microbiome
EXPLORING THE WILDERNESS WITHIN

2 A body map of bugs  4 How they impact your health
12 Snake oil or certainty?
There’s no treatment too bold for cancer. That’s why we’re developing tiny T cell-soaked sponges, which, when implanted on a tumor, release reservoirs of immunotherapy to eliminate cancer cells. Your support makes our work possible.

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A BODY MAP OF THE HUMAN MICROBIOME

Each of us contains trillions of inhuman cells — the bacteria, viruses, fungi and other tiny creatures that make up the human microbiome. By the latest estimate, a full half of our cells are not our own. Here is a quick peek at the microbiome zones most closely studied in biomedical research.

REPORTING BY RACHEL TOMPA
DESIGN BY JIM WOOLACE
ILLUSTRATION BY KIM CARNEY

AURA

Your microbiome is not technically contained to the edges of your body. Each of us exudes a cloud of microbes that might someday be used in forensics as a sort of bacterial fingerprint.

SKIN

The sticky surfaces of the lung are host to a variety of lung microbes, harmful or helpful organisms that live in the very region of the body designed to act as a barrier against harmful respiratory bacteria and viruses. Changes in the lung microbiome have been linked to COPD, asthma and cystic fibrosis.

MOUTH

Much like the skin, the oral cavity is home to different niches colonized by their own subsets of bacterial species. One bacteria, in particular, thrives here: Helicobacter pylori.

STOMACH

The stomach’s acidic contents make it particularly harsh environs for most microbes to set up shop. But one bacterium thrives here: the ulcer- and stomach-cancer-causing H. pylori.

LUNG

The lung’s sticky surfaces are beginning to scratch the surface of the eye microbiome. What is clear is that the surface of the eye — like our mouth — houses different bacteria than the conjunctiva, the inner eyelids. And early research suggests that conjunctiva can alter your ocular microbiome.

GUT

The human intestine is home to a vast diversity of microbes containing hundreds to more than 1,000 different bacterial species. Alterations in the gut microbiome can affect human health in myriad ways, from how people react to drugs to their susceptibility to infection to immune function — even changing the risk for certain cancers.

VAGINA

We generally think of diversity as beneficial in the human microbiome world. But the human vagina is an odd exception — a healthy vaginal microbiome is dominated by Lactobacillus bacteria, while the microbiomes of women with the common infection known as bacterial vaginosis, or BV, is much more diverse.

UTERUS & PLACENTA

Until very recently, the uterus — and, during pregnancy, the placenta — was thought to be a sterile environment. But new studies have shown that both the uterus and placenta harbor their own microbiomes, which may play a role in supporting healthy pregnancies.

ONE OF THE BEST THINGS ABOUT BEING A SCIENTIST is knowing that new frontiers are always waiting to be discovered. And sometimes, explorations into unknown or poorly understood areas of human biology lead us to better treatments and cures for diseases.

One of those exciting new frontiers is the human microbiome — the many different bacteria, fungi, viruses and more that inhabit our gut, skin, mouths, noses, lungs, and every other nook and cranny of our bodies. Latest estimates show that bacteria alone may make up a full half of our body’s cells.

At Fred Hutch, we lead the world in expertise on cancer, infectious diseases and the complex role of the human immune system in disease. Because of our long history in these areas, we’re uniquely positioned to better understand the intricate interplay between bacteria, cancer and our immune system to the ultimate benefit of patients with cancer and other diseases.

We have our fingers on the many delicate threads that connect our microbial partners to cancer and infectious disease. We are setting our sharpest minds and latest technologies to trace and understand those connections. I hope you’ll be as inspired as I am when you read about the exciting research and discoveries being made about these universes within us.

As always, we are thankful for your continued support in these exciting endeavors.

Cures start here,

Dr. Gary Gilliland
President and Director

FROM THE DIRECTOR

A new frontier that’s changing how we think about our bodies and cancer

Dr. Gary Gilliland

Photo by Robert Hood / Fred Hutch

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When Kimberly Loges rode the bus from her home in Seattle’s Ballard neighborhood to the Prevention Center at Fred Hutchinson Cancer Research Center, the healthy study volunteer kept a tight grip on the large paper bag she carried. “No, it’s not my lunch,” she would say when asked.

