

HUTCH

CURES START HERE

FRED HUTCHINSON CANCER RESEARCH CENTER



ANNUAL REPORT 2019

FROM THE DIRECTOR



Dr. Gary Gilliland

AS I REFLECT ON MY FIVE YEARS AS PRESIDENT AND DIRECTOR OF THIS REMARKABLE INSTITUTION, I feel both humbled and gratified to have been in this place at this time. I know it is a rare thing to lead an enterprise where everybody comes to work, every day, trying to do the best they can to help people who have terrible diseases.

That is the soul of Fred Hutchinson Cancer Research Center, and I am so pleased to complete my final year at the helm knowing we are in terrific shape.

From the beginning, I've tried to convey the sense of urgency I feel about our mission. I believe the most important action Fred Hutch can take to speed scientific discovery is to foster our culture of team science and to bring together the smartest people to work in collaboration across specialties. This has been a hallmark of our prior success, and we have vigorously expanded upon that. Your support has been instrumental in pursuing this strategy.

Our 2019 fiscal year brought important, measurable progress. We added 12 exceptional faculty members to our team and established eight new endowed chairs to support and attract more world-renowned faculty. We also launched our Translational Data Science Integrated Research Center to facilitate out-of-the box thinking and creative collaborations across the data and technology landscapes, work that is only possible here. Bringing in the best and breaking down walls to collaboration is also our goal with the expansion into the Lake Union Steam Plant. I believe the investment we're making to transform the iconic building into a nexus of immunotherapy and data science research will dramatically speed the development of personalized therapies.

The Hutch is in an excellent position, and I am delighted to report that it will continue to prosper under the leadership of Dr. Thomas J. Lynch Jr., who will become the sixth president in our 45-year history starting in February 2020. A highly respected oncologist, world-renowned scientist and successful cancer-center leader, Dr. Lynch is the ideal leader to advance Fred Hutch's mission.

Thank you again for your deep investment in us. Because of you, we're much closer to a world where every cancer, and every patient, has a cure.

Cures start here,

A handwritten signature in blue ink that reads "G. Gilliland". The signature is fluid and cursive, with a large initial "G" and a stylized "Gilliland" following.

Dr. Gary Gilliland
President and Director

RESEARCH HIGHLIGHTS 2019

Fred Hutch researchers continue to explore the edge of human knowledge as they seek cures for cancer, HIV and other diseases. Here we highlight a sampling of the most interesting and important research from the past year.



Y-shaped antibodies specific for individual CMV strains [depicted by same color] can prevent the virus from reactivating after transplantation. Image courtesy of Dr. Mariapia Degli-Esposti, Lions Eye Institute, Perth, Western Australia

Rethinking an old viral foe

YOU MAY NOT HAVE HEARD OF CYTOMEGALOVIRUS, but the two of you have likely met.

In fact, odds are it's dozing inside you right now.

Cytomegalovirus, or CMV, infects at least half of all adults worldwide. Most are unaware they're infected because their healthy immune system keeps it in check. The virus slips into dormancy, becoming a passive and lifelong passenger.

But CMV can roar back to life in anyone with a compromised immune system. The results can be life-threatening, and the virus has plagued bone marrow transplant patients for decades.

A study in the journal *Science* may rewrite the story of why the virus wreaks such havoc — and hint at how to stop it.

The research challenges long-held theories about how the body controls CMV. The twist: The immune system's defense

against CMV isn't a solo performance. After years of studying a mouse model, a team of researchers led by Dr. Geoffrey Hill shows that an unsung actor — antibodies — plays a vital role.

Antibodies are one of the body's chief ways of defending itself against infection.

Hill's insight could pave the way for cheaper, safer therapies using antibodies to protect transplant patients against CMV. The researchers found that a dose of the right antibodies after transplantation can keep the virus dormant in mice, without the need for any other immune cells.

"This is a big deal for the transplant field," said Hill, the study's senior author and director of Hematopoietic Stem Cell Transplantation at Fred Hutch. "We're turning dogma on its head, and that could meet the urgent need for inexpensive and nontoxic therapies to improve patient outcomes."

Mystery solved: How graft-vs.-host disease starts in the gut

BONE MARROW TRANSPLANTS have been curing some blood cancers for decades. But for just as long, a potentially fatal complication has lurked in the background.

