

2014 ANNUAL REPORT

CURES START HERE

ROBERT M. ARNOLD BUILDING



FRED HUTCH
CURES START HERE

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At Fred Hutch, our sights are set on a cancer-free future. This goal drives us to develop tomorrow's breakthroughs, today. As a Fred Hutch supporter, you propel our lifesaving research. Because of you, revolutionary discoveries, better treatments and healthier lives around the world are possible. Thank you.

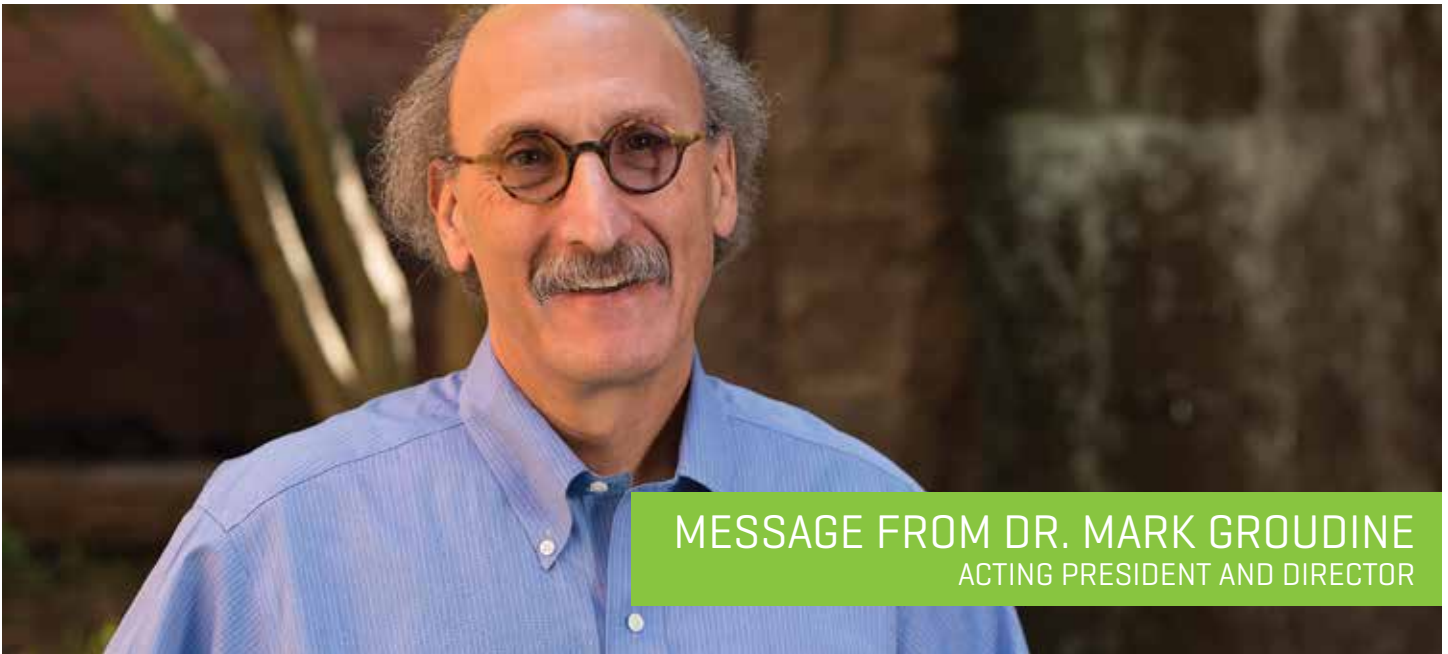


Photo by Bo Jungmayer / Fred Hutch

To all those who partner with us to make new cures possible, thank you.

I joined Fred Hutch in 1979, and since then, I've seen cures start here many times over. Much of our success in generating discoveries that produce meaningful improvements in human health is due to the Hutch's uniquely broad spectrum of research, from explorations of basic biology to patient trials of new medicines to population-based studies that shape public health guidelines.

Our annual report provides examples of that breadth, including stories on:

- ▶ Umbilical cord blood transplantation, a technique — built on fundamental breakthroughs made in Fred Hutch labs two decades ago — that is providing cures for cancer patients who had no other options
- ▶ An unanticipated discovery about combined hormone therapy and the risk of breast cancer that emerged from the Hutch-based Women's Health Initiative — findings that have since saved hundreds of thousands of lives and that also underscore the economic

value of high-quality research

- ▶ A yeast enzyme re-engineered by Fred Hutch scientists to work in humans that has become part of a new, targeted cancer therapy now being tested in patients with glioblastoma

You'll also read about some of the people who support and champion Fred Hutch by jump-starting research projects in immunotherapy or global oncology, for example, or by rallying friends to join in Obliteride.

To all the individuals and organizations who partner with us to make new cures possible, thank you. Your support is truly catalytic to Fred Hutch research. For example, approximately 90 percent of our annual research budget is derived from federal agencies such as the National Institutes of Health. As you may know, federal funding for biomedical research is becoming more precarious. Moreover, grants from these sources are committed to funding studies that are already far enough along to have documented

proof they can succeed. In contrast, philanthropic contributions fund novel, ahead-of-the-curve ideas. With that seed funding, our investigators can generate sufficient preliminary data to obtain more conventional funding. In addition, the dollars raised from philanthropy permit us to hire the best and brightest new investigators, who bring new ideas and approaches to the Hutch that will lead to more cures in the years ahead.

Finally, I want to thank Dr. Larry Corey, who ended his tenure as president and director this year to return to his laboratory and focus on research. It was my pleasure to work alongside my close friend and colleague while he led Fred Hutch. It is our good fortune that Larry will remain at the Hutch as president and director emeritus.

Thank you again to a community of contributors as diverse and dedicated as the researchers you support.



CATALYZING IMMUNOTHERAPY RESEARCH

Fred Hutch's Dr. Stanley Riddell [right] and his team members, Tyler Hill [left] and Dr. Daniel Sommermeyer [middle], are pioneering new approaches to battle cancer using killer immune cells — thanks in part to a boost from benefactors Rae and Mark Lembersky. *Photo by Bo Jungmayer / Fred Hutch*

Dr. Stanley Riddell's five-year partnership with Rae and Mark Lembersky has brought a promising cancer immunotherapy to the brink of clinical trial

By Dr. Rachel Tompa

Rae and Mark Lembersky met Fred Hutch's Dr. Stanley Riddell at a pivotal point of Riddell's research — he had just identified ROR1, a protein on certain leukemia cells that would later turn out to be a linchpin in a novel immunotherapy approach with the potential to help thousands of patients with many types of cancer.

Riddell and his Fred Hutch colleagues are world leaders in adoptive T-cell therapy, a technique that reprograms killer immune cells to specifically recognize and eliminate cancer cells, sparing healthy cells from the toxic damage of traditional cancer treatments. When the Lemberskys were first introduced to Riddell, his team had made great strides designing T cells loaded with chimeric antigen receptors (CARs), laboratory-engineered proteins that coat the surface of T cells and guide them to malignant cells by homing in on cancer-specific proteins.

The Lemberskys, already long-time supporters of Fred Hutch, connected with Riddell because Mark's aunt had been diagnosed with chronic lymphocytic leukemia (CLL), a blood cancer that afflicts B cells of the immune system. Riddell and his team were developing therapies for CLL and had just found that CLL cells are coated with

ROR1 protein in abundance, while healthy mature B cells are not, making it an ideal candidate target for their engineered killer T cells.

"What was scheduled to be a brief meeting turned into a long discussion," Mark said, as he was drawn into the innovation of Riddell's immunotherapy methods and learned about the difficulty the research team faced in garnering traditional funding for their "potentially breakthrough but unproven ideas."

