EARLE A. CHILES RESEARCH INSTITUTE
A division of Providence Cancer Institute at the Robert W. Franz Cancer Center

2018 Year in Review
## TABLE OF CONTENTS

- **DIRECTOR’S MESSAGE** ......................................................... 1
- **NEW & NOTEWORTHY** ..................................................... 2
- **RESEARCH HIGHLIGHTS** .................................................. 8
- **CORE FACILITIES** ............................................................ 14
- **EDUCATION & TRAINING** ................................................. 15
- **PROVIDENCE CANCER INSTITUTE** ................................... 16
- **PHILANTHROPY** ............................................................... 18
- **PUBLICATIONS** ............................................................... 20
- **FACTS & FIGURES** ........................................................... 22
- **LEADERSHIP** ................................................................. 23

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### ON THE COVER:

Mike Ritchey is healthy, happy and cancer-free thanks to an innovative clinical trial at Providence Cancer Institute combining immunotherapy and radiation therapy for patients with head and neck cancer. See Page 4.

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### EARLE A. CHILES RESEARCH INSTITUTE

A leader in cancer immunotherapy research and innovation since 1993, the Earle A. Chiles Research Institute is a world-class research facility, and home to a team of internationally known scientists and physicians.

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We are delighted to share with you our highlights from another exciting year in cancer medicine and research.

2018 marked a significant milestone in the era of cancer immunotherapy. The Nobel Prize in Physiology or Medicine was awarded to two immunotherapy researchers – James Allison, Ph.D., and Tasuku Honjo, M.D., Ph.D. – for their work uncovering how the immune system attacks cancer.

Their discoveries led to the development of the FDA-approved immune checkpoint therapies we have today. As the center which led the global clinical trial of one of those therapies – ipilimumab, we are delighted our contributions helped achieve this monumental honor and important recognition.

Another exciting advancement came with the FDA approval of the first immunotherapy for breast cancer, and we are proud of our contributions to the clinical trial which prompted the accelerated approval.

2018 also marked the expansion of clinical and research space at the Robert W. Franz Cancer Center. Our newly opened Franz Clinic allows us to serve more patients with cancer, and an additional 10,000 square feet of space dedicated to cancer research enables us to recruit more investigators.

From our humble beginnings, our team has grown to more than 150 investigators and research personnel, including 22 faculty members recognized globally for their pioneering contributions to cancer immunotherapy. From detecting and treating cancer in its earliest stages to developing new therapies for the most pernicious cancers, our researchers are united in their aim to advance cancer medicine.

With the growth of our genomics and bioinformatics teams, Providence oncologists can now recommend highly personalized treatment plans based on the unique genetic profiles of patients’ tumors. Coupled with the development of our adoptive cellular therapy programs, including CAR T-cell therapy, we are at the forefront of precision immuno-oncology.

Our growth would not have been possible without the support of major benefactors like Robert W. Franz and his sister, Elsie Franz Finley. Together, they helped equip us for state-of-the-art care and translational research for many years to come. Their generosity and leadership inspire us to press forward with an unwavering commitment to improving the lives of patients with cancer.

We all are touched by cancer, and we all have a role to play in the pursuit of a cancer-free future. I invite you to join us on our journey. With your support, together we can finish cancer.
NEW ADDITIONS AND NOTEWORTHY ACHIEVEMENTS

New labs enhance research portfolio
With the addition of 10,000 square feet of lab and office space in the Earle A. Chiles Research Institute – located on the second floor of the Robert W. Franz Cancer Center, we are expanding the scope of our investigations to treat and cure cancer. The $5 million expansion was funded by a bequest from Robert W. Franz. The space includes a beautiful conference room named in honor of his sister, the late Elsie Franz Finley. Space for highly specialized equipment, tissue culture rooms and 13 new lab bays allows us to recruit more investigators. These include cancer immunologist Thomas Duhen, Ph.D., genomic scientist Brian Piening, Ph.D., and computational and systems biologist Brady Bernard, Ph.D., who joined our faculty as assistant members to embark on promising new areas of cancer research.

Dr. Duhen served as senior scientist at AgonOx, a biotech spinoff led by Andrew D. Weinberg, Ph.D., member and Judith Ann Hartmann Endowed Chair for the Laboratory of Basic Immunology. Working in partnership with his Providence colleagues, Dr. Duhen identified a novel immune cell population capable of recognizing and eradicating tumors. The discovery led to a prominent article in Nature Communication, and may provide clinicians with therapeutic strategies for cancer patients for many years to come. Dr. Duhen’s newly formed Anti-Cancer Immune Response Lab will continue his research in tumor-reactive T cells with a focus on colorectal cancer and head and neck cancers.

Drs. Piening and Bernard were instrumental to the recent expansion of the Portland-based Molecular Genomics Lab, which has grown from a regional genome sequencing resource to the flagship center of the Providence St. Joseph Health Personalized Medicine Program. In addition to his role as technical director of Clinical Genomics, Dr. Piening leads the Cancer Immuno-Genomics Lab, while Dr. Bernard leads the Computational Immuno-Oncology Lab along with his ongoing efforts as associate director of Bioinformatics. Learn more on Page 10.

