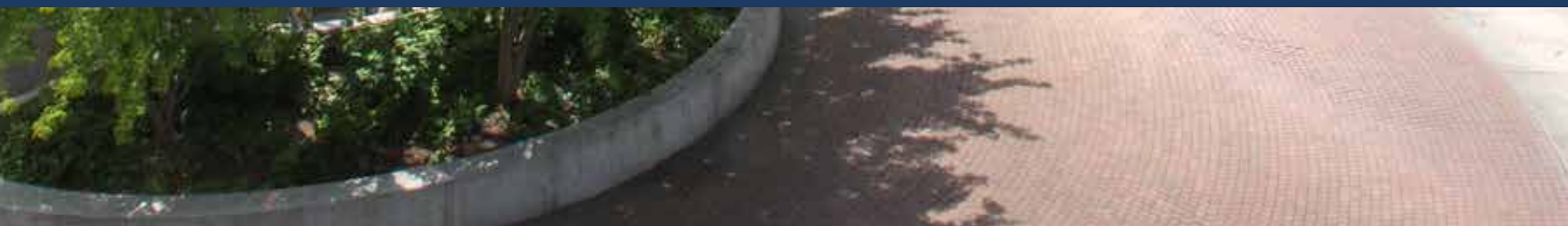
HUTCH

CURES START HERE

FRED HUTCHINSON CANCER RESEARCH CENTER | 2019 ANNUAL REPORT

ANNUAL REPORT 2019



Fred Hutch's passionate researchers are changing lives with their breakthrough science. Get the latest news at ***fredhutch.org.***

FROM THE DIRECTOR

2019 Annual Report letter

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 and 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.

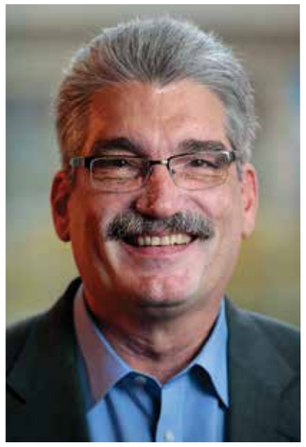
From the beginning, I've tried to convey the sense of urgency I feel about our mission. I believe the most important actions Fred Hutch can take to speed scientific discovery is to foster our culture of team science and to bring together the smartest people to work in collaboration across specialties. This has been a hallmark of our prior success, and we 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 will dramatically speed the development of personalized therapies.

The institution is in an excellent position, thanks in no small part to your partnership. Thank you again for your deep investment in Fred Hutch. Because of you, we're much closer to a world where every cancer, and every patient, has a cure.

Cures start here,

Dr. Gary Gilliland
President and Director



Dr. Gary Gilliland
Photo by Robert Hood / Fred Hutch

RESEARCH HIGHLIGHTS 2019

FRED HUTCHINSON CANCER RESEARCH CENTER researchers continued 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.

Rethinking an old viral foe

WHY DOES A COMMON VIRUS PLAGUE bone marrow transplant patients? New study challenges dogma, opens door to new therapies.

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 new study in 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. These Y-shaped proteins can bind, like a lock and key, to bad actors and neutralize them.

Hill's insight could pave the way for cheaper, safer therapies using antibodies to protect transplant patients against CMV. In a tantalizing hint, 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 Hutchinson Cancer Research Center. "We're turning dogma on its head, and that could meet the urgent need for inexpensive and nontoxic therapies to improve patient outcomes."

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

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

MICROBIOME TRIGGERS TOP KILLER after bone marrow transplant — and there's a potential way to stop it

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.

If GVHD occurs in the gut, it can be lethal. But how the disease occurs has been a mystery. Until now. A new 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 Hutchinson Cancer Research Center, 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. The question was never just academic. 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, who directs Hematopoietic Stem Cell Transplantation at Fred Hutch. "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."