In a bone marrow transplant, a patient's diseased blood-forming stem cells are wiped out and then replaced by a donor's healthy cells. Those donor cells are the key to the cure; they recognize and attack the patient's cancer cells.

But sometimes they attack the patient's healthy cells, too. This condition, called graft-vs.-host disease, can develop throughout the patient's body in organs like the skin, liver, eyes and lungs.



Dr. Motoko Koyama

If GVHD occurs in the gut, it can be lethal. How the disease occurs has been a mystery. Until now. A study published in the journal *Immunity* identifies the complex chain of events that triggers GVHD in the gut. It involves a large cast of cells and molecules, including some from a surprising source: the trillions of tiny organisms that live in and on us known as the microbiome.

The scientists, led by Drs. Motoko Koyama and Geoffrey Hill of Fred Hutch, also found a promising clue as they traced the disease's complicated pathway. One of the key players in that pathway is a chemical signal called interleukin 12. By snuffing out that signal, the researchers could prevent the disease from happening in mice. They are now applying for funding to test this approach in transplant patients via a clinical trial.

For Hill and Koyama, the study caps years of experiments trying to solve this whodunit. Both have seen transplant patients suffer and die from GVHD.

"Whether you live or die after a [donor] bone marrow transplant can, to a large extent, depend on whether or not you get graft-vs.-host disease of the gut," said Hill. "Now that we understand that the gut both initiates and is itself the target of GVHD, we might be able to intervene to stop the whole process from starting."

RESEARCH HIGHLIGHTS 2019

How a common cancer mutation actually drives cancer — and how to correct it

GENETIC MUTATIONS ARE THE SPARK AND FUEL

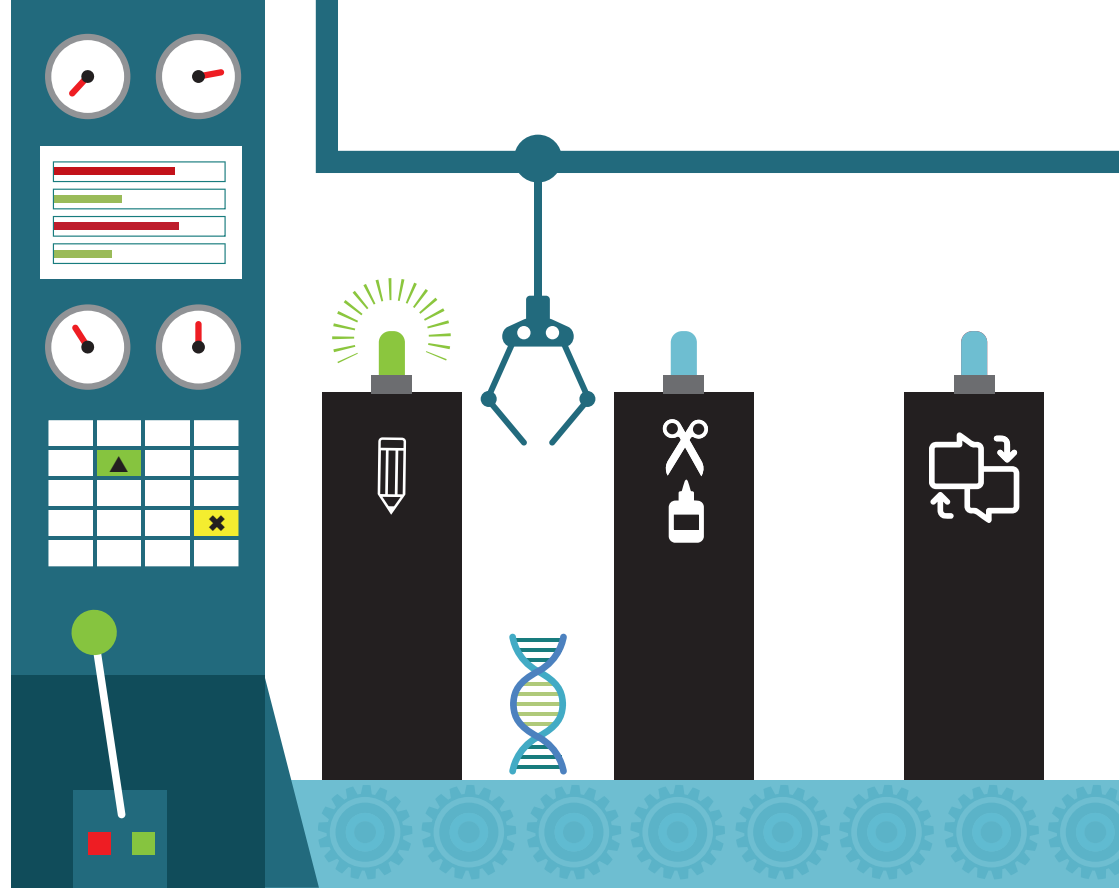
for cancer. Hundreds of DNA mutations have been linked to human cancers, and they're easier than ever to find and catalog, thanks to new genomic technologies.

