



PROVIDENCE CANCER INSTITUTE • 2023 STEWARDSHIP REPORT

Your generosity at work

Herb Anderson was running out of treatment options for his rare skin cancer until he enrolled in a new clinical trial at Providence Cancer Institute. Now he is cancer free and celebrated his 50th wedding anniversary in Hawaii.

#FINISHCANCER

 **PROVIDENCE**
Cancer Institute

Personal message from the director



Dear friends,

Each year I have the privilege of addressing you through our annual Stewardship Report. As we reflect on this past year at Providence Cancer Institute, we are filled with immense pride and gratitude for your unwavering support.

Together we have continued to put patients first, while relentlessly pursuing groundbreaking research and compassionate care. Your generosity and commitment have allowed us to achieve remarkable milestones despite the challenges that have come our way.

Our team remains committed to our Mission to make a positive impact on cancer treatment and prevention. We are thrilled to share some of the incredible achievements that your support has made possible:

Expanding horizons in adoptive cellular therapy

As home to the first research laboratory in Oregon for adoptive cellular therapy, our researchers continue to explore groundbreaking personalized immunotherapy, including significant strides in T cell transfer therapy and tumor-infiltrating lymphocytes.

Empowering pioneering development

Thanks to your belief in our vision and your generous support at this year's Creating Hope gala, Matthew Taylor, M.D., and his laboratory continue to develop an antibody that has the potential to improve currently available therapeutics.

Bringing world-class cancer care closer to home

We know that healing begins at home and that by bringing the advanced, compassionate care to the patient means better outcomes. In March, Providence Cancer Institute of Oregon was thrilled to open the Carol D. Suzuki Cancer Center at Providence Willamette Falls Medical Center. The expansion of our services to Clackamas County brings care closer to home for so many.

As we look back on these achievements, we must acknowledge that none of this would have been possible without your support. Your generosity makes a difference in the lives of our patients, family and friends.

We invite you to read and share in the highlights of our past year where we describe some of the incredible journeys of hope, courage and resilience made possible by your contributions. Together, we celebrate each step taken closer to finishing cancer.

Grateful for you,

Walter J. Urba, M.D., Ph.D.

*Chief Medical Officer
Director and Endowed Chair, Earle A. Chiles Research Institute
Physician Executive, Providence Cancer Institute
Physician Executive for Research, Providence St. Joseph Health*

Inner journey turns to forward thinking

Battling cancer can compel a person to turn inward. “My radiation oncologist told me, ‘This is your job. Your job is to eat and drink something every day.’”

That was **Mike Larson’s** focus during the grueling regimen of surgery, radiation and chemotherapy that cured his oropharyngeal cancer. His wife, **Mary Otto**, helped by preparing nutritious soups, then pureeing them so that they slid easily down Mike’s raw throat.

“It was the hardest experience in my life,” Mike remembered.

But after his treatment, Mike and Mary’s focus turned back outward. Mike volunteered for the Robert W. Franz Cancer Center Leadership Cabinet and as a peer counselor for other patients. Mary trained to advise caregivers like her how to cook and care for loved ones with head and neck cancers.

Then they made a big decision. They would dedicate a significant portion of their estate to advance research and improve care for patients like Mike, a gift that will establish the **Michael Larson & Mary Otto Endowed Fund for Head and Neck Cancer Research**.

“It’s a way to help cure cancer or develop treatments that make quality of life a lot better during treatment and after,” said Mike. “I still have trouble swallowing at times, and that won’t go away. So if we can find treatments that let people return to life as it was before, that would be great. We feel strongly about that.”

Mary agreed. “We’re excited. We wanted the money that we worked for and saved to go to something that matters to us and that will help other people. Of all the cancers, you don’t hear about head and neck very much, so it’s important. We’re excited that we made a decision about how we would like that money to be used. And we are confident about it.”

Mike and Mary will be honored as part of Providence’s Heritage Club for those who choose to include Providence as part of their estate plans.



