



Providence Cancer Institute Stewardship Report

#FINISHCANCER

Eric Tran, Ph.D., and Rom Leidner, M.D.
reported the world's first case of
metastatic pancreatic cancer regression
through T-cell transfer therapy with
genetically-engineered T cells.

 **PROVIDENCE**
Foundations of Oregon

Personal Message from the Director

Dear Friends,



At Providence Cancer Institute, we put patients first and continuously pursue the very best research and care possible.

This was a year marked with incredible achievement by our team. Despite a record heat wave that scorched the Pacific Northwest and evolving COVID-19 safety measures, our research team enrolled new patients in more than 100 clinical trials, shared important findings with colleagues across the globe, and treated those in our care with compassion and dignity.

I am especially proud of the researchers at the Earle A. Chiles Research Institute, a division of the Providence Cancer Institute at the Robert W. Franz Cancer Center, for the advancements made in immunotherapy research. Our strength is our ability to respond quickly to new ideas and collaborations, allowing us to offer new investigator-led clinical trials and first-in-human opportunities for patients.

- Rom Leidner, M.D., Eric Tran, Ph.D., and colleagues made a breakthrough discovery in adoptive cell therapy that may lead to better **treatments for some of the most difficult cancers**.
- **Three new labs** under the direction of Di Wen, Ph.D., Terry Medler, Ph.D., and Jianguo Huang, Ph.D., were added to perform independent cancer research.
- Providence became the first health system in the world to offer **Galleri, a diagnostic tool for the early detection** of many types of cancer.

Thank you for your support. I invite you to read the vignettes that follow and join me in celebrating each life saved and every groundbreaking discovery.

Grateful for you,

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

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

CANCER RESEARCH By the Numbers

It takes a robust team to fund, conduct and report on cancer research. Your support allows us to enhance the quantity and quality of clinical trials we offer to our patients. Your support impacts families throughout Oregon and southwest Washington, and helps us assemble the knowledge that will ultimately finish cancer.



119
New clinical trials
enrolling patients



24
Principal investigators
leading new trials



711
Newly enrolled patient
volunteers



70%
Funded by philanthropy



149
Medical journal
publications by faculty



67
Conference
presentations by faculty

Adoptive Cell Therapy reduced tumors in patient with pancreatic cancer

The Earle A. Chiles Research Institute is among a handful of centers in the world capable of developing and administering adoptive cell therapy, a highly personalized type of immunotherapy. In our Adoptive Cell Therapy Lab, T cells are obtained from a patient's blood and undergo TCR gene-engineering to target hotspot mutations expressed by the patient's cancer. Then they are amplified in magnitude and potency, and returned to the patient through intravenous infusion.

Despite decades of research, pancreatic cancer remains one of the deadliest forms of cancer. Most patients do not experience a lasting response to treatment. However, Kathy Wilkes of Florida experienced significant benefit after receiving adoptive cell therapy.

Kathy had metastatic pancreatic cancer that did not respond to chemotherapy, surgery or radiation. As part of a single-patient clinical trial at Providence Cancer Institute, co-led by **Eric Tran, Ph.D.**, and **Rom Leidner, M.D.**, Kathy received one infusion of her gene-modified T cells.

In one month, Kathy's tumors shrunk by 62%. Six months later, the tumors had shrunk by 72%.



Within six months of receiving adoptive cell therapy, Kathy's tumors shrunk by 72%.

"The fact that a single infusion of reprogrammed T cells could cause Kathy's metastatic pancreatic cancer to shrink for over six months makes me optimistic that we are on the right track. Now we have to make this therapy more potent and work for more patients."

– **Eric Tran, Ph.D.**, assistant member, Adoptive Cell Therapy Lab

Wilkes's success was detailed in a heralded article, "Neoantigen T-cell Receptor-Gene Therapy in Pancreatic Cancer" appearing in the June issue of The New England Journal of Medicine.

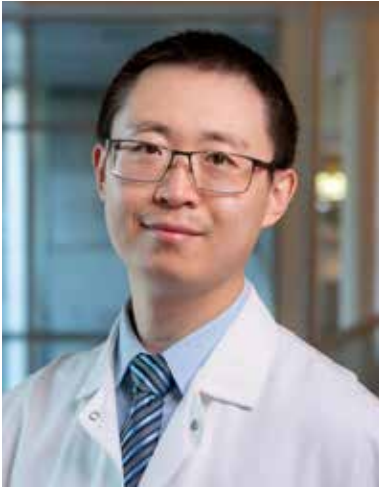
Drs. Tran and Leidner have opened a new clinical trial to provide cellular therapy to more patients. In this trial, like Wilkes's treatment, a patient's T cells will be genetically engineered to express a new receptor that redirects the T cells to attack a specific cancer mutation present in the patient's cancer cells. Patients will receive these gene-engineered T cells along with two additional immunotherapy agents to enhance the activity and efficacy of the transferred T cells.