Indeed. Inside that bag was a newly collected sample of stool, swirling in a liquid preservative. Also in the bag: a white, wide-mouth water bottle, sloshing with every drop of her urine from the past 24 hours. Four times over a half-year stretch she made the trip, delivering her specimens to researchers without incident.

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Write to Sabin Russell at srussell@fredhutch.org

In the name of science, sometimes decorum has to be set aside. And it helps to have a sense of humor. “It was awkward. It’s an awkward subject,” Loges said. “But the researchers made it easy. The only bizarre thing was delivery by bus.” She and nearly 50 other brave souls were enrolled in Flax FX, a Fred Hutch dietary study. They are among the thousands of volunteers who have joined with scientists around the world to explore the usually unseen — and sometimes unmentionable — frontiers of the human microbiome.

Researchers are also examining how the mix of microbial communities inside us may be tied to obesity, heart disease, mental health and how we respond to treatments for cancer. Mouse studies suggest that chemotherapy can be less effective against tumors if antibiotic treatments have destroyed the balance of gut microbes. And microbial communities help regulate our immune system, which has important implications for new therapies that harness immune defenses to fight cancer. “We know the bacteria in our bodies, which we call the microbiome, actually impacts the way people respond to immunotherapies,” said Dr. Phil Greenberg, an immunologist at Fred Hutch, during a recent American Association for Cancer Research conference in New York.

Not long ago, studies of the microbiomes were a medical research sideline, an obscure field that only aroused the curiosity of scientists unfazed by the subject matter. Yet new techniques began revealing the enormous diversity of the human microbiome and its role in health. Then came word of “fecal transplants” — restoring your unhealthy gut microbiome with someone else’s — and the topic made headlines. For some patients, these transplants were an effective treatment for a potentially deadly bacterial infection. Clostridium difficile, or C. diff, strikes patients, often elderly or immunocompromised, who have had their microbiomes radically altered by courses of antibiotics. Why a healthy gut microbiome has a broad mix of bacterial species, antibiotics can wipe out healthy bugs — leaving the field wide-open for bad actors. Fecal transplants may restore a more natural balance of bugs that keep C. diff under control.

Soon however, fecal transplant “spas” sprang up, making a host of unsurpassed claims. Now, a major industry has arisen selling products purporting to help consumers improve their own microbiome — drawing the attention of the U.S. Food and Drug Administration. Until more definitive studies emerge on so-called probiotics and microbial transplants, the best advice for consumers is the old watchword, “buyer beware” (See “Separating snake oil from certainty,” Page 12).

Nevertheless, the microbiome beckons serious researchers, at Fred Hutch and across the country, with the allure of a newly discovered frontier. It is a medical wilderness now being scouted with every tool of modern science, from the humble cotton swab to the supercomputer. Someday, understanding our unique, individual microbiomes could be critical to developing more precise, personalized medicine — and nothing is more personal than your microbiome.

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that picking apart these interactions will help Fredricks’s team “come up with novel ways of treating it through manipulation of the microbiota,” he said.

Information about the microbiome may also help doctors manage the risk of infectious diseases in patients after cancer therapy or a transplant. “We might be able to generate, in real time, information that would tell us we are seeing a bloom of a species, such as C. diff, and that we should tweak their antibiotics or alter their microbiota to reduce infectious complications,” Fredricks said.

Fredricks began exploring the microbiome at Stanford in the 1990s and developed genomic tools that have since helped his own microbiome-detection research at Fred Hutch, where he has worked since 2001. With grants from the National Institutes of Health and its Human Microbiome Project, he carried out some of the first comprehensive studies of the microbial populations that cause bacterial vaginosis, or BV, which affects nearly one in three women in the United States. Unpleasant and embarrassing, BV is also associated with preterm infections, including HIV.