Progress on two paths toward groundbreaking therapy

Researchers at the Earle A. Chiles Research Institute are taking two approaches to adoptive cell therapy, the strategy of growing cells capable of a strong immune response outside of a cancer patient's body and infusing the patient with those cells to fight the cancer.



The Adoptive Cell Therapy Laboratory led by **Eric Tran, Ph.D.**, assumes that not all patients are able to produce T cells that can recognize and eliminate their cancer cells. To overcome this challenge, Tran lab researchers genetically modify T cells from a patient's blood to recognize mutations expressed by the patient's cancer. In 2022 Dr. Tran and **Rom S. Leidner, M.D.**, published results using this approach in a patient with metastatic pancreatic cancer, a mostly donor-funded proof-of-concept effort. The New England Journal of Medicine characterized the world-first results as "remarkable."

Drs. Tran and Leidner are currently leading a Phase I clinical trial evaluating these engineered T cells for patients with incurable cancers. "The goal is to generate personalized and potent T-cell therapies to target an individual's unique cancer cells," said Dr. Tran.

A different approach is being taken by **Brendan D. Curti, M.D.**, and **Andrew D. Weinberg, Ph.D.**, who have identified cancer-specific T cells in the tumors of most patients with solid malignancies. The number of these T cells in the tumor correlates with survival of patients with advanced head and neck cancer.

"Most tumors have a few thousand or tens of thousands of the cancer-specific T cells," Dr. Curti explained. "With our approach, after a surgeon removes a tumor, we recover the tumor-infiltrating T cells from it, isolate the cancer-specific T cells, expand their number from thousands to billions in the lab and then give them back to the patient to fight the remaining tumors."

After seven years of research, Drs. Curti and Weinberg recently launched a Phase I trial testing this approach. Expected to last two to three years, to date the study has enrolled four patients.



One challenge is that it currently takes six weeks to grow the T cells in the lab. That's too long for **Walter J. Urba, M.D., Ph.D.**, Director and endowed chair of the Earle A. Chiles Research Institute. "We're working to speed this up because cancer doesn't just sit around. We want to grow these cells in two weeks, rather than six weeks."

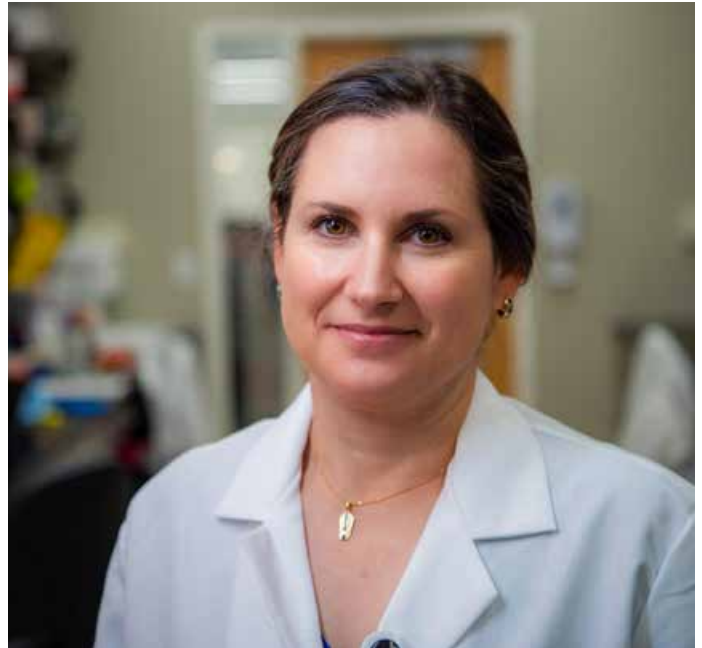
More effective and less toxic

Radiation oncologist **Kristina Young, M.D., Ph.D.**, and the Tumor Microenvironment Lab she leads are pairing radiation treatments with immunotherapy to shrink tumors more effectively, make their surgical removal easier and decrease treatment toxicity by reducing the need for post-surgical therapy.