"We are at the doorstep of what may be a breakthrough 'living drug.' There is no better place than the Earle A. Chiles Research Institute for the visionary and indefatigable commitment needed to develop this kind of groundbreaking cancer treatment."

– **Rom Leidner, M.D.**, co-medical director, Providence Head and Neck Cancer Program and associate member

Three new faculty recruited and labs established

Philanthropy allowed the Earle A. Chiles Research Institute to develop three new labs this year. These labs will be led by the following accomplished researchers:



Di Wen, Ph.D., leads the newly created Biomedical Engineering Laboratory.

During postdoctoral training, Dr. Wen pioneered a novel approach to cancer therapy by engineering fat cells and platelets for local drug delivery to enhance surgical effectiveness.

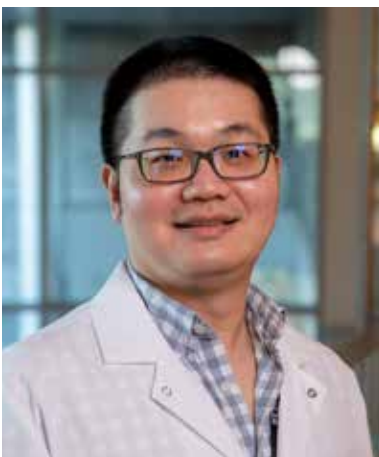
Dr. Wen is developing biomaterials and cellular therapies in partnership with notable Providence researchers including Bryan Bell, M.D., D.D.S., FACS, FRCS(Ed), medical director of the Providence Head and Neck Cancer Program and director of Surgical Oncology Research.

Dr. Wen and Dr. Bell are investigating methods of engineering cells to deliver various cancer therapies directly to the surgical site and tumor. They hope patients who receive the locally administered therapies will have better outcomes compared to traditional treatment methods.

"We are already working towards translating this approach from the lab bench to the patient bedside. Dr. Wen has the expertise to lead this effort and he has hit the ground running."

– **Bryan Bell, M.D., D.D.S., FACS, FRCS(Ed)**

The Biomedical Engineering Laboratory is supported, in part, by a generous donation from Steve and Cindy Harder.



Jianguo Huang, Ph.D., is an assistant member at the Earle A. Chiles Research Institute. He has extensive expertise in cell therapy and gene editing.

Dr. Huang is focused on finding ways to improve therapeutic strategies for patients with soft tissue sarcoma. In 2020, he was awarded a K22 grant by the National Institutes of Health to study the coding genes and noncoding RNAs that regulate sarcoma development. The grant allows Dr. Huang to carry his research forward at Providence, leading the Preclinical Cancer Therapy Laboratory. He is studying methods to eliminate sarcoma cells at primary and metastatic sites by targeting critical cellular pathways.

"I want to fill the gap in sarcoma research, create a different type of screening approach and expand my specialty to a broader range of tumors."

– **Jianguo Huang, Ph.D.**



Terry Medler, Ph.D., is an assistant member at the Earle A. Chiles Research Institute. Dr. Medler received his doctoral degree at Northwestern University in the laboratory of Charles Clevenger, M.D., Ph.D., where he studied the role of hormones in breast cancer.

Previous study of the role of the immune system in cancer development and treatment led Dr. Medler to a postdoctoral fellowship at the Earle A. Chiles Research Institute with Marka Crittenden, M.D., Ph.D., and Michael Gough, Ph.D. Dr. Medler studies innate immunity and investigates methods to improve antigen-specific CD8 T cell responses to cancer.

“The biggest draw for a translational researcher to come to Providence is the researchers in the lab are constantly in contact with the physicians who treat patients. These discussions keep our research focused on the clinically relevant questions and

boost the likelihood of our research being translated to the clinic. It truly brings a synergy that can’t be overstated.”

– Terry Medler, Ph.D.



Jack Locker Center for Cardio-Oncology is immediate success

It holds true that radiation, chemotherapy and immunotherapy help patients live longer or beat cancer altogether. However, these very same cancer treatments pose a risk to the heart. Data from cancer registries consistently show that individuals who received certain forms of cancer treatment have a significantly higher likelihood of developing cardiovascular disease than their counterparts without cancer.