That's where the Lemberskys stepped in. A few weeks after meeting with Riddell, they made a gift that launched the ROR1 project and supported the team's first year of research. With that initial support, the scientists crafted the first CARs specific for ROR1 and conducted preliminary experiments to better understand this potentially life-changing but mysterious protein. Less than a year later, Riddell used that preliminary data to obtain a National Institutes of Health grant to support his ROR1 and other immunotherapy research worth 20 times the Lemberskys' initial investment.

Riddell's team was the first to show the promise of ROR1 for T-cell therapy, and in the year following began testing the therapy's safety and cancer-killing power in preclinical models. They also continued their exploration of ROR1's role in cancer and found, to

their surprise, that the protein dots the surface of many other types of cancer cells, including mantle cell lymphoma, lung, pancreatic and prostate cancer, and some types of breast and brain cancer.

Riddell and his colleagues were delighted to find that what started as a possible therapy for one type of leukemia might have a much broader reach. Riddell has since led groundbreaking research showing for the first time that T cells bearing ROR1-CARs can eliminate breast cancer and mantle cell lymphoma in the laboratory.

Although Riddell received government support for part of his work, there were other funding gaps along the path from this initial research to clinical trial. Traditional granting agencies simply don't cover every stage of translational research, and that's why Riddell is so thankful for the Lemberskys' continued partnership. For example, a gift from the Lemberskys allowed Riddell to develop a technique to examine ROR1's activity in solid tumors, a technique that is essential to bring the power of ROR1 immunotherapy to cancers beyond leukemia.

"Fortunately for us they continued to catalyze the project at very critical stages," Riddell said. "At every step where we faced a need to generate critical preliminary data to move the project forward, they were there for us."

Now, Riddell and his team are poised to bring ROR1-immunotherapy to patients with a clinical trial that will launch in early 2015. Another gift from the Lemberskys has allowed Riddell to include patients with solid tumors in the trial, in addition to blood cancer patients.

Mark's aunt is still alive and thriving, and although the Lemberskys originally connected with Riddell to find out more about CLL, they are happy their investment has the potential to reach even more people.

"We were very motivated to help Stan's work that not only might help CLL sufferers but also a broad array of cancer patients. That remains our motivation today," Mark said.

Riddell is grateful for the Lemberskys' financial support — "We would probably never have started with ROR1 if it wasn't for that initial gift," he said — but he also deeply appreciates their engagement with him and his research.

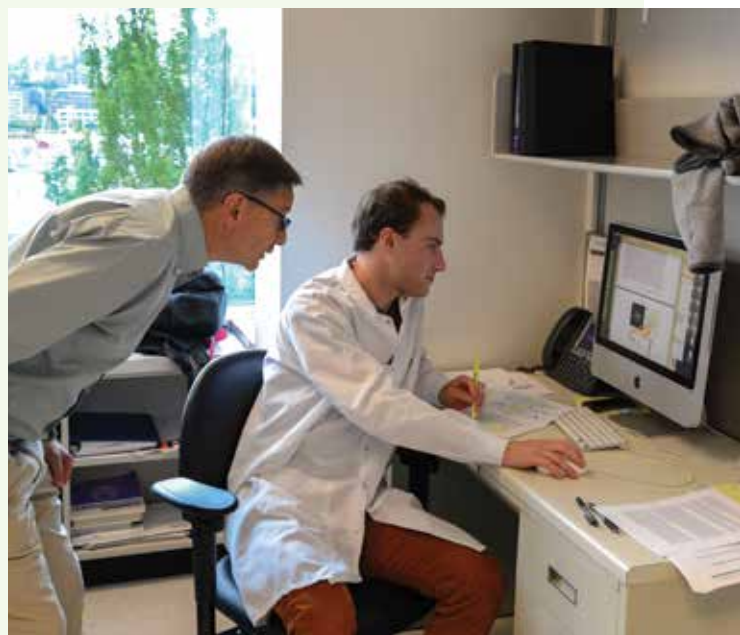
"They really want to know that you're working hard on this, and they want to understand what your obstacles are and how they can help solve them. It's that kind of partnership that really makes it a lot of fun," Riddell said. "The NIH does not take a personal interest, whereas the Lemberskys are as excited as we are at the prospect of making this idea a reality."

The partnership has also been rewarding for the Lemberskys. "Interacting with Stan has been a real pleasure," they said. "Plus, we have been given the opportunity to play a small part in what may well become a major safe and effective treatment for not only CLL, but a number of other cancers as well. What more could donors ask for?"

Immunotherapy takes off

Dr. Stanley Riddell's groundbreaking research on ROR1 is just one advance in Fred Hutch's decades-long history of harnessing the immune system to save lives. This year, Fred Hutch's leadership in immunotherapy led to two landmark developments that are opening new doors to cancer cures:

- ▶ In December 2013, Fred Hutch partnered with Memorial Sloan Kettering Cancer Center and Seattle Children's Research Institute to launch Juno Therapeutics Inc. The cancer immunotherapy startup, which raised \$310 million in investments its first year, will leverage its impressive array of scientific talent and technology to more rapidly advance promising new treatments to patients.
- ▶ In April 2014, Fred Hutch received its largest donation ever: a \$20 million gift from the Bezos family to boost immunotherapy research and extend the successes seen so far in patients with blood cancers to those with lung, colon, breast, pancreatic, ovarian and other solid-tumor cancers.



Dr. Stanley Riddell, left, and Alex Salter discuss their latest research findings in Riddell's immunotherapy lab in Fred Hutch's Clinical Research Division. Photo by Bo Jungmayer / Fred Hutch



Dr. Larry Corey stepped down as Fred Hutch president and director this year to return to the lab and his passion of hands-on research. Photo by Robert Hood / Fred Hutch

Dr. Larry Corey steps down as Fred Hutch president and director, sets sights on achieving an AIDS-free world through hands-on research

By Linda Dahlstrom

At the helm of Fred Hutch, Dr. Larry Corey championed high-impact initiatives and encouraged everyone around him to share the story of Fred Hutch's lifesaving research and the people conducting it.

After three and a half successful years leading Fred Hutch, Corey stepped down June 30 as president and director.

"I've loved this job. The notion that cures start here now permeates the place," Corey said. "We are no longer looking backward — we are looking forward."

Corey, who for decades dedicated his career to unlocking the secrets of HIV and AIDS and other infectious diseases and finding treatments that have now saved countless lives, has returned to his passion — making a difference through hands-on research.

Corey is now working full-time with his lab and colleagues in the Vaccine and Infectious Disease Division. He's a member of the faculty, and has the title of president and director emeritus. Dr. Mark Groudine is serving as Fred Hutch's acting president and director while the Board of Trustees conducts a national search for Corey's successor.

"The Hutch's loss of Larry as president and director is a major gain for the field of HIV vaccine research," said Dr. Anthony S. Fauci, director of the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health.

Dr. Robert Day, former president and director of Fred Hutch, was one of the people who recruited Corey as a researcher in 1996.

"I'm a big fan of Larry. This is a very difficult time for biomedical research and he's dealt with that difficulty very well," Day said. "Now he'll be able to apply his full attention [to research] and I think it's a good time for that."

While better treatments have been developed for people living with AIDS, Corey has set his sights on a vaccine. He's the founder and director of the HIV Vaccine Trials Network, a collaboration of scientists around the world working toward an HIV vaccine.

"I want my grandchildren to grow up in the AIDS-free world that I did," Corey said. "I want them to be able to get vaccinated for HIV and for herpes and to not have to worry. That's the dream."

There is much to do, and after all these years, Corey still feels the same sense of urgency and is eager to get back to it.

"Miracles really do happen in the labs," he said.



FROM YEAST TO BRAIN, ENGINEERING A NEW CANCER TREATMENT

Dr. Barry Stoddard and his team used a new approach to engineer a molecule in yeast that is now being tested to treat brain cancer. Photo by Scott Streble for Fred Hutch

Enzyme redesigned at Fred Hutch makes headway in clinical trial

By Susan Keown

Some engineers build skyscrapers, but Dr. Barry Stoddard works on a much smaller scale. Using computer modeling software and genetic manipulation techniques, Stoddard tinkers with molecules.