Oncologists have used radiation to treat cancer for decades. The radiation damages the DNA of cancer cells and healthy cells alike. But while healthy cells can repair that damage, tumor cells typically lose that ability and die or fail to reproduce. That has been the well understood mechanism of radiation treatments for cancer.

But according to Dr. Young, in the past 20 years she and other researchers began to realize that more was going on. "Radiation also creates an inflammatory response in the tumor microenvironment that draws in cancer-fighting T cells, which is a good thing," she explained. "It also draws things that can suppress T cells' effectiveness. We're trying to figure out how to enhance the positive effects of the radiation and reduce T cell suppression."

Dr. Young and the Tumor Microenvironment Lab have demonstrated that pairing radiation with immunotherapy makes both treatments more effective. The radiation attracts T cells and improves their access to the tumor by altering its blood vessels, while immunotherapy helps T cells overcome some of the tumor's immunosuppressive mechanisms.



"When I'm in clinic, the thing that is most emotionally challenging is when my patients don't have any good options or there aren't good treatments for the stage of their disease," said Dr. Young, who lost a loved one to breast cancer. "I want my research to give them more options - longer lives, better quality of life and more time with their loved ones."



Creating new tools for the immune system

Matthew Taylor, M.D., wants to give the immune system a bulletproof vest. Cancer can kill T cells by commandeering one of the immune system's normal regulatory processes. Dr. Taylor and his team in the Developmental Cancer Therapeutics Laboratory are researching how to overcome that hijacking.

T cells are one of the most effective components of the immune system, searching for and attacking infections and tumors. Normally after an infection, the body uses a protein, fas ligand, to rid itself of unneeded T cells. But many cancers take over this mechanism, using fas ligand to kill T cells trying to attack their tumors. Compounding the problem, the fas ligand protein also stimulates tumor cell growth and metastasis.

Dr. Taylor is developing an antibody to block the protein, with the goal of making immunotherapies for advanced cancers more effective. "We want to protect the immune cells

from being killed by the tumor and block the tumor-promoting properties of fas ligand," said Dr. Taylor.

Dr. Taylor's team has successfully developed a drug prototype with very promising characteristics. They have engaged a manufacturer to produce enough of the prototype for toxicology testing and a Phase I clinical trial. The trial, which Dr. Taylor anticipates will start in late Summer 2024, will determine the drug's safety in humans, enrolling patients with a variety of advanced cancers that have become resistant to standard treatments.

"I've spent the last 13 years of my career conducting Phase I clinical trials, and it's been gratifying to see how new drugs have changed patients' lives," Dr. Taylor said. "This will be an extension of that experience but testing a drug that we've made here at Providence Cancer Institute."

Final option wins lifesaving success

Unless he could find a new treatment, **Herb Anderson** was going to die.

The retired public utility district worker from Longview, Washington, had metastatic Merkel cell carcinoma, a rare skin cancer that started with a lump in his armpit. Because it can grow fast and spread quickly, Herb and his wife, Debbie, cancelled a long-planned vacation and allocated their resources for a long fight. But, despite two-and-a-half years of treatment that included Pembrolizumab, combination therapy with Ipilimumab and Nivolumab, as well as radiation therapy, the cancer spread to his lymph nodes, throat and abdomen.

"I kept thinking, 'We are out of options. We are out of options,'" recalled Debbie.

But Herb's oncologist, **Matthew Taylor, M.D.**, a physician researcher at Providence Cancer Institute, had one more option, a newly launched clinical trial by the biotech company Immune-Onc. Herb would be one of just 30 patients nationwide receiving a new immunotherapy drug called IO-108, which helps activate T cells to fight cancer.