The full set of human genes varies from that of chimpanzees by only about 4 percent, but the microbial mix within a human gut microbiome may differ by two-thirds from one person to the next. Those diverse legions of bugs in the colon ferment the fibers and other organic substances that can’t be broken down by enzymes in the stomach and small intestine. As such, they are also consumers of the food we digest, and they may have the means to signal what they prefer to eat. “When you eat a meat,” said Lampe, “you are not just eating for one.”

Liz Wagner, a Seattle digital products manager for a large coffee company, volunteered for the Hutch’s Flax FX study in hopes of helping others. Just like Loges, she and other participants were assigned to either a daily flaxseed preparation or an identical-looking sugar pill — a placebo — to be taken for 60 days. She was not told which one she was assigned. Wagner collected and delivered her own urine and stool specimens, and had blood drawn at the lab. After a pause of several months, the 60-day process was repeated. Whether she was assigned flaxseed or placebo in the first round, she received the opposite pill in the second.

The internet is periodically plagued with rumors that facial hair is a nest of nasty germs. Quite to the contrary, a 2014 study of 408 male hospital workers, published in the Journal of Hospital Infection, found bacterial colonization rates were roughly the same among those with beards and the clean-shaven — and bearded men were less likely to be harboring the most dangerous bacteria such as MRSA.

Seattle digital products manager Liz Wagner volunteered for the Hutch’s Flax FX study in hopes of helping others. As part of the study, she was assigned to take a daily pill — either flaxseed or placebo — for 60 days.

The human genome differs from that of the chimpanzee by only four percent. One person’s microbiome may differ from another’s by about 60 percent.

Don’t fear the beard. You can see the full story at hutch.org.

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More microbiome factoids

Newborns are first exposed to microbial communities on their skin as they pass down the birth canal. It takes about 21 days for a newborn to begin developing a personalized microbiome; up to two years for their own unique microbiome to become established in the gut.

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rRNA sequencing — the name refers to that ancient gene — where Salama received her postdoctoral training, this 16S sequencing machine could run a barcode census of entire communities of bacteria, spotting every species in a matter of days, with no need to isolate or grow any of them. Instead, scientists would not try to catalog a microbiome because it took months to isolate, grow and identify a single species. Now, a gene-sequencing machine could run a barcode census of entire communities of bacteria by their genetic fingerprints. Scientists learned to zero in on an ancient gene common to almost all hordes of bacteria by their genetic fingerprints. Scientists now are helping us understand why healthy foods which revealed the vast complexity of microbial life in the human gut, are now helping us understand why healthy foods might work for one person but might not for someone else. As Lampe pointed out, “It’s the microbes that are producing the compounds that are beneficial or detrimental.”

unlocking clues to stomach cancer

Dr. Nina Salama, a Fred Hutch Human Biology Division researcher and holder of the Dr. Penny E. Peterson Memorial Chair of Lymphoma Research, has been exploring the microbiome for more than 15 years with a singular focus: Helicobacter pylori. It is a bug that thrives in the acidic environment of the human stomach and is implicated in stomach cancer, the world’s third leading cause of cancer death. However, with half the world’s population infected with H. pylori, only a fraction are diagnosed with stomach cancer. Salama and her Hutch colleagues are asking whether the cancer-causing mechanisms of this bug are tied up in complex interactions with other microbes and the enzymes and tissues of their human hosts. “We have to be less ‘one-bug-centric,’” she said.