But it's remained difficult to find out what those mutations are doing to drive cancer growth so that scientists can design new treatments to intervene.

In research published in the journal *Nature*, a group of collaborators applied a powerful new method to do just that. The team showed how one commonly mutated gene actually drives cancer growth and how, potentially, to counteract it.

"Even for very well-studied mutations, it's frequently not obvious what the specific underlying processes are that promote cancer growth," said the study's co-leader, Dr. Robert Bradley of Fred Hutch. "When we understand how to map a mutation to the development of cancer, then we can start to think about how to block that process for therapy."

The gene Bradley and collaborators studied, called SF3B1, was mutated in 19 different ways in several different cancers. That gene is so critical to a fundamental cell process that when it is



A broken machine on a factory assembly line leads to defective widgets that must be weeded out. Researchers at Fred Hutch and their collaborators mapped out a similar process in cancer, caused by a mutation in the cell's molecular machinery for processing DNA instructions into proteins. In the lab, a strategy they developed for compensating for the broken machine stopped tumor growth in its tracks. Illustration by Kim Carney

mutated, things get 'screwed up' all over the cell.

The biggest surprise to the scientists was that, out of all this complexity, an elegantly simple answer emerged. No matter how SF3B1 was mutated, no matter in what type of cancer they examined, no matter what else was out of whack in the cells, just one key process was central in driving cancer growth.

Once they knew what the problematic

mechanism was, the scientists could intervene. In mice, implanted human tumors started to shrink when injected with the researchers' custom-designed molecular repair kit.

The experimental "treatment" they designed is years away from human patients. For now, they hope their work prompts other researchers to study this mechanism to prove that it's happening in many cancers with SF3B1 mutations.

Is it possible to prevent breast cancer metastasis?

RESEARCHERS AT FRED HUTCH MAY HAVE FOUND

a way to essentially smother cancer cells in their sleep, preventing them from ever waking up and forming deadly metastatic tumors.

The work, led by translational researcher Dr. Cyrus Ghajar, has also turned on its ear the longstanding belief that chemotherapy can't kill dormant disseminated tumor cells — cancer cells that escape early on and hide out in other regions of the body — because those cells are in a "sleeping state." They've stopped growing so chemo, which blindly targets all fast-growing cells, healthy and otherwise, doesn't work.

That's not quite the case.

"It's always been assumed that dormant cells cannot be killed by any kind of chemotherapy because they're not dividing," said Ghajar, who runs the Laboratory for the Study of Metastatic Microenvironments at Fred Hutch. "But what we're showing is that's not true. They're relying on survival signaling in their microenvironment, in this case specifically from blood vessels within the bone marrow. And if you can take away that signaling, you can sensitize them to chemotherapy."

Ghajar's paper, published in *Nature Cell Biology*, proposes both a paradigm shift in how we view dormant disseminated tumor cells — and a new therapy to potentially slay this sleeping giant.

Ghajar and his team slashed the metastatic relapse rate in his mice by more than two-thirds.

Cancer doesn't just spread because a primary tumor has reached a certain size or stage. Disseminated tumor cells, or DTCs, can break off before a tumor has even formed and travel to distant sites in the body where they lie dormant until something "wakes them up" and they start the deadly process of metastasis, or cancer spread/colonization.

One common hideout for these sleepy creeps is the bone marrow. Past research has shown an association between DTCs in the bone marrow of cancer patients and metastatic recurrence — and not necessarily just bone metastasis.

RESEARCH HIGHLIGHTS 2019

How to boost cancer clinical trial participation

New study suggests loosening criteria would open trials to thousands of patients

A study led by Dr. Joseph Unger offers a tantalizing solution to low clinical trial participation: loosen up the strict eligibility criteria. Low participation is a problem that's plagued cancer researchers for decades, with most estimates putting adult cancer patient involvement at less than 5%. In many cases, the patients' clinical status excludes them from even being considered for a trial.