Today, one molecule reengineered in the Stoddard Lab is getting its chance to prove itself as part of a groundbreaking new therapy for glioblastoma, a fast-growing brain cancer.

Last year, a San Diego-based biotech company began early-phase clinical trials of a yeast enzyme reengineered in 2005 by Stoddard and his collaborators. [An enzyme is a molecule that helps the chemical reactions of life happen.] Thanks to three tweaks that the Stoddard Lab made to its structure, the engineered enzyme is more stable and more precisely honed to its target, which has made it better for use in human therapeutics.

“At that time, that type of protein engineering hadn’t been done before,” Stoddard said. “Structure-based, computer-aided redesign to alter the properties of an enzyme, to make it better.”

In the ongoing trials, researchers infect patients’ cancer cells [and not their healthy cells] with a special virus that instructs the cells to make the engineered enzyme. Then, patients take pills containing a compound that is harmless to normal human cells, but fatal to the cancer cells once their new enzyme converts the compound into a poison. Unlike conventional chemotherapy, this type of targeted gene therapy leaves healthy cells untouched.

Stoddard’s original goal was to figure out this enzyme’s structure and how it works. Once he’d done that and successfully engineered a new version, his team shared their redesigned enzyme with the scientific community, which is how it made its way into a starring role in the glioblastoma trial.

This trial is “a really good example of a basic scientific study unexpectedly getting turned into a clinical application,” said Stoddard.

It’s still too early to know whether the treatment will shrink the tumors as intended or if it might need further refining, but some patients have shown encouraging improvements.

“That there are people walking around with glioblastomas that are getting therapeutic benefit, partly from something we worked on, just blows my mind,” said Stoddard, whose mother died of glioblastoma shortly after he came to the Hutch. “To have been able to contribute in a small way to efforts to fight such a terrible disease has been a tremendous blessing.”

THROUGH THEIR GENEROUS SUPPORT AT THE 2013 HUTCH HOLIDAY GALA, AND AS MEMBERS OF FRED HUTCH’S PRESIDENT’S CIRCLE, BRUCE AND PEGGY WANTA HELP FUEL BASIC SCIENCE RESEARCH AT FRED HUTCH — LIKE DR. STODDARD’S — THAT PAVES THE WAY TO LIFESAVING MEDICAL ADVANCES.



BRINGING THE CURATIVE POWER OF CORD BLOOD TO THE WORLD

Dr. Colleen Delaney (far left) updates (L to R) Daniella, David and Jacquie Bayley on her team's research progress, along with lab technician David Oliver (far right). Photo by Bo Jungmayer / Fred Hutch

Bayley family supports Dr. Colleen Delaney's quest to make cord blood transplantation available to all who need it

By Dr. Sabrina Richards

Bone marrow transplantation was pioneered at Fred Hutch as a cure for many types of leukemias and lymphomas. This groundbreaking procedure has since been performed over 1 million times worldwide, but hope for a cure remains out of reach for many patients who lack genetically matched donors. To help them, Fred Hutch is again nurturing a future cure: a next-generation blood stem cell transplant that could put the lifesaving treatment within reach of any patient in need. The treatment relies on umbilical cord blood.

Cord blood harbors the same blood stem cells that can replace a patient's cancerous bone marrow, but it doesn't need to be nearly as well-matched to the patient as adult blood stem cells do. This makes it a good option for patients who can't find a matched adult donor, many of whom are ethnic minorities or of mixed race.

Dr. Colleen Delaney, who heads Fred Hutch's Cord Blood Program, is designing a product that harnesses cord blood's advantages (no need for perfect matching) while overcoming its disadvantage (the low number of key blood stem cells found in

each sample). Her goal is to create an off-the-shelf cord blood product available to anyone, anywhere, in need of a transplant — irrespective of their genetic make-up.

Delaney's progress has been impressive — thanks to critical private support, including contributions from the Bayley family, which shares her vision of a future where no transplant patient goes wanting. It is a dream close to their hearts.

In 2004, Jacquie and Björn Bayley's 17-year-old son, David, noticed an unusual lethargy during soccer practice. Blood tests showed he had acute myeloid leukemia. After initially successful chemotherapy, he relapsed in 2006. Doctors prescribed a bone marrow transplant.

David's medical team found a donor in Germany whose DNA matched at nine out of ten genetic sites. The transplant worked. "I feel so lucky I came through it so well," explains David, who's been cancer-free ever since, with only one lingering side effect, a slight dryness to his eyes, to remind him of the procedure. "But I saw many who weren't as successful." He knew patients whose transplants didn't "take" or who struggled with debilitating graft-vs.-host disease, a complication in which donor immune cells attack the patient's healthy tissues.

The Bayleys knew they wanted to give back and help other cancer patients in need. "I firmly believe if you can give, you do," explains Jacquie.

They turned to Fred Hutch as part of the community that provided care through David's illness. As the family considered three potential projects — two that addressed cancer survivors' concerns, and one related to Delaney's ambitious cord blood therapy — David had an epiphany: Delaney's research provided hope for a gentler, yet curative, option for cancer patients. Not only could cord blood help save lives, it would help improve them by dramatically reducing the complications that plagued even successful transplants.

"I thought, if Dr. Delaney's project succeeds, you wouldn't need the other two projects," recalls David.

And so a collaboration was born. Over the years, funds from the Bayley Family Foundation

have enabled Delaney to buy vital equipment, retain critical laboratory staff, continue her clinical trials, and support basic research investigating exactly how cord blood works its magic.

And in her hands, the material is magical. Building on fundamental discoveries first made in Fred Hutch labs about how blood stem cells divide and mature, Delaney developed a method to multiply, or expand, the few precious blood stem cells from the teaspoon-sized cord blood samples up to 500 times over. The expanded product protects transplant patients against chemotherapy toxicity, infection and cancer relapse, improving not only survival but quality of life.

In addition, Delaney discovered that cord blood's healing power is not limited to transplant patients. Chemotherapy patients who receive her expanded cord blood cells are also protected

against infection and see their chemo-impaired immune systems rebound in just a couple weeks, rather than a month or more. This can make a huge difference to the patient's quality of life.

As the possible curative applications keep unfolding, Delaney keeps dreaming bigger, and the Bayleys are helping propel her dreams forward. In particular, their contributions have supported

postdoctoral fellow Dr. Jianqiang Li's investigations into double cord-blood transplantation. In this procedure, patients are given cord blood from two different donors. Double cord blood transplants have a higher success rate than transplants from a single donor and they're better at preventing cancer relapse.

Delaney and her team demonstrated that this is because of a battle waged between the immune cells found in each cord blood sample; one donor "wins" the battle, and these donor's cells become the source of new, healthy bone marrow.

"It's like two different people fighting inside another person," explains Delaney, "and the winner becomes even stronger in its ability to fight the cancer."