Salama attributes the surge in interest in the microbiome to the arrival of new tools that finally made it possible to identify hordes of bacteria by their genetic fingerprints. Scientists learned to zero in on an ancient gene common to almost all bacteria. Embedded within that gene is a strip of DNA that is different for every species and can be read almost like a bar code. Scientists would not try to catalog a microbiome because it took months to isolate, grow and identify a single species. Now, a gene-sequencing machine could run a barcode census of entire communities of bacteria, spotting every species in a matter of days, with no need to isolate or grow any of them. Refined during the 1990s at universities such as Stanford, where Salama received her postdoctoral training, this 16S rRNA sequencing — the name refers to that ancient gene — revolutionized the field. Like a microscope that suddenly throws an invisible world of tiny, living creatures into focus, these genomic tools cracked open the microbiome. Since those early days, the resolution of these genomic microscopes has substantially improved. So-called “next generation” gene sequences — blending fast and highly automated — are bringing greater precision to microbiome analysis. The technology allows researchers to identify not only bacterial species but specific strains. “I work on H. pylori and we know that not all strains are created equal,” Salama said. With this better tool, she is researching H. pylori strains that pose an even higher risk of stomach cancer. These strains, which carry a suspect gene, are more prevalent in some East Asian populations that have more gastric cancers than others. “The association is clear, but nobody has come up with a causal mechanism to explain it,” said Salama. So, one discovery leads to another puzzle, the process that drives science at the leading edge.

adding to our understanding of how to prevent and control obesity, which is linked to increased risk of certain cancers,” said Hullar. To probe this gut-brain link, brain-imaging scans, including MRIs, are being offered to 100 women participants in Hawaii, who also fill out standardized behavioral surveys. These scans will add data on brain chemistry and structure to the other health information already gathered. It is a breathtaking illustration of how sophisticated microbiome research has become. A project that began with stool samples now has high-speed computers crunching big data from genomic screens, proton spectrographs and MRI readouts.

the brain and the microbiome

Dr. Meredith Hullar is a microbial ecologist at Fred Hutch who got her start at Harvard studying the complex metabolism of microorganisms in the sea. She collaborates closely with Lampe on dietary research and the role of microbial metabolism in human health. Hullar is a fan of large studies that bring together huge amounts of disparate data, searching for patterns. One such project she and Lampe are involved in is the Multi-Ethnic Cohort study, which is comparing the microbiome profiles of 8,000 men and women from five different ethnic groups in Hawaii and California. It’s a massive undertaking, sequencing microbial genes from 7,200 stool samples and matching data from questionnaires, medical exams and whole-genome screens that can spot gene variants in each participant. The goal is to link the makeup and function of the gut microbiome to risks of obesity and cancer.

But the study is also exploring the connection between gut bugs, the brain and behavior. While signals from the gut to the brain help determine whether a person “feels full” after a meal, certain gut bacteria may alter that communication, influencing behavior linked to weight gain. “Understanding how the gut microbiome influences the brain’s regulation of body fat may add to our understanding of how to prevent and control obesity, which is linked to increased risk of certain cancers,” said Hullar.

Hullar and Lampe are working to understand the mechanisms by which components of diet, particularly constituents of plant foods, alter risk factors for cancer. Hullar and Lampe are working to understand the mechanisms by which components of diet, particularly constituents of plant foods, alter risk factors for cancer. It is a field that keeps the big picture in mind.

new chapter of exploration

When the microbiome is taken into account, it changes how we think of the human body. In the more traditional model, a human being is like a machine with important moving parts: Think heart, lungs, brain, liver, intestines. When trillions of microorganisms are added to the picture, the model morphs into an ecosystem, chock-full of complicated interactions, cycles and interdependent relationships — not just among organs but among different species. It becomes a little harder to determine what actually makes us human: the cells that define our bodies, or the relationships our own cells forge with their surrounding environment. In this ecological model, our health is intertwined with that of the microbial world that surrounds us.

Early interest in the human microbiome, in fact, was driven by research from microbial ecologists who study the community of bugs that inhabit soils, oceans, decaying matter on forest floors, and even extreme environments like volcanic hot springs. It is a field that leaps the big picture in mind. To do that, the exploration of the human microbiome is a story of hints. Finding associations between obesity and the microbiome are not the same as finding cause and effect. The field is still young, and its findings, while often intriguing, will have to stand up to the scrutiny that comes with volumes of studies, large surveys and replication of results. Those hints, however, are firing the imagination of researchers who scour for every possible edge against cancer and other deadly diseases. At Fred Hutch, the microbiome has come into focus, and a new chapter of exploration has begun.