In February 2022, Herb began infusions of the therapy every three weeks. By April his tumors were starting to shrink. While immunotherapy typically can bring some tough side effects, Herb felt great. "Good enough to golf!" he said.

By June 2023 the cancer could not be seen on any scans. "We hope other cancer patients can benefit from this trial and see the same positive results," said Dr. Taylor.



Herb and Debbie celebrated their 50th wedding anniversary in 2023 with a family trip to Hawaii. "We love Providence. They make you feel comfortable and hopeful," said Debbie. Herb added, "Cancer touches all of us at some point. By supporting cancer research, you are changing people's lives – extending lives. And, when we finish cancer, you get to say you helped play a part."

Multi-faceted team spurs growth in gynecologic cancer treatment and research

In just three years, the Providence Gynecologic Oncology program has grown into the largest gynecologic cancer research center in Oregon, serving women up and down the West Coast.

Christopher Darus, M.D., MS, who joined Providence Cancer Institute in October 2020, leads a multi-faceted team of researchers and caregivers, including a donor-supported nurse practitioner who helps women with physical and psychosocial sexual health needs resulting from their treatment.

“Every great cancer program should represent every aspect of cancer care,” explained Dr. Darus. “And we have a wonderful opportunity to build on Providence’s research infrastructure.”

Patients at Providence Cancer Institute are five times more likely to be enrolled in clinical trials than the national average, and patients in the gynecologic cancer program are no exception.

“We have about nine Phase II and III clinical trials open and five more in the pipeline,” said Dr. Darus. “There is no single ovarian cancer or endometrial cancer. There are specific sub-types, and we can’t assume that they or their treatments will be the same. So, we’re approaching this from a lot of different directions.”

One of the team’s key focuses, endometrial cancer, illustrates this approach. The cancer begins in the layer of cells that form the lining (endometrium) of the uterus. Over the past 25 years, diagnoses have skyrocketed. The program’s patients are participating in clinical trials testing new treatments for four major subtypes of the disease.



“We’re looking at their unique proteins and DNA mutations,” Dr. Darus said. “All cancer care should be individualized because every cancer is different.”



New center brings world-class care close to home

On March 2, 2023, **Lisa Hammond** received a diagnosis of Stage III breast cancer. “It was my birthday,” she recalled. “I never thought in a million years that I would have two weeks to figure out my life.”

Thanks to outstanding donor support, one thing Lisa did not have to figure out was where to receive her chemotherapy. She was one of the first patients at the newly opened Carol Danielson Suzuki Cancer Center at Providence Willamette Falls Medical Center, just “a mile and change” away from her home in Gladstone.

Donors gave more than \$3.5 million to help build the center, which has eased access to world-class care at Providence Cancer Institute. At the Suzuki Cancer Center, patients can access chemotherapy and immunotherapy treatments, as well as consultations, clinic visits and surgery. The center brings innovative research from the

researchers at the Earle A. Chiles Research Institute directly to the patients.

“The new center makes it easier for Clackamas County residents to participate in innovative treatments and clinical trials that offer the very latest in cancer care,” said **Lyn Dobrunick, MN, FNP, AOCN**, executive director, Providence Cancer Institute.

Lisa did not relish the idea of driving to Portland for chemotherapy. “I wasn’t sure how I would feel after my treatments,” she said. “I was so excited I could have them at Willamette Falls. Having them close to home was very helpful.”

Lisa looks at the donor wall in the Suzuki Cancer Center each time she visits. “I don’t know if they have been through cancer, but I am very thankful for the people who donate. I feel a lot of gratitude.”