Dr. Motoko Koyama, a staff scientist at Fred Hutch, has spent years trying to untangle the pathway of GVHD of the gut. Photo by Robert Hood / Fred Hutch News Service

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

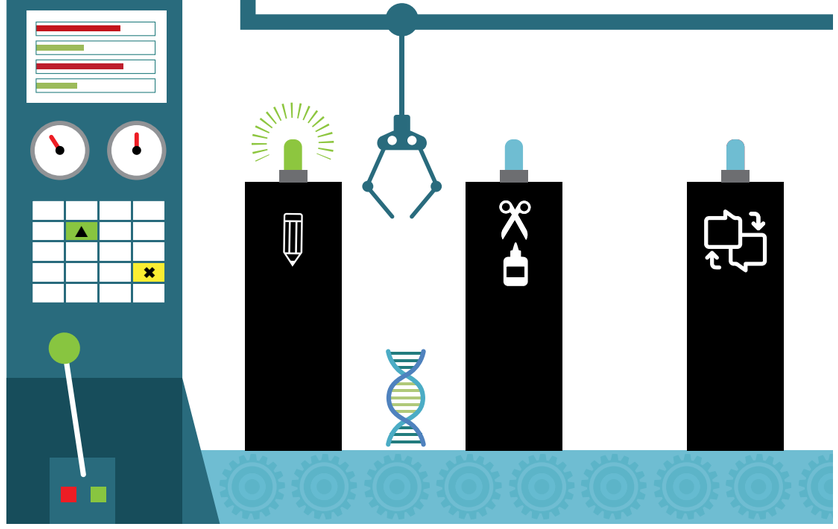
HIGH-TECH APPROACH SOLVES 'REAL MYSTERY' in many cancers

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 new research published in the journal Nature, a coast-to-coast 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 Hutchinson Cancer Research Center in Seattle. "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."



A broken machine on a factory assembly line leads to defective widgets that must be weeded out. Researchers at Fred Hutchinson Cancer Research Center 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. Animation by Kim Carney / Fred Hutch News Service

The gene Bradley and collaborators studied, called SF3B1, was mutated in 19 different ways in the several different cancer types they looked at. That gene is so critical to a fundamental cell process that when it is 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?

Study reveals how blood vessels in the bone marrow protect dormant tumor cells, suggests a way to kill them in their sleep

BY DIANE MAPES / FRED HUTCH NEWS SERVICE

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 "sleeper 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, is the culmination of more than four years' work and proposes both a paradigm shift in how we view dormant disseminated tumor cells — and a new therapy to potentially slay this sleeping giant. Although it's still early days, 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. Dormant tumor cells have been found in the bone marrow of breast cancer patients at the very earliest stage of the disease — DCIS or stage 0 — and Ghajar said they're mostly likely present in other patients with early-stage disease, as well.

Past research has shown an association between DTCs in the bone marrow of cancer patients and metastatic recurrence — and not necessarily just bone metastasis.

ADDITIONAL READING

Signature studies, read full list on *fredhutch.org*

Failed Alzheimer's drug boosts CAR T-cell therapy

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

They may not have made a dent against Alzheimer's. But it turns out experimental drugs called gamma secretase inhibitors, or GSIs, sure can bedevil cancer. Fred Hutch research 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.

How to boost cancer clinical trial participation

New study suggests loosening strict comorbidity criteria would open trials to thousands of previously exempt patients

A new 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 percent. In many cases, the patients' clinical status — that is, their various medical conditions — exclude 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 at Fred Hutch 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 vaccine researchers were able to use a tiny chunk of protein as bait to fish for extremely rare white blood cells hidden within ordinary blood.

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 created at Fred Hutch 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.

"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

The statistics are grim: 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 these patients. Scientists used engineered T cells to prevent relapse in 12 AML patients after a bone marrow transplant put their disease in remission. They all remain cancer-free after a median follow-up of more than three years.

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 without causing bodywide toxicities.