To read more about Fred Hutch’s latest research and stories, go to fredhutch.org/news.
Some researchers use a Twitter hashtag to call out such quackery: "#microbiomania." Early understanding of the microbiome provides ripe space for scientists — and marketers.

**BY BILL BRIGGS | ILLUSTRATION BY BREANNA WELSH**

**SOME OF THE TINIEST LIFE FORMS** are generating some of the biggest hype. Our microbiomes — ecological communities of bacteria and other microbes residing within us — are fertile ground for shaky medical claims and shady websites vowing to cure everything from anxiety to autism.

" Hackers hoping to profit from the legitimate excitement springing from this Lilliputian landscape are increasingly drawing criticism from scientists working to crack the microbiome's tantalizing promise. Some researchers use a Twitter hashtag to call out such quackery: "microbiomania." "The science here has enormous potential and I do not want that potential to be damaged by this BS and the hype," said Dr. Jonathan Eisen, an evolutionary biologist at the University of California, Davis. He uses his science blog, "The Tree of Life," to pick apart what he sees as microbiome lies or misconceptions.

Jonathan Eisen, an evolutionary biologist at the University of California, Davis. He uses his science blog, "The Tree of Life," to pick apart what he sees as microbiome lies or misconceptions.

"The microbiome is ripe for snake oil because it is so complex and oversell," Eisen said. "This is part of microbiomania where people somehow have forgotten about infectious disease and how, not only did it kill billions, it still is one of the biggest killers on the planet," said Eisen.

"No, rolling around in dirt or licking the floor or your toilet is not a good idea," he said. "Yes, increasing microbial exposure on average can be beneficial.

Changing your microbiome will curb depression, cut anxiety and boost your mood.

The theory is called the "gut-brain connection" — the idea that bacteria in your digestive tract may have some influence on your thoughts and feelings. A 2013 study led by researchers at the California Institute of Technology found that when mice with autism-like symptoms were fed a common bug called Bacteroides fragilis, it changed their microbiome and appeared to make them less anxious.

"Many large-scale, spurious claims are (nonetheless) being made" about the health benefits of swapping out your gut bugs, Dinan told the FiveThirtyEight blog. For example, a psychology magazine recently published six steps to balance your microbiome and appeared to make them less anxious.

Welcome to the "hygiene hypothesis," which posits that exposing kids to germs early will prevent asthma later. In 2013, a New York City geneticist told journalists, "I would advise any new parent to roll their child on the floor of the New York subway."

"This is part of microbiomania where people somehow have forgotten about infectious disease and how, not only did it kill billions, it still is one of the biggest killers on the planet," said Eisen.

"No, rolling around in dirt or licking the floor or your toilet is not a good idea," he said. "Yes, increasing microbial exposure on average can be beneficial."

And when it comes to scrubbing away germs, the FDA says there's no evidence that antibacterial soaps stave off illness any better than plain ol' soap and water.

**Fecal transplants cure Parkinson’s disease, multiple sclerosis and autism.**

For some patients whose bodies harbor the potentially lethal bacteria Clostridium difficile, transplanting donated poop from a healthy person via colonoscopy may restore the natural balance of bugs that restrain C. diff. For now, that’s the most definitive statement scientists can make on the procedure.

But a handful of physicians are stretching that truth. At a national medical conference in 2012, a well-known gastroenterologist said "even more exciting is the use of fecal transplantation for a wide range of diseases (including) Parkinson’s disease, multiple sclerosis (and) autism."

Citing that same doctor, an alternative-medicine website now proclaims that fecal transplants have "been proven to be a highly effective treatment" for patients with Parkinson’s disease, clinical depression, and multiple sclerosis. The website shows readers how to do DIY fecal transplants by liquefying donated feces with a kitchen blender, putting the poop into a rectal syringe, emptying the syringe into the rectum and advising readers to keep the "liquefied feces inside your colon for at least 2 hours or longer" to be cured.

"This is not true," said Fred Hutch’s Dr. David Fredricks, who studies patterns of gut bugs in cancer patients who have blood stem cell transplants. "Indeed, the probiotic strains of bacteria tend to be minority species. The normal inhabitants still dominate."