Baiting for B cells: A clever new way to make an AIDS vaccine

Researchers fish for rare blood cells that can evolve into HIV blockers

Scientists have developed a new strategy to counter the frustrating ability of HIV to sidestep vaccines designed to block it. It is a scheme that relies on one of the oldest tricks in the book for a fisherman: Use the right bait. The researchers were able to use a tiny chunk of protein as bait to fish for extremely rare white blood cells hidden within ordinary blood.



Failed Alzheimer's drug boosts CAR T-cell therapy

Engineered immune cells get a helping hand in new clinical trial for multiple myeloma patients

It turns out experimental drugs called gamma secretase inhibitors, or GSIs, sure can bedevil cancer. A Fred Hutch study describes how GSIs can reverse a crafty disappearing act that multiple myeloma pulls on the immune system. That ability to vanish even tricks T cells that are genetically programmed to home in on and attack myeloma cells.

Public health throws shade on tanning, and it works

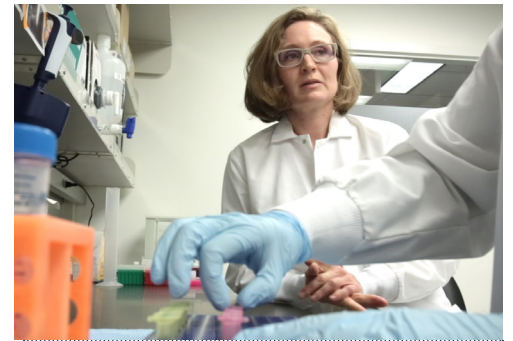
New study shows sharp drop in melanoma rates in people under 30

In a "big win" for cancer prevention, Fred Hutch and University of Washington researchers found a "sustained, statistically and clinically significant downtrend" in melanoma rates in people under 30 — a near 25% drop over 10 years' time.

Nanotech turns pro-tumor immune cells into cancer-killing triple agents

Strategy doubles survival in mice with cancer

Our immune cells usually do a great job of keeping us healthy, staving off infection and killing tumor cells. But sometimes, they betray us and join the enemy: cancer. Tumors often release factors that convince immune cells to help tumors instead of hurting them. But what if these double agent immune cells could be convinced to switch allegiance yet again? Nanotechnology could be the key to redirecting specialized immune cells to attack and shrink tumors. Research showed in mice that minuscule, dissolving polymer particles can ferry genetic instructions that temporarily rewire certain immune-suppressing cells into cancer fighters.



"These patients don't have any options when it comes to preventing relapse, but here we feel we have a signal," said Dr. Aude Chapuis.

Immunotherapy prevents relapse in small leukemia trial

Engineered T cells kept leukemia from returning in 12 high-risk patients

For patients with high-risk acute myeloid leukemia, more than 60% will relapse within two years of a bone marrow transplant. The return of their cancer is the leading cause of death for these patients. But results from a small trial of genetically modified immune cells hint at a way of protecting them. Dr. Aude Chapuis and colleagues used engineered T cells to prevent relapse in 12 AML patients after a bone marrow transplant put their disease in remission.

Special delivery: Gold nanoparticles ship CRISPR cargo

Scientists used their new golden courier to edit genes tied to HIV, genetic blood disorders

Tiny golden delivery trucks can ship CRISPR into human blood stem cells, offering a potential way to treat diseases like HIV and sickle cell anemia. And the researchers behind those trucks have even bigger distribution dreams.

Read the full articles at fredhutch.org/annual-report-2019



Dr. Jen Adair, left, speaks with Seattle Mayor Jenny Durkan during a lab tour at Fred Hutch.



Above: A rider at the Obliteride finish.