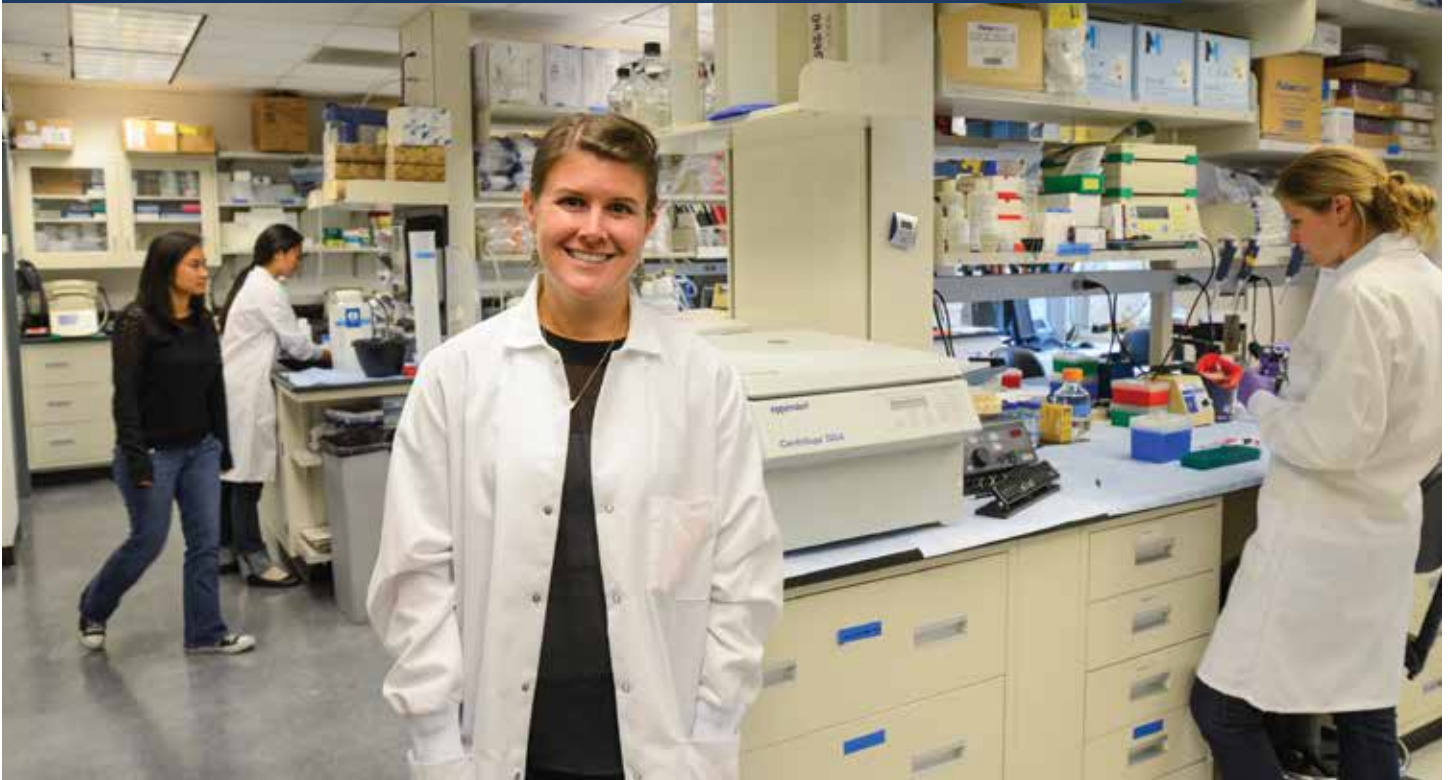
But which cells will win? And how does the competition itself help the winner go on to defeat the cancer? Li is working to answer these questions. His insights will help transplant oncologists pick the winning donor cells even before transplantation, and perhaps enable Delaney's team to develop a cord blood-based immunotherapy that can better target cancer cells and enhance protection against relapse.

It is this vision — to understand and utilize all of cord blood's potential, sparking countless more cures — that the Bayleys continue to support, year after year. As Jacquie explains, "I think it's the way of the future."



The Bayley family's collaboration with Dr. Delaney has accelerated important insights into cord blood's potential. Photo by Bo Jungmayer / Fred Hutch

IN PICTURES: GETTING INVOLVED TO GET CURES STARTED



Fred Hutch employee Andrea Towlerton is a curestarter — on and off the clock

By Dr. Sabrina Richards

TOP: Research technician Andrea Towlerton trekked from Midland, Michigan, to Seattle to join Dr. Hootie Warren's lab at Fred Hutch four years ago. Towlerton had studied everything from bats to nanotechnology, but when she learned of Fred Hutch's lifesaving clinical trials from the cancer patients with whom she volunteered in her hometown, she made it her mission to be a part of bringing cures to the bedside. "Dr. Warren combines passion and compassion: He's enthusiastic about research but also really understands the sacrifices patients make," said Towlerton. "It's truly a gift to wake up each day and know that what you're doing is helping others." *Photo by Bo Jungmayer / Fred Hutch*

RIGHT: In the Warren Lab, Towlerton and her colleagues focus on developing immunotherapy strategies for cancer patients. Not long after starting her new position, she joined Innovators Network, a group of young professionals committed to funding early-stage research, to get more involved in the Fred Hutch community and learn about the fantastic research being done across her new workplace. "Working in this environment is absolutely awesome: People work here because their motivation in life is to help others. IN helps keep these brilliant minds here." *Fred Hutch file photo*





ABOVE: “It takes teamwork to do science right, and giving back can be part of a team effort too,” said Towlerton. Last year, she and her lab mates joined the “T cells” immunotherapy team to ride and raise money for cancer research through Obliterate, Fred Hutch’s annual bike riding fundraiser. “It was a whole new — and very fun — way for us to support innovative research together,” she said. *Photo courtesy of Andrea Towlerton*

RIGHT: Her 50-mile ride supporting cancer research came just three weeks after a 19,340-foot climb. As part of another Fred Hutch fundraiser, the Climb to Fight Breast Cancer, Towlerton summited Mount Kilimanjaro in Tanzania. That adventure combined two of her loves, mountain climbing and giving to her community, and raised more than \$10,000 — half of that in small donations of a few dollars each. Towlerton explained, “My parents instilled a desire to give back, whatever your resources. Over my four years here, I’ve been able to contribute more than \$15,000 to Fred Hutch, and I’m just one person!” *Photo courtesy of Andrea Towlerton*



Why give back so much personal time — and a seemingly endless supply of energy — to the same place where she already devotes so many hours in the lab working on cancer cures? “I feel it’s important to give back to a place that gives so much to patients,” she said. “Every therapy starts with research. In our lab, we understand the importance of research and clinical care working together, and private philanthropy helps support our quest to create lifesaving therapies.” Towlerton’s dedication to her colleagues and the patients they’re striving to help runs deep — and is now an enduring piece of Fred Hutch itself. The engraved brick she bought as a Christmas present “to commemorate the Warren Lab and every amazing scientist who passes through” sits in the courtyard outside her building and serves as a daily reminder of the mission that unites all Fred Hutch supporters *Fred Hutch File*





DR. ERIC HOLLAND'S VISION
TO TRANSFORM HOW SOLID
TUMORS ARE TREATED

Dr. Eric Holland is bringing together researchers, data and big ideas to revolutionize treatment for patients with solid-tumor cancers. Photo by Bo Jungmayer / Fred Hutch

Big ideas and Big Data promise big improvements for patients

By Linda Dahlstrom and Deborah Bach

Dr. Eric Holland aims to do something that hasn't happened in more than a half century: Find a better strategy for treating the deadliest brain tumors.

Holland specializes in glioblastoma, a brain cancer that spreads quickly and is notorious for its ability to weave inside brain tissue. That makes it almost impossible for surgeons to completely remove the tumors, called gliomas. The best available treatment — an aggressive combination of surgery, chemotherapy and radiation — can cause brain damage, yet the tumors almost always come back within months.

Holland has dedicated his career to finding more effective therapies with fewer side effects. Last year, he and 11 members of his team left Memorial Sloan Kettering Cancer Center in New York,

where over 13 years he built a renowned brain cancer program, to come to Fred Hutch, which is known for pioneering treatments.

His bold vision? Revolutionize how solid tumors in nearly a dozen organs are treated.

Shortly after arriving at Fred Hutch, Holland's team launched the Solid Tumor Translational Research (STTR) effort, which brings together investigators and clinicians from Fred Hutch, UW Medicine and Seattle Cancer Care Alliance. STTR is focused on developing precision treatments for tumors that include those affecting the bladder, brain, breast, colon, head and neck, lung, ovary, pancreas and prostate.

One of the keys for achieving his vision is to build a first-of-its-kind database that researchers and clinicians can use to extract meaningful, potentially lifesaving, information from reams of raw data on patients and their diseases. "No one has ever done

what we are doing,” said Holland, who directs the Hutch’s Human Biology Division and the Nancy and Buster Alvord Brain Tumor Center at the University of Washington.