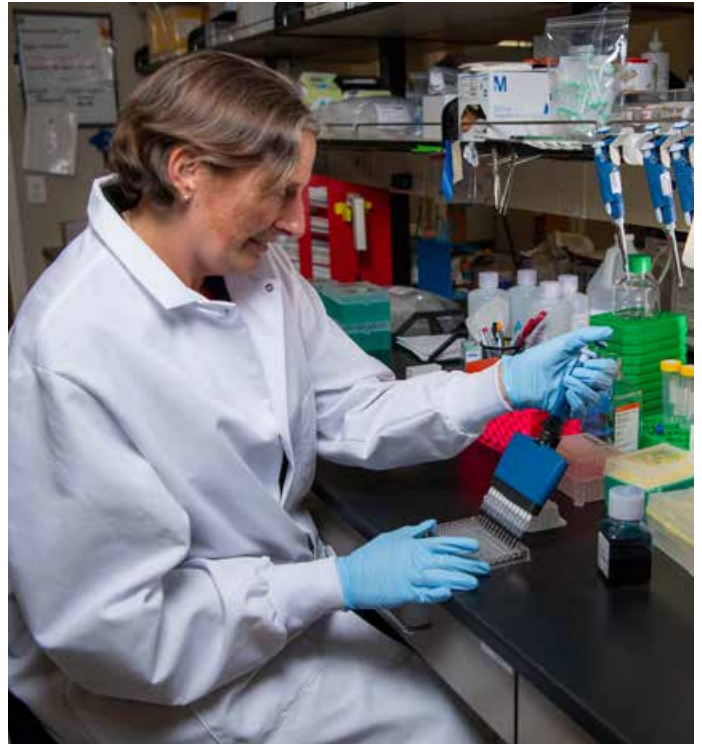
A vaccine to prevent breast cancer

Sasha Stanton, M.D., Ph.D., hopes to make protecting oneself from breast cancer as easy as getting a shot for the measles.

"I'd like to make a vaccine that you can use right off the shelf, something that would work for anyone at risk anywhere in the world," she said.

Dr. Stanton is taking an approach similar to that used for the mRNA COVID-19 vaccines: using pieces of proteins associated with breast cancer growth to teach the immune system to respond to the cancer itself. Her research currently focuses on patients with early forms of breast cancer, but Dr. Stanton's goal is to create a vaccine for people who have never had evidence of the disease but are at high risk of developing it.

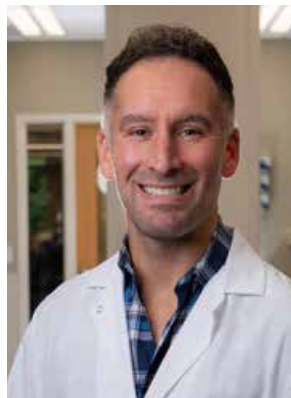
"I want to give people a treatment that could prevent the need for surgery and radiation, a treatment that is durable and easily tolerated."



Stopping cancer from taking over immune system communications

Terry Medler, Ph.D., and the Innate Immunology Laboratory are seeking new ways to prevent cancer from commandeering the immune system's communications.

According to Dr. Medler, cancer frequently breaks down the communication pathways between the innate nonspecific immune response that constantly patrols the body and the adaptive immune response with cells specifically targeted for different types of infection or cancer. "Cancer



manipulates these pathways to its advantage," he explained. "The innate system keeps calling in a futile response rather than helping to clear the cancer. The whole process goes awry."

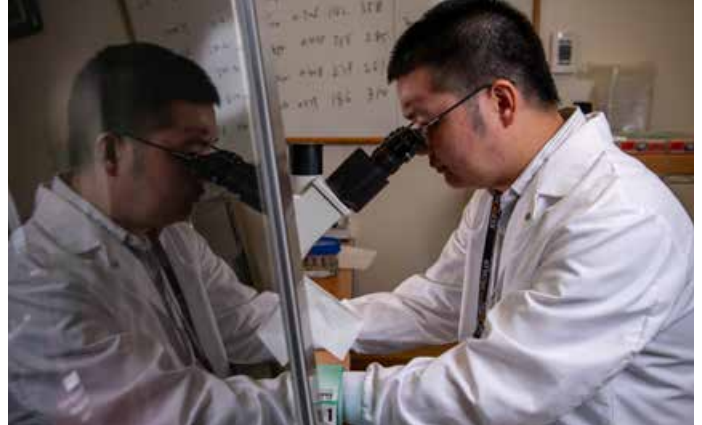
Dr. Medler hopes to identify innate pathways that might operate in certain cancers or subsets of patients. "If we can target an innate pathway that is thwarting the response of the adaptive immune system," he said, "we may be able to improve outcomes for patients who are not responding to available treatments. We've made great strides in treating cancer, and they work extremely well in certain patients. Our goal is to understand innate pathways that lead to treatment failure so these therapies work in more people."