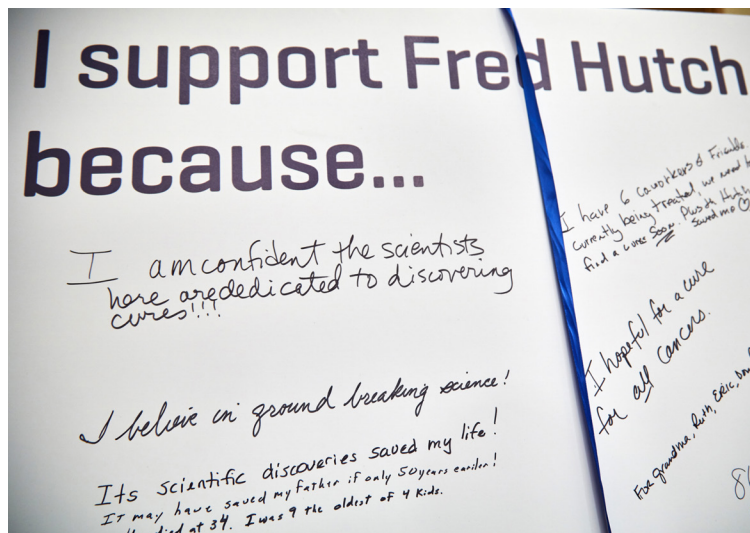


Above right: The Mariner Moose poses with Fred Hutchinson's son, Joe Hutchinson; Hutch President and Director Dr. Gary Gilliland; and Fred Hutch staff member Michael Ferguson during Fred Hutchinson's 100th birthday celebration at T-Mobile Park in July.



Right: Donors share why they give to Fred Hutch at a President's Circle event in April.

Far Right: Luke Timmerman's Climb to Fight Cancer team at Mount Kilimanjaro.



EVENT HIGHLIGHTS 2019

Engaging our community

From presenting our research at premiere scientific conferences to cycling across the Seattle area with a record number of participants in Obliteride to throwing out the first pitch at a Mariners game for the 100th birthday of our namesake, 2019 was packed with opportunities for us to engage with our community.

We enjoy increasingly strong philanthropic support from our donors, drawing 63,000 donations from more than 39,000 donors in FY19, both new records. Thousands of people participated in our events — scaling mountains,

climbing stairs, pedaling across the Puget Sound, shredding the slopes and hitting the dance floor. And thousands more donated to our pioneering efforts through our campaigns, giving clubs and legacy programs to honor loved ones affected by cancer and other diseases.

We also traveled the world to share our science with our peers and collaborate with others working on cancer, HIV and related diseases. We participated in hundreds of events and conferences, and met with partners to build connections that can help bring cures to patients as quickly as possible.



From the top: Faculty and staff enjoy a cookout during the annual Fred Hutch-SCCA Employee Celebration. Pitcher Jim Abbott gives the keynote address at the Hutch Award Luncheon. Meet Mitch winner Kim Lefler, a teacher at South Kitsap Elementary, brought some of her students to meet the Mariners star before a game in September. An attendee raises her paddle during the 44th annual Hutch Holiday Gala, which raised over \$13 million from donors Dec. 7.