Public health throws shade on tanning, and it works

New study shows sharp drop in melanoma rates in people under 30, but skin cancer rates still going up in those over 40

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

To see more Philanthropy Events, visit fredhutch.org/ways-to-give

EVENT HIGHLIGHTS 2019

Engaging our community throughout 2019

From presenting our research at premiere scientific conferences to throwing out the first pitch at a Mariners game to celebrate the 100th birthday of our namesake, 2019 was packed with opportunities for us to engage with our communities.

Those communities include the donors who help support our cutting-edge research, the participants in our fundraising events that scale mountains around the world or pedal across the Puget Sound region, the other researchers and institutions that we collaborate with to learn more about cancer, HIV and other diseases, and the businesses that we partner with to bring potential cures to patients as quickly as possible.

There are hundreds of events that we either host here in Seattle or participate in throughout the year. And we travel around the world to connect with our communities and show our appreciation for their collaboration and support.

GALA
raised a record $13 million

UGANDA
Sue Desmond-Hellmann, CEO with the Bill and Melinda Gates Foundation, center, and Fred Hutch President Dr. Gary Gilliland visit with the medical staff during a visit to the **Uganda Cancer Institute**

CLIMB
Fred Hutch's Climb to Fight Cancer Team at Mount Kilimanjaro

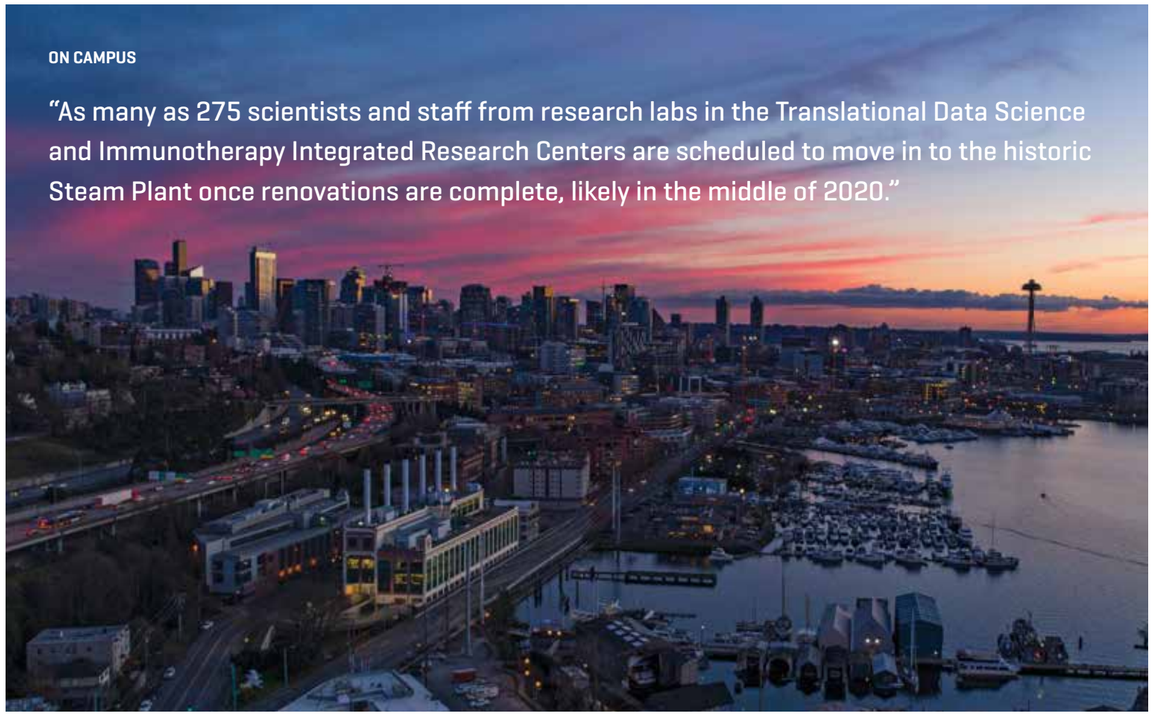
CAMPUS AND EMPLOYEE PICNIC (BELOW)

FRED HUTCHINSON'S
100TH BIRTHDAY EVENT

2019 "Meet Mitch" winner Kim Lefler (far right), who teaches fourth grade in Port Orchard, Washington at South Kitsap Elementary, brought a group of students to meet Mitch Haniger of the Mariners.