He’s starting with the brain. At MSK, he created the world’s most comprehensive brain tumor database. Based on tumor samples from hundreds of patients, the database contains a complete genetic profile of each tumor, plus details on how each patient was treated and how they responded. Now Holland is building a similar database using several thousand tissue samples collected by UW’s Department of Neurological Surgery.

The goal is for every new patient’s tumor to be profiled. Doctors can then compare that profile to other tumors in the database and select the most effective therapy.

“This is personalized medicine — making decisions that are tailored to the tumor,” said Holland, who also is a practicing brain surgeon and a UW professor of neurological surgery.

In addition to using Big Data to start transforming how tumors are treated, Holland is investigating ways to make current treatments more effective by better understanding tumors.

Many glioblastoma patients are treated with radiation after surgery, but recently researchers realized that some cells in an immature state [similar to stem cells] are resistant. What’s more, the cancer cells can toggle between being mature and immature; imagine water sloshing back and forth, Holland explains. But

what if instead of administering radiation at uniform intervals where cycling cells were always at the same point each time, a staggered schedule was used to radiate cells when they were most vulnerable? If researchers like Holland can figure out the formula of how and when that’s happening, radiation could be timed to increase the chances of killing every cancer cell. Holland has already shown staggered radiation can extend the lifespan of mice with glioblastomas.

These kinds of findings energize Holland. The thing he enjoys most about being a scientist, he said, is “looking for the truth — and sometimes finding it.”

The truth of what he’s learning in the lab — and the information the tumor database will provide — are just beginning to redefine how he, and many other

physicians around the world, treat their cancer patients.

“I love surgery — operating on someone lets you directly improve their life,” Holland said, “and I love research because it’s a chance to have an impact on many, many more people.”



Desert Horse-Grant (left) directs strategy and operations for the Solid Tumor Translational Research network. She’s one of 11 team members who came with Holland from New York to develop new tumor therapies. Photo by Robert Hood / Fred Hutch

INNOVATIVE SOLID TUMOR TRANSLATIONAL RESEARCH, LIKE THAT BEING LED BY DR. ERIC HOLLAND, IS ACCELERATED BY GENEROUS SUPPORT FROM INDIVIDUAL BENEFACTORS, INCLUDING ELDON “BUD” MOUNT.



Drs. Garnet Anderson [left] and Joshua Roth of Fred Hutch's Public Health Sciences Division share findings with WHI participant and Hutch supporter Jean Rolfe regarding the thousands of lives and billions of dollars saved by a landmark combined hormone therapy study. *Photo by Bo Jungmayer / Fred Hutch*

Public investment and personal involvement in prevention research produce lifesaving dividends

By Diane Mapes

The Women's Health Initiative, launched in 1993, is one of the largest and most ambitious prevention studies ever conducted in the U.S.

Designed to address research inequities and provide strategies to thwart heart disease, breast and colorectal cancer, and other leading causes of death and disability in older women, the WHI has gathered health information from 161,000-plus post-menopausal women for nearly a quarter of a century. That wealth of data has been systematically managed and analyzed at Fred Hutch, the WHI's Clinical Coordinating Center, so researchers can glean from it crucial, lifesaving insights.

Powered by an initial \$625 million grant from the National Institutes of Health, the WHI has tackled everything from the health effects of hormone therapy and diet to life and longevity after cancer.

Given its expense, the WHI's perceived worth has also been

bandied about for decades. But a newly published Fred Hutch study has gone far to lay that discussion to rest.

Dr. Joshua Roth, a postdoctoral fellow in the Hutchinson Institute for Cancer Outcomes Research [HICOR], analyzed the return on investment of just a portion of the WHI's work, the landmark finding that combined hormone therapy, or CHT, significantly raised a woman's chance of developing cardiovascular disease, stroke and breast cancer.

"The economic return from the trial is substantial," Roth said when announcing his results in May. "The original NIH trial cost was \$260 million [in 2012 dollars] and the net economic return was \$37.1 billion. That's a return of approximately \$140 on every dollar invested in the trial."

Roth, who used a mathematical model to estimate the influence of a "no WHI world," showed the CHT finding also directly led to 126,000 fewer breast cancer cases, 76,000 fewer cases of heart disease and stroke and 80,000 fewer cases of venous thromboembolism between 2003 and 2012.

“It really brings the point home when you crunch the numbers,” he said. “You see that millions of U.S. women likely stopped or never used CHT and that this change resulted in important reductions in disease incidence and associated medical spending.”

Former Fred Hutch board member Jean Rolfe is one of the thousands of women who not only participated in WHI’s work but, along with her three daughters, stood to benefit from it. The longtime civic leader said Roth’s study brings a new and necessary perspective to the WHI’s findings.

“This really substantiates what the research accomplished,” she said.

Although Rolfe was not part of the CHT investigation, for five years she provided WHI researchers with vital health data for another study arm.

Her involvement was just part of a pattern of public health service that started when she was a young girl.

“My mother was a very big volunteer at [Seattle] Children’s, and I would go with her during the summer and that whetted my appetite,” she said. “My husband said I’d been practicing without a license for a very long time.”

Rolfe’s long-standing relationship with Fred Hutch began in the 1980s and has included stints as board and senior council member, public speaker, donor and Board of Ambassadors co-chair.

“They would report findings to us as board members and I always felt a great sense of accomplishment that I had something to do with it,” she said of her WHI participation. “It really appealed to me because it was women my children’s age and my age and above.”

Rolfe, who currently champions Fred Hutch by emceeding events that

introduce Hutch science to the community, said her involvement gave her a unique perspective on cancer prevention research.

“Not everybody understands public health so doing something within the [Public Health Sciences] division better enabled me to speak to [that],” she said.

Dr. Garnet Anderson, principal investigator for WHI’s Clinical Coordinating Center and director of the Hutch’s Public Health Sciences Division, emphasized the incredible value of the contributions made by Rolfe and other participants.

“That data has been used extensively,” Anderson told Rolfe. “We have probably published over 1,000 papers using data that you’ve contributed to.”

Anderson also hailed Roth’s study for highlighting WHI’s impact both in terms of saving money and human lives.

“This is what prevention studies can do and we’re trying to get that word out,” she said. “These findings underscore the significant role clinical trials play in science and the importance of continuing to find ways to strategically invest public research funds to maximize value to society. It’s brought a new perspective to think about it as an investment.”



Longtime civic leader and former Fred Hutch board member Jean Rolfe is also a WHI participant. “I always felt a great sense of accomplishment that I had something to do with it,” she said. *Photo by Bo Jungmayer / Fred Hutch*



'PERFECT PLACE' FOR INNOVATION

A tiny liquid droplet, magnified under a microscope, glowing green to indicate that it contains a T-cell gene. Drs. Jason Bielas and Harlan Robins first developed QuanTILfy using this droplet-based technology to count unique T-cell DNA molecules. *Photo courtesy of the Bielas and Ghajar Labs*

Shared ideas lead to new test for cancer prognosis

By Susan Keown

Last year, a diverse group of collaborators at Fred Hutch demonstrated a new and powerful assay for predicting patients' outcomes after cancer.

Their assay, named QuanTILfy, counts and sorts cancer-fighting immune cells called tumor-infiltrating lymphocytes. Patients with greater numbers of TILs tend to survive longer after diagnosis; however, there has never been a way to reliably and consistently measure TILs — until now.

"What [our research] shows is that for the first time, you can actually count the number of T cells that infiltrate into a tumor, reproducibly. That hasn't been done before," said Dr. Jason Bielas, associate member of the Public Health Sciences and Human Biology Divisions at Fred Hutch. Bielas, a cancer geneticist, led the team that developed and tested this method for the first time, in ovarian cancer.