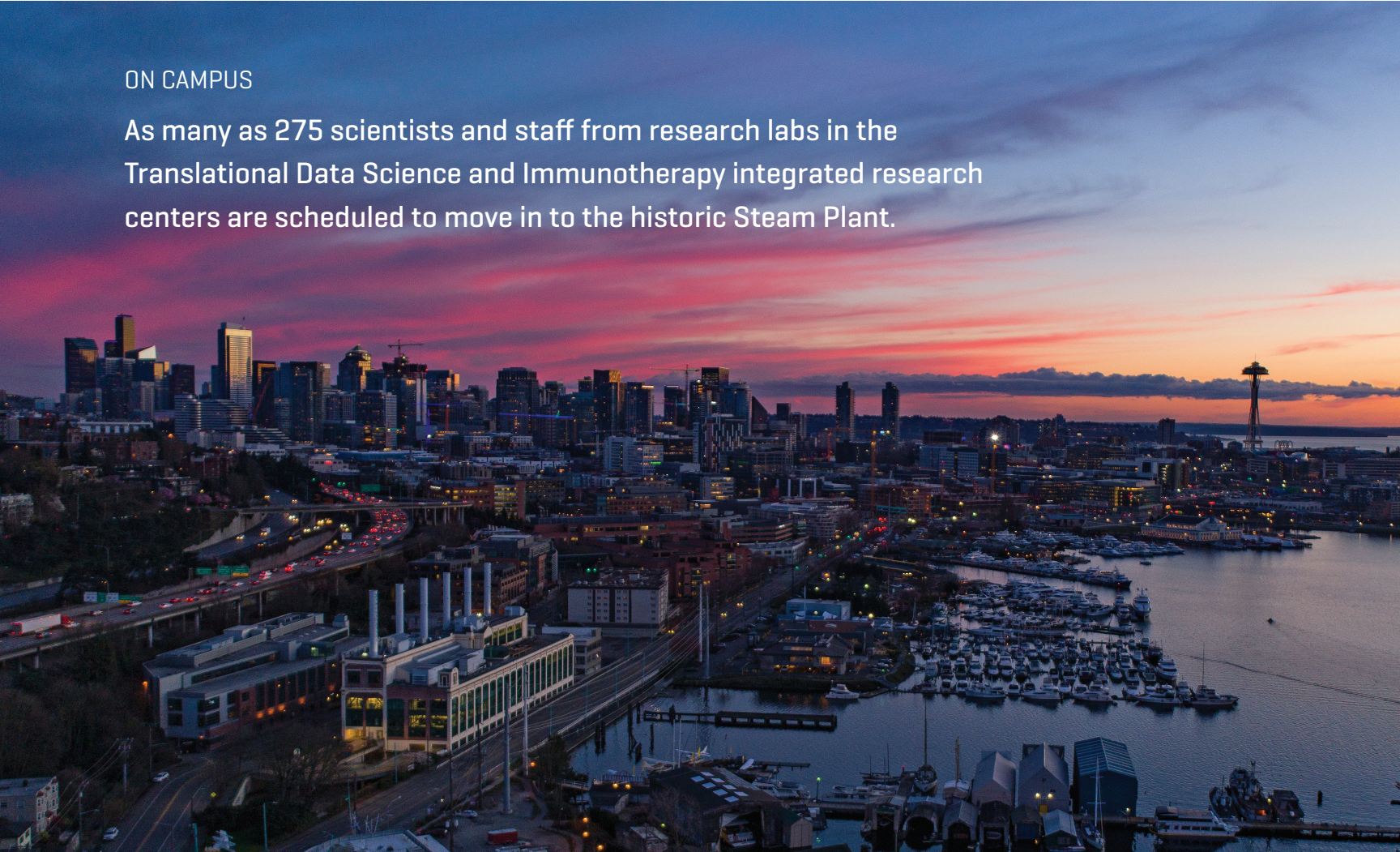
Below: Dr. Gary Gilliland speaks at an event announcing a new collaboration with Aga Khan University.



Looking Ahead to 2020

ON CAMPUS

As many as 275 scientists and staff from research labs in the Translational Data Science and Immunotherapy integrated research centers are scheduled to move in to the historic Steam Plant.

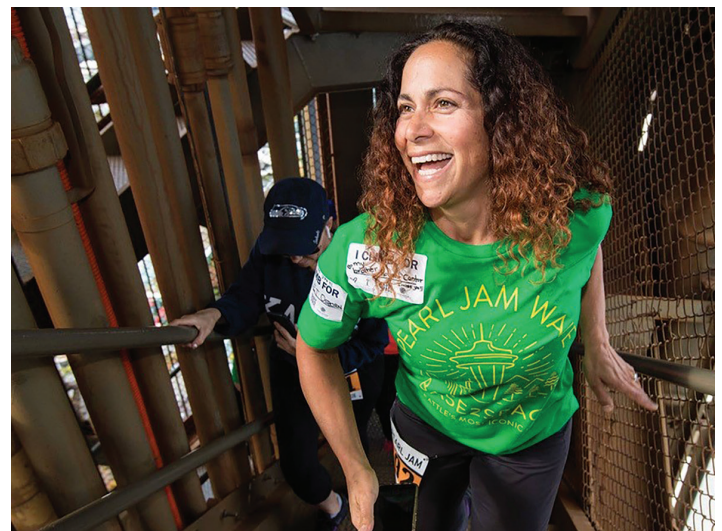


JOIN WITH US

We have a full calendar of opportunities throughout the year for you to join in our mission. Our Philanthropy team and our partners host events like Obliteride and Base 2 Space [photo at right] that draw thousands of participants to raise funds that fuel our efforts. This year's Everest Base Camp Trek will raise the level of adventure while other summits will be scaled by Fred Hutch teams as part of Climb to Fight Cancer.

And this summer our eighth Bone Marrow Transplant Survivor Reunion will gather hundreds of patients — some of whom were transplanted over 40 years ago — and their families to connect with each other and, in some cases, with their donors.

