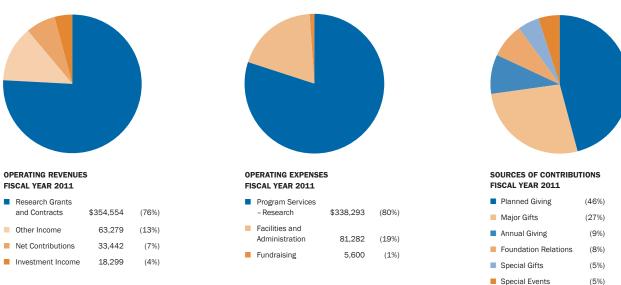
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Published by the External Affairs and Communications Department

Fred Hutchinson Cancer Research Center Mail Stop J5-200

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