To see more Philanthropy Events, visit fredhutch.org/ways-to-give

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 once renovations are complete, likely in the middle of 2020."

IN OUR COMMUNITY

"Thousands of people will participate in the dozens of events and expeditions, from chef's dinners to trekking to Everest Base Camp, hosted by our Philanthropy team and our partners that raise funds to fuel hundreds of Fred Hutch laboratories and projects working to prevent, treat, and cure cancer and other diseases."

IN SCIENCE

"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. Robert Bradley, a computational biologist and biophysicist

"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."

- Dr. Hans-Peter Kiem, and oncologist, stem cell and gene therapy researcher who holds the Stephanus Family Endowed Chair for Cell and Gene Therapy.

"Genetic engineering technologies 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 costs."

- Dr. Aude Chapuis, an expert in blood stem cell transplantation and immunotherapy

"QUOTE FROM SUE IS COMING ABOUT WHY CRYO-EM IS SO AMAZING," Dr. Sue Biggins, who studies how cells sort their genetic material and is director of the Basic Sciences Division.

"In 2020, new approaches to HIV prevention will be discovered, broadly neutralizing antibodies will be shown to be useful, and a new era will begin with the use of combination antibodies, which, like combinations of antiviral drugs, hit the virus from multiple points of attack."

- Dr. Larry Corey, an expert in virology, immunology and vaccine development and Fred Hutch president and director emeritus.

Dr. Robert Bradley. Photo by Robert Hood / Fred Hutch

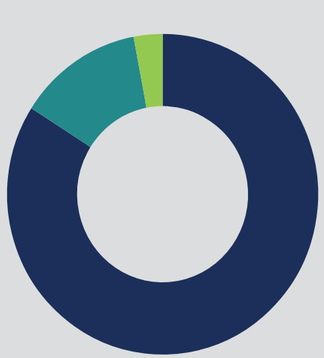
Dr. Aude Chapuis

By the Numbers

Fred Hutchinson Cancer Research Center, fiscal year 2019 (audited)

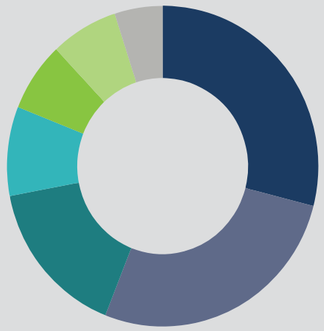
OPERATING REVENUES, FISCAL YEAR 2019

Research Grants and Contracts	**$465,852,230**	**(65%)**
Other Income	**$149,853,715**	**(21%)**
Contributions	**$54,354,208**	**(8%)**
Investment Income	**$43,894,658**	**(6%)**
TOTAL	**$713,954,811**	



OPERATING EXPENSES, FISCAL YEAR 2019

Program Services – Research	**$548,873,658**	**(84%)**
Management and General	**$82,288,115**	**(13%)**
Fundraising	**$17,741,457**	**(3%)**
TOTAL	**$648,903,230**	



SOURCES OF PRIVATE CONTRIBUTIONS, FISCAL YEAR 2019

Major Gifts	**29%**
Corporate and Foundation Relations	**27%**
Planned Giving	**16%**
Annual Giving	**9%**
Gifts of $10,000 – $49,999	**7%**
Events	**7%**
Obliteride	**4%**

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

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AWARDS AND ENDOWED CHAIRS

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 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 each elected Fellows of the AACR Academy

ENDOWED CHAIRS RECIPIENTS

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

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

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

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

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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Hutch Magazine staff
EDITORS: David Patton and Kristen Woodward

DESIGNERS: Kim Carney, Corey Hage and Jim Woolace

PHOTOGRAPHER: Robert Hood

communications@fredhutch.org

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