"Many large-scale, spurious claims are (nonetheless) being made" about the health benefits of swapping out your gut bugs, Dinan told the FiveThirtyEight blog. For example, a psychology magazine recently published six steps to balance your intestinal bugs in order to balance your moods. One of their suggested steps: "Eat probiotic foods."
THE HUMAN MICROBIOME had been largely uncharted until the last decade, when high-speed gene sequencing machines cracked it open for study and researchers began pouring into the field. In the past few years alone, the number of studies published in academic journals on microbiome research has soared. To highlight the breadth and excitement of new discoveries about the human microbiome, here is a snapshot of just five surprising and important findings that may affect your health.

A SAMPLE OF KEY SCIENTIFIC DISCOVERIES ABOUT THE BUGS INSIDE YOU

BY SABIN RUSSELL

5

The wrong balance of gut bugs could trigger gut illnesses

Disruptions to the balance of microbial species in the human gut have been associated with several gastrointestinal diseases, including inflammatory bowel disease, irritable bowel syndrome, nonalcoholic fatty liver disease and bowel cancers.

Cleaner water may be tied to diabetes risk

A study by the Providence Saint John’s Health Center in Santa Monica, California, found that women with a history of breast cancer had a distinctively different community of microbes in their breast ducts compared to healthy controls. Until recently, it was assumed that breast tissue, nipple aspirate fluid and milk were sterile. Studies are underway to find out if the bacteria found in breast fluid could promote or inhibit DNA damage that can turn cells cancerous.

Gut bugs may affect how vaccines work

When a once-promising HIV vaccine failed completely in a global trial three years ago, scientists wanted to know why. Last year came a revelation: It may have been interference from common bacteria in the human gut. Duke Medicine researchers, with help from Fred Hutch scientists, found the candidate vaccine essentially stirred up the wrong antibodies — showing for the first time that gut bacteria can modify an immune response to a vaccine.

Antibodies are proteins that our immune system generates to target features on the surface of invading microbes. But instead of producing new antibodies against HIV, this experimental vaccine awakened old antibodies formed against gut bacteria acquired during early childhood.

Dr. Jim Kubit of Fred Hutch’s Vaccine and Infectious Disease Division helped oversee the HIV vaccine trial, and this fall was awarded a five-year, $45 million grant from the National Institute of Allergy and Infectious Diseases to study exactly how gut microbes can alter immune responses. The study could not only lead to a better HIV vaccine, it could show how the immune response to gut bacteria might be tapped to build more effective vaccines of all kinds.

Gut bacteria could make immunotherapy more effective

A pair of mouse studies, conducted continents apart, has shown that specific kinds of gut bacteria can directly affect the immune system’s response against cancer. A University of Chicago study found that mice with the common gut bacterium Bifidobacterium had better anti-tumor activity against melanoma than mice without it. Significantly, an immunotherapy drug known as a checkpoint inhibitor — the same treatment credited with saving former President Jimmy Carter’s life — worked better in the mice with Bifidobacterium.

A French study of a different checkpoint inhibitor found that the drug failed against melanoma in “germ free” mice, but the anti-cancer properties of the drug were restored when the mice were fed Bacteroides fragilis. Checkpoint inhibitor therapy works for some patients, not for others. Both studies suggest that changes in a patient’s microbiome might improve the efficacy of immunotherapy.

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AN EXPLOSION OF MICROBIOME SCIENCE

Citations of microbiome research in academic papers are soaring.

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FORTY. That’s how old Shubang Gan, a now-retired aerodynamics engineer was when he immigrated to the U.S. from Shanghai to attend Princeton. 2004. That’s the year he was diagnosed with a rare cancer known as NK T-cell lymphoma.

Seventeen, he said, is the number of days it took for new bone marrow to start growing after his doctors knocked out his immune system with chemo and radiation therapy, and then performed a blood stem cell transplant to eradicate the cancer. 

Two thousand. That’s how many calories a day of “really bad” hospital food Gan had to consume before his doctors would let him go home (“The waffle was thick like a brick!” he recalled).