Now a valuable research tool, QuanTILfy has the potential to become a standardized clinical test for guiding treatment

decisions. For example, a patient found to have fewer TILs [meaning a less favorable prognosis] might choose to start more aggressive treatments first, which could help prolong the patient's life.

QuanTILfy leverages a technology co-created by team member Dr. Harlan Robins, a computational biologist and associate member of the Public Health Sciences and Human Biology Divisions at Fred Hutch. Robins' powerful genetic technology can map the unique surface markers of this diverse class of cells, which are otherwise difficult to characterize. The QuanTILfy team formed after Bielas heard Robins speak about his technology and the two began to seek a way to apply it to tumors.

"We were in the perfect place," Bielas said about their Fred Hutch-based team. "I think this is a very collaborative environment: Ideas are shared even before they're published, just when they're beginning." Sharing research in its early stages provides scientists from different fields with opportunities to collaborate, Bielas said, which can open doors to new lines of inquiry that might otherwise go unexplored or lead to new insights

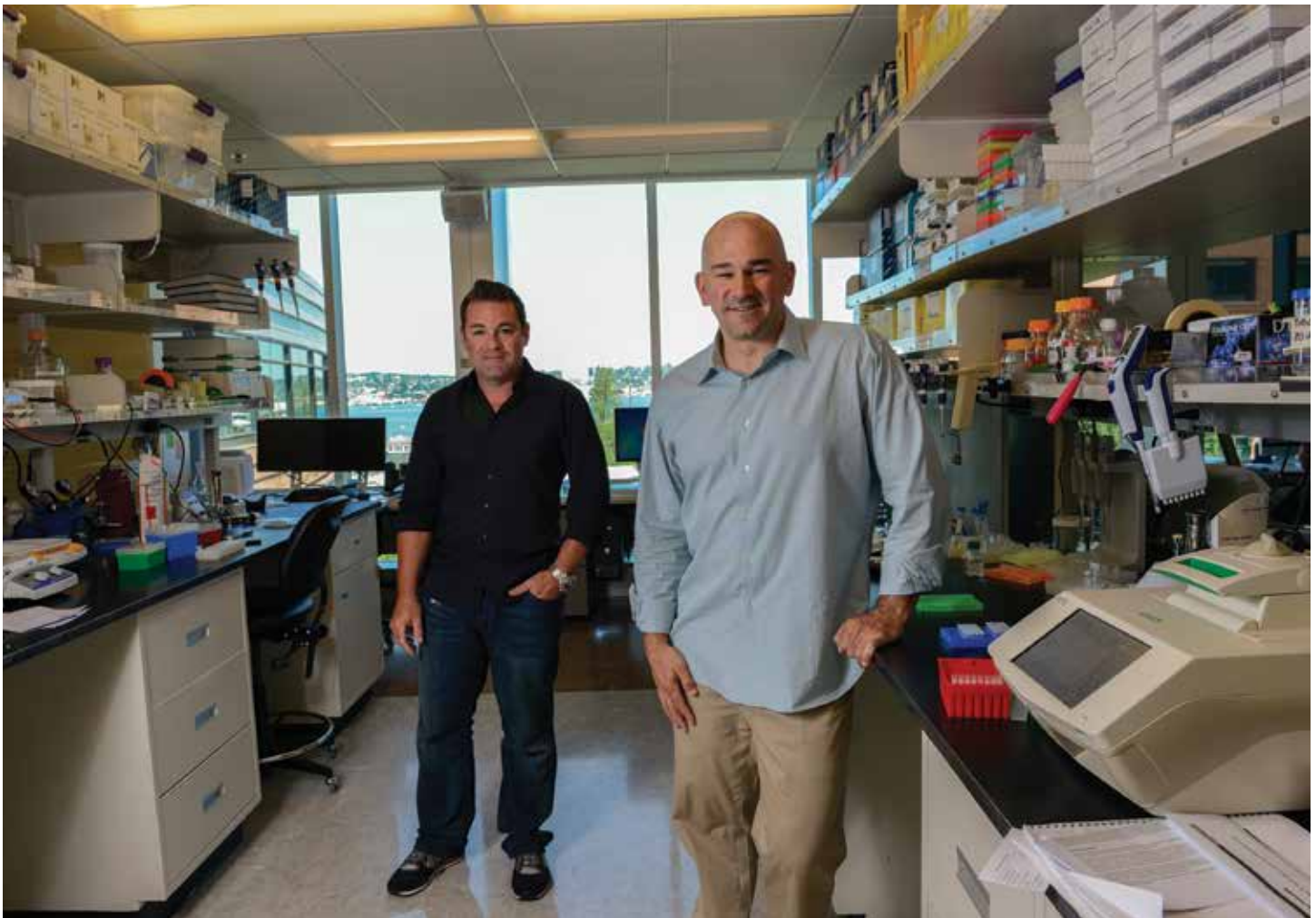
more quickly by bringing fresh perspectives to challenging problems.

Now that QuanTILfy has proven its potential, researchers at Fred Hutch and at biomedical companies are using it in studies of TILs in many types of solid tumors, from melanoma to lung cancer. What they learn could offer an unprecedented view of the interactions between the immune system and tumors. This knowledge will help scientists design new therapeutic strategies — for example, strengthening an existing immune reaction or removing a tumor’s protective barriers — that capitalize on each patient’s unique situation.

Adaptive Biotechnologies, a firm co-founded by Robins and two Fred Hutch colleagues, holds the license for both QuanTILfy and its underlying genetic sequencing technology. Within the last year,

Adaptive has significantly upgraded QuanTILfy’s methodology and is leading further testing with the goal of launching a clinical version by 2015. Thanks to this unique partnership, built in the hallways and labs of Fred Hutch, we are seeing the birth of a tool that could soon help doctors and their patients make the most effective treatment choices.

SUPPORT FROM CHUCK GOGGIO AND OTHER MEMBERS OF THE PRESIDENT’S CIRCLE FUELS THE WORK OF FRED HUTCH SCIENTISTS TO DEVELOP GROUNDBREAKING NEW TOOLS FOR CANCER RESEARCH AND TREATMENT, LIKE QUANTILFY.



Drs. Jason Bielas (left) and Harlan Robins (right) collaborated on a new tool for predicting prognosis in cancer patients. Photo by Bo Jungmayer / Fred Hutch



NEIGHBORS REACH OUT TO HELP CHILDREN A WORLD AWAY

Naheni Teopista played with her 6-year-old granddaughter, Naula Kamondi, who was feeling better after starting treatment for Burkitt lymphoma. Naula's care was provided through a joint Fred Hutch-Uganda Cancer Institute research project funded in part by Lisa Martin and Ken Fabert. *Photo by Robert Hood / Fred Hutch*

Benefactors Lisa Martin and Ken Fabert help launch research program to cure children with cancer in Uganda

By Dr. Rachel Tompa

When Fred Hutch's Dr. Corey Casper first visited the Uganda Cancer Institute (UCI) in Kampala, Uganda, he was disturbed by the arresting sight of children with the most common pediatric cancer in Uganda, Burkitt lymphoma. The disease, triggered by the Epstein-Barr virus, causes fast-growing and disfiguring tumors, usually on the jaw.

An expert in infection-related cancers, Casper understood all too well the senseless tragedy of what he saw. Burkitt lymphoma is highly curable — in the U.S., a simple chemotherapy regimen cures up to 95 percent of kids with this disease. When Casper first visited Uganda's sole cancer treatment facility in 2004, only an estimated 30 to 40 percent of Ugandan children with the cancer survived a year past diagnosis. And those were the ones who got treatment. Many do not have access to care.

When he returned to the U.S., Casper and his family sent a personal donation to the UCI for chemotherapy for Burkitt

lymphoma patients, but the next time he visited it became clear the funds had not gone far enough. How could they? The facility had limited pain medications, running water and electricity. There was only one oncologist to serve the entire country.