See the full list of events and opportunities to connect at fredhutch.org/events



IN SCIENCE



Dr. Robert Bradley

Computational biologist and biophysicist

“We’ll see an increased focus on using cancer genomics to inform precision medicine in real time, so that patient-care decisions can be made using the latest tools and analysis strategies.”

Dr. Aude Chapuis

Blood stem cell transplantation and immunotherapy expert

“Genetic engineering technologies will continue to advance, and become more cost-effective and accessible to mainstream science, so that immune T cells can be efficiently engineered to target a wide variety of cancers at less cost.”



Dr. Larry Corey

Fred Hutch president and director emeritus

Expert in virology, immunology and vaccine development

“In 2020, new approaches to HIV prevention will be discovered, broadly neutralizing antibodies will be shown to be useful, and a new era of combination antibody therapy — where injections of two or more different broadly neutralizing antibodies are used to prevent infectious diseases — will begin.”



Dr. Hans-Peter Kiem

Oncologist and stem cell and gene therapy researcher

Stephanus Family Endowed Chair for Cell and Gene Therapy

“I predict that there will be increasing interest in ‘in vivo’ delivery platforms” — meaning ways to edit genes directly in a patient’s body, without needing a lab — “to make both gene therapy and editing more scalable.”



By the Numbers

Fiscal Year 2019 [audited]



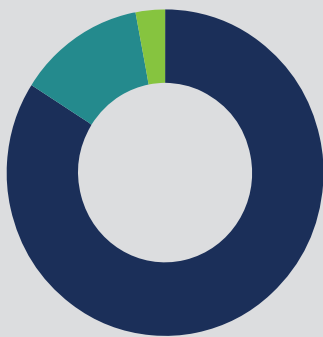
OPERATING REVENUES

Contracts and Government Grants	\$403,052	(56%)
Gifts and Philanthropic Grants	\$117,154	(16%)
Investment Income	\$43,895	(6%)
Other Income	\$149,858	(21%)
TOTAL	\$713,959	



SOURCES OF PHILANTHROPIC CONTRIBUTIONS

Philanthropic Grants	47%
Gifts from Individuals	28%
Planned Gifts	10%
Corporate Gifts	8%
Fundraising and Community Events/Gifts	7%



OPERATING EXPENSES

Program Services - Research	\$543,003	(84%)
Management and General	\$88,174	(13%)
Fundraising	\$17,726	(3%)
TOTAL	\$648,903	

Rounded to the nearest \$1,000. Percentages may not total 100% due to rounding.

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Raisbeck chairholders Drs. Nina Salama, Nancy Davidson and Sunil Hingorani. Standing: Dr. Gary Gilliland, Sherry Raisbeck, Dr. Fred Appelbaum and James Raisbeck.

SCIENTIFIC AWARDS

Evolutionary biologist **Dr. Harmit Malik** was elected a fellow of the **American Association for the Advancement of Science** and a member of the **National Academy of Sciences**.

Statistician **Dr. M. Elizabeth "Betz" Halloran** was elected to the **National Academy of Medicine**.

Dr. Fred Appelbaum, executive vice president and deputy director of the Hutch, and **Dr. Phil Greenberg**, head of the Program in Immunology, were elected fellows of the **American Association for Cancer Research Academy**.

ENDOWED CHAIR RECIPIENTS

Dr. Fred Appelbaum received the **Metcalfe Family/Frederick Appelbaum Endowed Chair in Cancer Research**.

Breast cancer oncologist **Dr. Nancy E. Davidson**, senior vice president and director of the Clinical Research Division, received the **Raisbeck Endowed Chair for Collaborative Research**.

Leukemia researcher **Dr. Jerry Radich** received the **Kurt Enslein Endowed Chair**.

Hematology oncologist **Dr. Cameron Turtle** received the **Anderson Family Endowed Chair for Immunotherapy**.

NEW ENDOWED CHAIRS

The **Helen G. Edson Endowed Chair for Breast Cancer Research** was established in August 2019.

The **John C. and Karyl K. Hughes Endowed Chair** was established in November 2019.

About Fred Hutch

Fred Hutch is a world-renowned 501(c)(3) nonprofit research organization working to eliminate cancer and related diseases. Located near Seattle's South Lake Union, we are proud to be home to three Nobel laureates.

fredhutch.org

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Your support makes our lifesaving breakthroughs possible. Together, we can eradicate cancer and related diseases.
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