It took one year for Gan to fully recover from his transplant and boldly quit his job in order to pursue a passion project that would provide “something meaningful for the human race.” His quest led him to Alaska, the 49th state of the union, which was seeking innovative, sustainable energy solutions.

Three. That’s the number of blades on a wind turbine, which Gan knew would be a better energy source for the remote reaches of Alaska than trucked-in diesel fuel, which typically freezes at 10 to 15 degrees Fahrenheit. Alaska’s limited roads and rail lines, however, made transporting the huge turbine blades a problem. Tapping his aerodynamics expertise and his manufacturing savvy, Gan designed and shepherded the production and shipment (via container ship across the Pacific, then barge to Alaska) of dozens of 70-foot-long, 600-pound fiberglass blades. Wind turbines now provide electricity in 28 small Alaskan villages 365 days a year.

Four is how many items, including the wind project, Gan has now checked off his post-diagnosis “bucket list.” Seeing the 48-mile-long Panama Canal was another; ditto for participating in a Fred Hutch fundraiser. Still active at 69, Gan was one of more than 1,200 supporters who climbed 832 steps to the top of the Space Needle as part of Base 2 Space on Oct. 2. The event raised more than $145,000. It took the Bothell, Washington, resident 24 minutes to make the climb, he said, which he did while wearing a pair of glasses—printed on his 3-D printer—in the shape of the number 5,005. “That’s how many days he’d been alive since his transplant, he says proudly.

Gan recently commemorated both his survivorship and the “wonderful” team that cared for him during his cancer treatment with a 12-inch by 24-inch slate on Fred Hutch campus engraved with Chinese characters expressing his deep appreciation. “It’s a very Chinese tradition to send something to the doctor or physician to show thanks,” he said. “Every doctor and every nurse was so kind.”

How many people helped him get to this point? Too many to count, he said, with a laugh.
Fred Hutch recruits world-renowned oncologist for key leadership role

Remissions after experimental immunotherapy

A GIANT IN THE CANCER RESEARCH

CLINICAL TRIALS

Incredibly ambitious’ trial in a deadly cancer

Emotions

Seattle Mariners GM, broadcaster visit Fred Hutch

DR. NANCY E. DAVIDSON

CAMPUS LIFE

BASEBALL BROUGHT THEM TOGETHER.

Clinical researchers are building a new generation of cancer fighters.

“Amazing ambition’’ trial in a deadly cancer

The Seattle Mariners General Manager Jerry Dipoto and the play-by-play broadcaster Dave Sims have brought them closer.

Mariners General Manager Jerry Dipoto, looking through the microscope, and broadcaster Dave Sims behind him, visit the lab of Fred Hutch’s Dr. Pete Nelson, September 2016. Photo by Stefanie Felix.

In September, Dipoto, a thyroid cancer survivor, and Sims, a prostate cancer survivor, visited Fred Hutch to learn about the science driving promising cancer therapies.

In the trial, 32 participants received an infusion of CAR T cells following chemotherapy, called lymphodepletion, which was given to make space in the body for the infused engineered cells. The team found that the CAR T cells most effectively knocked out the cancer in a group of 11 patients who received a two-drug combination chemotherapy followed by an intermediate dose of the engineered T cells.

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Seven of these participants, or 69 percent, went into complete remission — “which is very high” — given the advanced stage of these patients’ cancers, said Dr. Cameron Turtle, one of the study leaders.

These data demonstrate how dialing in the treatment parameters can make these cells more effective cancer fighters in patients with this particular type of cancer, Turtle said.

Graphical illustration showing genetically engineered immune cells attacking a cancer cell.

Mariners General Manager Jerry Dipoto, looking through the microscope, and broadcaster Dave Sims behind him, visit the lab of Fred Hutch’s Dr. Pete Nelson, in blue, September 2016. Photo by Robert Ham/ Fred Hutch.

“On one hand, it’s incredibly ambitious,” he said, “and on the other hand it’s exactly where we need to be to treat this cancer.”