With gratitude to Lynn Locker and multiple supporters, Providence opened the Jack Locker Center for Cardio-Oncology this past year. Led by cardiologist **Michael Layoun, M.D.**, the goal is to help physicians keep their patients on life-saving cancer treatments for as long as possible while keeping the heart healthy.

Dr. Layoun provides personalized treatment plans for each patient and collaborates with other cardiologists and oncologists to ensure that negative effects on heart health can be minimized through cancer treatment.



Michael Layoun, M.D.

Your Generosity at Work

The Jack Locker Center for Cardio-Oncology would not be possible without Providence supporters. You helped us fund positions for medical director and nurse navigator – first steps toward creating a dedicated facility.

This program is in excellent hands with Dr. Layoun as the medical director. In one year, he conducted 110 in-person and multiple virtual consultations. Dr. Layoun plans to assemble an internal review board to facilitate sharing data with the international cardio-oncology registry. This will allow us to share what we are learning with providers caring for similar patients across the globe.

Kate Lenahan was recently hired to fill the cardio-oncology nurse navigator position. She will help Dr. Layoun identify and triage urgent cases and connect patients with support services, as needed.

Excellence in Colorectal Cancer Treatment

Colorectal cancer remains the third most common cancer among people in the United States. Although new diagnoses have dropped steadily among older adults, the incidence of colorectal cancer is increasing in people aged 50 years and younger.

Patients who come to Providence for treatment of colorectal cancer can expect a greater chance of success. This is due to access to multiple clinical trials, strict patient care standards and our amazing caregivers who provide the best multidisciplinary care.

Young Mother Now Cancer-free

“Sasha” continued to experience gastrointestinal complications six weeks after giving birth. In her thirties and with no known family history of colorectal cancer, her physician was surprised to find a 4-centimeter cancerous tumor in her colon.

Sasha was offered the chance to participate in an immunotherapy clinical trial. Providence Medical Director of Radiation Oncology Kristina Young, M.D., Ph.D., leads an investigator-initiated Phase II clinical trial testing galunisertib, an experimental immunotherapy for people with colorectal cancer.

Sasha took galunisertib every day for two weeks before starting radiation and chemotherapy. When it came time for surgery, she had completed four weeks of immunotherapy concurrent with six weeks of chemoradiation and experienced few side effects.

This treatment significantly reduced the size of Sasha’s tumor allowing her to recover and better care for her family. This past year, a second colonoscopy revealed she was disease-free.



Galunisertib is an experimental immunotherapy drug.

It attacks cancer at multiple levels, from the mechanisms involved in cancer cell growth to the reinforcement of anticancer immune responses.

When given as an immune-boosting treatment prior to standard care, galunisertib may help more people respond to therapy.



Hagen Kennecke, M.D., joined the Providence Cancer Institute as Medical Oncologist and Medical Director of Gastrointestinal Oncology. He is an active clinician researcher and has received multiple research awards.

Dr. Kennecke is the current chair of the United States National Cancer Institute Rectal-Anal Cancer Task Force.

National Accreditation

Providence Cancer Institute received accreditation by the National Accreditation Program for Rectal Cancer. To achieve NAPRC accreditation, a center must demonstrate compliance with numerous NAPRC standards.

Each rectal cancer program must undergo a rigorous evaluation. For example, as patients prepare for surgery, their medical team needs to prepare clinical regimens of the highest standards. Providence meets this standard by deploying a multidisciplinary rectal cancer team—surgeons, pathologists, radiologists, radiation oncologists, medical oncologists and nurses—who carefully review each patient’s case and work as a team to decide the best plan for care.

Providence Genomics offers faster tumor analysis and more accurate diagnosis

“I see us standing at the precipice of a new era that we could hardly imagine 10 or 20 years ago. People are now eligible for therapies that would have never been given to a patient.”

– Carlo Bifulco, M.D., CMO, Providence Genomics

When cancer is discovered at an advanced stage, every day matters. Thanks to donor support, the Providence team was able to purchase an Illumina NovaSeq 6000 instrument to begin to assess the genetic make-up of tumor cells. The NovaSeq 6000 enables us to significantly increase our throughput and offer comprehensive genomic profiling to all Providence cancer patients.

Comprehensive genomic profiling provides detailed information about a patient’s cancer cells that allows physicians to recommend a personalized treatment plan. Of the 10,000 patients tested at Providence, comprehensive genomic profiling provided actionable results in more than half of the patients tested.

Advocating for Genomic Testing

Comprehensive genomic profiling is mainly performed for patients with late-stage cancer and only after they have exhausted treatment options. Our wish is to make comprehensive genetic testing available to all patients with cancer, regardless of tumor type or previous treatment.