Using leading-edge technology to target new therapies

A new member of the Earle A. Chiles Research Institute is using the game-changing CRISPR gene editor to discover the genes most likely to initiate and spread several rare but deadly cancers.

Jianguo Huang, Ph.D., joined the institute in 2022 to lead the Preclinical Cancer Therapy laboratory where he is developing targeted therapies and immunotherapies for soft tissue sarcomas and other cancers with similar gene mutations.

CRISPR has transformed a years-long and expensive gene-editing process into one that is quick and much less costly. Dr. Huang uses it to identify the mutated genes driving soft tissue sarcomas.

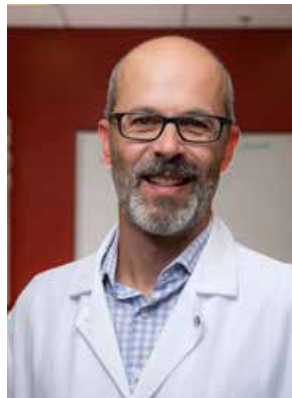


Preliminary tests of therapies targeting those genes and key proteins associated with them have shown promising results. Dr. Huang plans to continue researching sarcomas, comparing their mutations with those found in other cancers to learn more about what might be driving them.

“The next 10 years will see the development of many CRISPR-based treatments,” said Dr. Huang. “The past decade is only the beginning.”

Understanding how T cells interact with cancer

For four years, **Thomas Duhon, Ph.D.**, has led the Anti-Cancer Immune Response Lab to advance understanding of how different types of T cells interact with cancer cells. The lab has contributed to groundbreaking discoveries on tumor-killing T cells that have the potential to greatly improve the anti-tumor immune response.



Tumors contain a diverse mix of T cells. Some, the tumor-reactive T cells, work to destroy the tumor. Others, the regulatory T cells, which normally prevent inflammation and autoimmune responses,

promote tumor growth by fighting off their tumor-killing brethren.

Dr. Duhon seeks to promote the activity of the tumor-reactive T cells without completely blocking the regulatory T cells, as this could cause devastating side effects. He hopes to work with other group leaders within the institute to harness his research and together translate it into more effective therapies.

“We are looking for ways to make the good, tumor-reactive T cells stronger and more effective, while concomitantly blocking the effects of the regulatory T cells that aim to suppress them,” he explained. “We are upstream of Dr. Eric Tran’s lab. He is translating discoveries to treat patients. Our goal is to discover more basic mechanisms that he can take in his lab to create novel therapies.”

Don Mark grateful for care

Diagnosed with prostate cancer, **Don Mark** was on his way to the Mayo Clinic when a friend told him to go to Providence Portland Medical Center emergency department instead. "Less than 24 hours after I arrived, I'd had two imaging appointments and my first radiation treatment," he recalled.

Today Don's cancer is gone. "People need to know that they have your back – from the ED team to the cancer center," he said. "I just don't know where I would be if I hadn't been steered to Providence. They're in the business of helping people."



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OUR MISSION

As expressions of God's healing love, witnessed through the ministry of Jesus, we are steadfast in serving all, especially those who are poor and vulnerable.

OUR VALUES

Compassion, Dignity, Justice,
Excellence, Integrity

ProvidenceFoundations.org/cancer