“We believe that you can both learn, in a deep way, about the strategy you’re applying and actually maximally benefit that patient at the same time,” Hingorani said. This approach is exactly what this deadly malignancy needs, he said.

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**Dr. Marie Bleakley**

12 questions about life outside the lab for the Fred Hutch pediatric immunotherapy and transplantation researcher

**BY SUSAN KEOWN**

Dr. Marie Bleakley followed her grandfather into medicine. A native Australian, she came to the U.S., and Fred Hutch, in 2002 for a fellowship in pediatric hematology-oncology. Through her research on blood stem cell transplant and targeted immune therapies, Bleakley aims to improve survival and reduce treatment side effects in patients, especially children, who have high-risk leukemia. Recently, she sat down to talk about:

**Your grandfather?**

He was a family physician in the days where they did everything, including delivering babies. He was very tall and British and quite elegant in his doctoring and family life. He emigrated from the U.K. to Australia. His sideline was that he started the Canberra Food and Wine Club.

**I noticed bottles of wine in your office … ?**

They’re accumulating because I’m too busy to drink them. [They’re from] students — I’m not sure if they’re gifts or bribes.

(Laughs)

**What do you miss about where you grew up?**

Easy contact with family and friends, the climate, bird songs and the smell of eucalyptus.

**Did you grow up doing outdoorsy things?**

Oh yes. And Seattle in the summer is fantastic for hiking and biking. But then you have those long periods where — well, the skiing is great, but November here is hard before the snow starts, and the days are short.

**Did you plan on staying in the U.S.?**

(My husband) thought we were coming here for a year. I thought we were coming for three, and here we are 24 years later, with two kids and a dog. He’s a very tolerant man.

**How did you meet?**

At university, through the track club.

**Are you still a runner?**

We do fun runs quite frequently. We do the Shore Run [a Seattle 5K/10K event] each year to raise money for the Hutch. I do the woman’s run around Green Lake with my daughter. We do trail running.

If I’m pushing in one direction, I don’t like to push in another, so the running is more recreational now.

**One object you would bring to a desert island, assuming you had food and water?**

My Kindle, and an electricity supply.

**Do you have a favorite genre?**

Biography. I find it relaxing and educational at the same time. Having a broader view of what’s happened in the world — it’s more enjoyable seeing it through the eyes of an individual.

**The most compelling biographies you’ve read?**

Obama’s was really inspirational. Also Rosalind Franklin [who helped solve the structure of DNA] — just her determination to follow the science and excel despite the challenges that she had as a woman in science at the time.

**If you could be any animal what would you be?**

A dog. My border collie, Gypsy, has a good life.

OK, now you’re a person again, but you can choose a superpower.

Can I clone myself? An army of clones doing everything I need to do, and a couple that are resting and enjoying life with the family.

Fred Hutch is a global leader in discovering therapies for kids with cancer. With funds raised at the 2016 Hutch Holiday Gala, we intend to make our biggest investment yet in pediatric cancer research. Learn more at fredhutch.org/givenow.
Dr. David Maloney has been appointed the first medical director for cellular immunotherapy at Fred Hutch and the recently opened Bezos Family Immunotherapy Clinic at Seattle Cancer Care Alliance (SCCA).

Maloney is an immunotherapy researcher and blood cancer physician at Fred Hutch, SCCA and the University of Washington, and holds the Leonard and Norma Klorfine Endowed Chair for Clinical Research at Fred Hutch. In his role as medical director for cellular immunotherapy at the Hutch, Maloney has oversight of critical clinical trials infrastructure and provides expertise for effective research operations. As medical director of the new immunotherapy clinic, Maloney leads the clinic’s physicians and oversees research and patient care.

He played a key role in the development of the clinic — the only one of its kind in the nation that’s designed to meet the needs of patients participating in immunotherapy clinical trials.

The clinic bears the name of the Bezos family, which has provided catalytic philanthropic gifts and galvanized the community to join them in support of our groundbreaking and lifesaving immunotherapy research.

Photo by Robert Hood / Fred Hutch