Dr. Corey Casper, head of Fred Hutch's Program in Global Oncology, is working to find sustainable solutions for cancer patients in Uganda — and beyond. *Photo by Robert Hood / Fred Hutch*

"I realized that unless we deal with this cancer holistically, there's no point," said Casper, who also heads Fred Hutch's Program in Global Oncology.

Casper and his Fred Hutch colleagues built a partnership with the UCI to start tackling the problem at its roots. Through the UCI/Hutchinson Center Cancer Alliance, they laid the groundwork for improving cancer research and care, from bringing Ugandan doctors to Seattle for cutting-edge oncology training to ensuring UCI nurses had enough latex gloves to administer chemotherapy. And they began planning a program to treat every Burkitt lymphoma patient at the UCI.

Later, a fortuitous chance drew Casper together with benefactors Lisa Martin and Ken Fabert, himself a practicing family physician. The couple already supported Fred Hutch research, but when Erica Sessle, at the time the managing director of the UCI/Hutchinson Center Cancer Alliance, moved in next door to Martin and Fabert, neighborly small talk led to the next step in their giving.

"It was literally an over the backyard fence kind of thing," Fabert said. "We had a few social chats about [Sessle's work]. We said, 'How's it funded, how's it structured, what are you doing?' and one thing led to another."

Through Sessle, they met Casper and others on the Fred Hutch team. The more they learned, the more intrigued they became.

"There's a mantra in philanthropy: As much or more than institutions or organizations, you fund people," Fabert said. Martin added, "There are a lot of good people there!"

Through their family foundation, the couple made a three-year pledge to support the team's work. Their gift in combination with funding from the Burkitt Lymphoma Fund for Africa and the National Cancer Institute launched the Burkitt Lymphoma Project. Private support is integral to the researchers' comprehensive approach, Casper said. Most grants he could apply for were restricted to research, but first and foremost, the children needed treatment — treatment this funding allowed them to provide.

Although UCI researchers established combination chemotherapy's power to cure Burkitt lymphoma nearly 50 years ago, Casper's team needed to show the power of their system

to overcome all barriers Ugandan children with the disease face, from awareness and diagnosis to completed treatment. The Burkitt Lymphoma Project topples these barriers by purchasing chemotherapy during shortages in government-supplied drugs, reimbursing families for transportation to and from the UCI, creating an electronic tracking system, supplying daily meals to patients, and pairing families with case managers for one-on-one assistance.

Since it began enrolling patients in 2012, the Burkitt Lymphoma Project has seen 125 children with the disease. The team is already documenting incredible changes [see story below], all of which are adding up for their patients. Now, more than 60 percent of these kids survive for a year or more past treatment, almost double the survival rate before the Fred Hutch program began.

Dr. Innocent Mutyaba is one of the Ugandan doctors who trained in oncology at Fred Hutch. Now he coordinates the Burkitt Lymphoma Project on site in Kampala, and he's pleased with their progress.

"For Burkitt, we have fantastic success stories," Mutyaba said.

To cure even more children, the team is working with Ugandan dental providers to refer suspected cases

earlier, since dental problems are common early signs of Burkitt lymphoma. And they are improving diagnostic techniques, eagerly anticipating the on-site pathology lab that will be part of a new Fred Hutch/UCI facility slated to open early in 2015.

They've also set a track record to be emulated. UCI clinicians treating patients with Wilms tumor, a pediatric kidney cancer, are now implementing some of the tools the Burkitt Lymphoma Project put in place, including case managers, electronic medical records and transportation reimbursement.

Martin and Fabert have been pleased to see the immediate effect their support has had in Uganda and how far their dollars have gone to save lives there.

"The amounts of money that our grant covered aren't huge amounts," Fabert said. "It's nice to think that there are niches ... where relatively modest grants can potentially have a significant impact."



Lisa Martin and Ken Fabert have been pleased with the progress of the Burkitt Lymphoma Project, which their contributions helped to launch.
Photo by Bo Jungmayer / Fred Hutch



On a visit to the Uganda Cancer Institute, Ronald Lumala cuddled his 4-year-old son, Mike Kiragga, who was successfully treated for Burkitt lymphoma. *Photo by Robert Hood / Fred Hutch*

A father's greatest gift: His son's life

By **Mary Engel**

Looking at the bright-eyed boy sitting on his father's lap at the Uganda Cancer Institute, it's hard to believe that 4-year-old Mike Kiragga once had a tumor on his jaw so huge he couldn't turn his head.

Kiragga had Burkitt lymphoma, one of the fastest growing cancers and the leading cause of cancer deaths in children in sub-Saharan Africa — but one that is highly curable if treated in time with chemotherapy.

But his father, Ronald Lumala, a farmer from a small village in west-central Uganda, originally had his own explanation for the mysterious swelling that appeared in December 2012: He feared Kiragga had been bewitched.

How else to explain a lump that kept growing and growing? No one in his village had seen anything like it, and his neighbors agreed that witchcraft was involved.

Lumala took his son to traditional healers, trading goats for care. Nothing helped. So he tried his village medical clinic, which referred him to Mulago Hospital, the nation's largest, in

Kampala. Eventually that hospital, after doing a biopsy, sent him to the UCI.

There he met Susan Nabakooza, a UCI nurse who also works as a case manager for the Burkitt Lymphoma Project, a joint initiative of Fred Hutch and the UCI. Kiragga was admitted to the UCI and treated for his fever and pain. Once the diagnosis was confirmed, he was immediately started on chemotherapy.

It was Feb. 13, 2013. Virtually overnight, the tumor shrank by almost half.

Kiragga spent two weeks as an inpatient at the UCI. After his second dose of chemotherapy, the tumor shrank yet again. He was discharged and his father was told to return every two weeks until the full regimen of six treatments was completed.

Kiragga completed his cancer therapy in May 2013, and he continues to come into the UCI for follow-ups. There is no sign of the cancer.

"He never believed he would have that child back," said Nabakooza. "Now every time he sees the child, he's just so happy."



Members of Team Society crossing the finish line in 2014. From L to R: Sim Rubenstein, Pete Kosowski, Hayley Duitch and Steve Burns. Photo by Lisi Wolf Photography

Obliteride participant's enthusiasm for Fred Hutch research inspires others to get involved

By Susan Keown

Hayley Duitch is proof that passion can have an outsized impact on advancing cancer research.

"I want to be part of finding a cure," said Duitch, who has watched many friends and family members struggle with cancer. Through fundraising, Duitch has forged a partnership with Fred Hutch that allows her to kick-start progress, even from outside the labs and clinics of cancer research.

"I'm not a scientist," she said. "I'm just a normal person that doesn't want anyone to have to go through it."

In 2013, Duitch, a resident of Mercer Island, Washington, and a business consultant, joined a small team of family and close friends to ride in the inaugural Obliteride in memory of a family friend who died of brain cancer in 2010. Duitch was drawn to the fact that all proceeds from Obliteride, an annual bike ride through the Puget Sound region, support cancer research at Fred Hutch.

Her first Obliteride finish, however, didn't come easy. While riding with a painful knee injury sustained during her training, it was the thought of the many people she knows with the disease that kept her going.

"That 50 miles was nothing compared to what they were going through," Duitch said. "Each stroke, I'd just say their names over and over and over again, just to get through it."

After such a difficult experience, some people would throw in the towel. But this year, Duitch rode again — and brought her entire company along.

"Our response was, 'Yes, how do we start?'" said Josiah Johnson, co-founder and vice president of Society Consulting, Duitch's employer, recalling Duitch's first conversation with company leadership about Obliteride.

Her pitch struck a chord with both Johnson and John Bergen, another cofounder and the president of Society Consulting. Obliteride offered a way for their company to combine two



Duitch's 2013 bike, covered with the names of people with cancer submitted by her supporters. As inspiration during her tough ride, Duitch repeated these names as a mantra. *Photo courtesy of Hayley Duitch*

important interests: support of local charitable causes and cycling — several staff members are dedicated cyclists and the company sponsors a competitive road and cyclocross racing team.