Over the next several years, we aim to use a patient’s genetic make-up to connect them with clinical trials for drugs designed to attack their specific mutations. We will also share with fellow physicians and scientists the benefits of implementing comprehensive genomic profiling immediately after diagnosis.

Molecular Tumor Board

The Providence Molecular Tumor Board is a crucial resource available to Providence caregivers whose patients have tumors with challenging molecular changes. Custom software allows caregivers to



Carlo Bifulco, M.D., uses the NovaSeq, housed at the Providence Molecular Genomics Lab, to study the genetic make-up of a tumor.



present their patient’s data virtually to a team of radiologists, pathologists, oncologists and experts in genetic medicine.

The virtual platform combines patient data from multiple sources allowing the board to analyze digital imaging, the oncology treatment timeline and the genomic profile of the tumor. Together they discuss the best course of treatment including mutation-specific clinical trials. Caregivers also can create cohorts, linking patients who have similar molecular abnormalities, to see how similar patients have fared on their treatments in the past.

Parr Fund provided rental assistance to father with cancer



The team at Providence St. Vincent Medical Center met with 21 patients this year who were exhausted from cancer treatment and unable to afford basic living expenses. The Dwight and Patricia Parr Endowment allowed us to offer emergency assistance to these families when they needed it most.

“Gary” and his young family received assistance from the Parr Fund. Diagnosed with metastatic cancer, Gary was unable to work full-time due to his treatments. Although his wife was working, her salary could not cover their household expenses in addition to Gary’s treatment.

The Parr Fund assisted this family with a \$2,000 grant to pay for three months of rent. This allowed the family to stay in their own home until Gary could resume work. It was also a powerful experience for Gary—that someone he never met cared enough to help him amid tragedy.

Endowed Chair Research Snapshot

“Endowed chairs make a significant difference in our ability to recruit the absolute best talent and creative people. It has been my great pleasure to see us recruit younger, talented individuals in immunology, precision medicine and clinical trials. The best innovative ideas come from these younger, talented colleagues.”

– **Brendan Curti, M.D.**, Robert W. Franz Endowed Chair

At the Earle A. Chiles Research Institute there are five endowed chair positions. They are funded by generous families and individuals who made a lasting gift to support cancer research.

Chair holders and their teams of investigators are collaborating with scientists throughout the field on multiple studies, looking for every way possible to finish cancer. The following is a brief sample of their important work.

Michael Kelley Endowed Chair for Cancer Research

Named in memory of Mike Kelley by his loving family and friends after he lost his battle with head and neck cancer.



Chair Holder: Marka Crittenden, M.D., Ph.D.

Lab Research: Identifying and observing a novel protein that may prevent cancer from detection by the immune system after radiation

Research Implications: If the novel protein can be shut off, patients may have more successful outcomes following radiation

Notes from Dr. Crittenden

“Having treated Mike Kelley, I saw when he was sad or scared. I also saw an enormous sense of strength. I feel a responsibility to him and to the people who cared about him enough to support cancer research.”

Robert W. Franz Endowed Chair for Clinical Research

Named in memory of Robert W. Franz after his lifetime of service to Providence and the greater Portland community



Chair Holder: Brendan Curti, M.D.

Top Research: Galectin-3 inhibition combined with anti-PD-1 immunotherapy in patients with advanced melanoma and head and neck cancer

Research Implications: Treatment combination has the potential of increasing response and decreasing side effects of checkpoint immunotherapy in several tumor types

Notes from Dr. Curti

“We have set the bar very high by focusing on solid tumors like melanoma, kidney cancer, pancreatic cancer, and head and neck cancer. If we can routinely cure those patients with advanced disease, then we will have made a huge difference in cancer therapy.”



New Drug in Development to Protect Immune Cells

Matthew Taylor, M.D., led a team in the development of an antibody to block fas ligand—a protein that leads to death of immune cells.

Dr. Taylor and his team developed a prototype drug (a monoclonal antibody) that may aid in protecting immune cells against death induced by fas ligand. If testing reveals the antibody to be safe and effective, we plan to produce large quantities in preparation for a clinical trial.

“Our work to develop a new therapy to support the immune system as it fights cancer is moving along very well. Thanks to the generosity of our donors, we have cleared a major hurdle in developing a prototype drug that protects the cells of the immune system.”

One of the major obstacles in treating cancer is that the cells of the immune system are frequently killed when they attempt to attack tumors. We are developing a drug that inactivates a critical protein within tumors that contributes to killing immune system cells.

We are now in the second phase of development which involves refining and improving the drug in preparation for clinical trial testing. We still have a lot of work to do but we are excited to see this work advancing rapidly.”

For more information contact:

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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