“On every level, from the DNA of our culture, to the values of what Obliteride stood for — with this world-class research organization right here in our community — it really just touched on everything that we stand for,” Bergen said. Society Consulting decided not just to form a team around co-captains Duitch and Johnson to fundraise and ride in the event, but to become an Obliteride sponsor as well.

Even with encouragement from the top, Duitch had to work to persuade some of her new colleagues to join the ride. She sent company-wide emails to rebut excuses she’d heard, from not having a bike [her reply: “We can find you one to borrow”] to the ride being hard [Duitch’s response: “My 14-year-old nephew did it”]. She stopped to talk to her coworkers in the halls.

Duitch laughs about her enthusiasm for recruiting new members to Team Society. “I don’t want to force people to do it,” Duitch said with a grin, “but I definitely think, at a very minimum, 25 miles isn’t that hard.”

Duitch’s persuasion paid off. On August 10, 2014, Team Society had 25 riders, one volunteer and one virtual rider, including all the members of Duitch’s 2013 team.

Last year, Duitch gathered almost \$3,000 in donations for Fred Hutch research as an Obliteride rider — no small feat on its own.



Team Yo Adrienne, Duitch’s 2013 Obliteride team. *Photo courtesy of Hayley Duitch.*

But this year, thanks to her ability to inspire others to get involved, more than ten times that was raised, including over \$10,000 in pledges that Bergen raised through his participation in Ride Across America, a cross-country bicycling race.

Duitch doesn’t have a medical degree. Neither does she have a Ph.D. But what she does have is a contagious passion. In partnership with an organization that channels passion into cures, that’s all it takes.



MESSAGE FROM PAULA REYNOLDS BOARD OF TRUSTEES CHAIR, FISCAL YEAR 2014

Photo by Robert Hood / Fred Hutch

Seeing Fred Hutch breakthroughs translate into lives saved

CURES START HERE.

That's the theme of this year's report and it succinctly captures the story of our center. Fred Hutch has historically had a reputation as the world leader in curing blood-borne cancers. But this remarkable accomplishment is only part of the story. Our scientists conduct research that relates to a wide spectrum of cancers — and a host of other diseases, too.

In this last year alone, our scientists have made dozens of scientific breakthroughs. Most widely covered in the media has been our work in the area of immunotherapy, which is among the most exciting developments in the search for cancer cures. But as you read this annual report, you can learn more about the myriad discoveries being made by Hutch scientists.

Fred Hutch, however, is not just a research institution. Our scientist-physicians apply research findings every

day in the real world. In the last year, over 7,000 patients were treated at Seattle Cancer Care Alliance (SCCA), our affiliated clinical branch where we join forces with Seattle Children's and UW Medicine. At SCCA, we translate our world-class science into patient care. SCCA treats more cancer cases than any other medical center in the region and is the place where patients with rare, complex and advanced cancers gain hope through novel therapies.

In the past year, Fred Hutch has faced a number of challenges, the greatest of which has been reduced funding from our largest supporters, the National Institutes of Health. Your Board of Trustees has embarked on a strategy to diversify our funding sources and ensure our success far into the future. Meanwhile, we have been heartened by the generosity of our donors. In this last fiscal year, Fred Hutch received the largest gift in our history — a \$20 million gift from the Bezos family — as

well as exceeded all previous records for donations.

In May, the Board accepted the resignation of Fred Hutch's president and director, Dr. Larry Corey, which took effect June 30, the end of our fiscal year. We are grateful for all that Dr. Corey accomplished in his tenure. The Board is conducting an international search for a successor and expects to announce a selection shortly. Meanwhile, we appreciate the leadership of our deputy directors, Dr. Mark Groudine and Dr. Fred Appelbaum, during this transition.

It is an honor to serve as the Chair of the Board of Trustees. My fellow trustees have shown singular dedication to Fred Hutch. In return, we are privileged to associate with extraordinary scientists. We see firsthand how their breakthroughs translate into saving lives. We are grateful to them for their unwavering commitment to lives of science — and to you, our benefactors, for your continued and generous support.

CURES START HERE

PRIVATE CONTRIBUTORS FISCAL YEAR 2014

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 thank each of the 31,202 benefactors who provided \$44,089,301 million in contributions, pledges and in-kind gifts between July 1, 2013 and June 30, 2014. Each of the individuals, corporations, foundations and organizations listed below contributed or pledged \$1,000 or more within the 2014 fiscal year.

We are grateful for the generous investment from all of our supporters in our relentless pursuit to improve the prevention, detection and treatment of cancer and related diseases.

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The Nobel Laureates Circle recognizes benefactors who have made cumulative gifts of \$1 million or more. These key contributors are permanent members of the Circle which was established to honor Fred Hutch's Nobel Prize recipients, Drs. E. 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 Fred Hutch's mission to eliminate cancer and related diseases as causes of human suffering and death.

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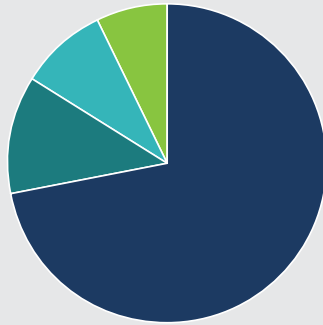
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*In FY14, giving to the SCCA included 3
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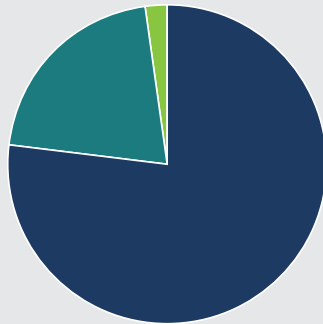
FINANCIAL SUMMARY

FRED HUTCHINSON CANCER RESEARCH CENTER FISCAL YEAR 2014



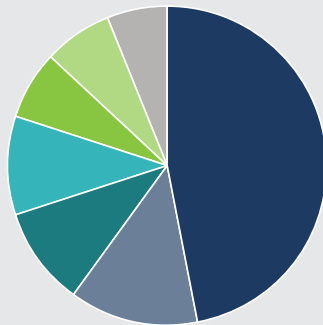
OPERATING REVENUES FISCAL YEAR 2014

■ Research Grants and Contracts	\$313,692,000	[72%]
■ Other Income	52,453,000	[12%]
■ Net Contributions	37,980,000	[9%]
■ Investment Income	31,385,000	[7%]



OPERATING EXPENSES FISCAL YEAR 2014

■ Program Services - Research	\$323,844,000	[77%]
■ Facilities and Administration	88,381,000	[21%]
■ Fundraising	8,257,000	[2%]



SOURCES OF CONTRIBUTIONS FISCAL YEAR 2014

■ Major Gifts	47%
■ Planned Giving	13%
■ Corporate and Foundation Relations	10%
■ Annual Giving	10%
■ Gifts of \$10K - \$49K	7%
■ Obliteride	7%
■ Events	6%

*Fiscal year 2014 numbers are preliminary and unaudited
Rounded to the nearest \$1,000*

THE POWER OF PHILANTHROPY

FEDERAL SUPPORT IS SHRINKING



The National Institutes of Health budget for U.S. biomedical research decreased **8.7%** over the past three fiscal years [a **13.2%** drop after adjusting for inflation].

FRED HUTCH FEELS THE IMPACT



Fred Hutch received **\$25.3** million less in NIH grants [approximately **7.4%** reduction] in FY14 than in FY12.

YOUR DONATIONS HELP CLOSE THE GAP



Fred Hutch benefactors contributed **\$16.5** million more in FY14 than in FY12 [a **37.4%** increase].

OUR COMMUNITY'S REACH

IN SEATTLE AND BEYOND



Fred Hutch employees **2,697**

Volunteers **1,500**

Study participants **25,000**

Donors **31,202**

ONLINE AND SOCIAL



Facebook likes **13,700**

Twitter followers **10,600**

Website visitors per year **1.15 million**

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FISCAL YEAR 2014

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