Inaugural Immuno-Oncology Fellowship
Launched in 2018, this 12-month research fellowship provides structured education and training in clinical cancer immunotherapeutics from our expert faculty. Fellows receive a foundation in research methodology to prepare them for successful academic careers in immuno- oncology. Curriculum includes protected time to conduct mentored, independent research, and rotations in medical oncology, inpatient immunotherapy service, immune monitoring and clinical trials. Learn more on Page 15.

First immunotherapy approval for breast cancer
Metastatic triple-negative breast cancer is a formidable disease. “The average survival is usually less than two years,” said Alison Conlin, M.D., MPH, associate member and medical director, Providence Breast Cancer Medical Program and High-Risk Breast Clinic. Thanks to researchers such as Dr. Conlin and patients who participated in a groundbreaking clinical trial, immunotherapy may improve survival for women with this aggressive form of breast cancer.

That’s the power of participating in a clinical trial.

From top left: Dr. Piening and Dr. Bernard; Dr. Duhen; new lab space; and inaugural immuno- oncology fellows Dr. Katherine Sanchez and Dr. Marcus Couey.

Breast Cancer Immunotherapy, were among the first investigators worldwide to open a clinical trial of atezolizumab – an immune checkpoint inhibitor – combined with a common chemotherapy. By inhibiting the immune checkpoint protein PD-L1, atezolizumab unleashes the immune system, enhancing the ability of immune cells to find and attack cancer cells.

“One of our first patients to join the trial more than three years ago continues in treatment today,” Dr. Conlin said. “It’s truly remarkable. These patients have helped change the lives of so many women after them. That’s the power of participating in a clinical trial.” The FDA granted accelerated approval in early 2019, marking the first immunotherapy approved for breast cancer.
Leading by example

Elsie Franz Finley and her brother Robert W. Franz were a major philanthropic and visionary force within Providence for more than 30 years. Their longstanding support helped us become one of the foremost cancer immunotherapy centers in the world. The Robert W. Franz Cancer Center, the Elsie Franz Finley Scholarship for Nursing Excellence and the Robert W. Franz Chair for Clinical Research are among the many tributes to honor their unmatched generosity to Providence Cancer Institute. Learn more on Page 18.

Franz Clinic serves more patients

The 11th floor of the Robert W. Franz Cancer Center opened in October 2018. This new space allows us to expand and consolidate our outpatient cancer services in the new Providence Cancer Institute Franz Clinic. This will enhance our care for the 6,000 oncology patients we see every year – and the hundreds more we will be able to serve. Services offered include thoracic surgery; head and neck surgery; a specialty dentistry clinic; a cancer genetics program and genetic risk clinic; expanded infusion spaces; and a specialty pharmacy. Having all these services located in one space eases the way for our patients and gives them increased access to clinical trials and promising new research.

Franz Chair for Clinical Research

Since his arrival at the Earle A. Chiles Research Institute in 2002, Brendan Curti, M.D., member and director, Cytokine and Adoptive Immunotherapy Program and Providence Melanoma Program, is determined to help patients receive the best treatment possible as they face cancer.

Dr. Curti is an expert in translational research – taking ideas generated by scientists in the lab and translating them into clinical trials for patients with melanoma, kidney, bladder, prostate and other types of cancer. He leads numerous clinical trials to improve patient survival rates, and more than half of his patients volunteer for experimental therapies. In recognition of his many achievements, Dr. Curti is the first recipient of our Robert W. Franz Endowed Chair for Clinical Research.
A rich reward

“What about immunotherapy?”

Those three words changed Mike Ritchey’s life.
Ritchey had been diagnosed with head and neck squamous cell carcinoma, commonly referred to as head and neck cancer. The 75-year-old saw his primary care doctor about a small bump on his neck. “It was just a tiny knot,” said Ritchey. But after an ultrasound revealed it was cancer, Ritchey found himself in the office of Allen Cheng, M.D., D.D.S., FACS, a head and neck surgeon affiliated with Providence Cancer Institute.

With his wife Susan at his side, Ritchey learned his outlook was promising. The cancer was detected very early, before it had spread. Dr. Cheng reviewed the standard treatment: surgery to remove the cancer, followed by a long course of chemotherapy and radiation therapy. “Dr. Cheng gave me the gruesome details of what was going to be my immediate future,” said Ritchey. “And it sounded awfully rugged, and he told me it was. He didn’t pull any punches.” They scheduled the surgery.

Then, just as they were leaving, Ritchey remembered those forward-thinking, progressive treatments he’d read about. A retired newspaper publisher and journalist, he’d always been interested in medical advances. “What about immunotherapy?” he asked.

Dr. Cheng stopped in his tracks. He shares a clinical practice with Bryan Bell, M.D., D.D.S., FACS, associate member and medical director, Providence Head and Neck Cancer Program and Clinic. Dr. Bell and his colleagues at Providence Cancer Institute are leaders in immunotherapy for head and neck cancer.

“I know of a clinical trial about to get started,” said Dr. Cheng. “And it sounded awfully rugged, and he told me it was. He didn’t pull any punches.” They scheduled the surgery.

In the Name of Science
The illustration on the postcard showed a medical attendant wheeling in a gurney to the surprise of a healthy, living patient. The caption read, “You the guy who donated your body to science?”

It was from Mike Ritchey, with a personal inscription: “Hello, Dr. Leidner. Colorado misses you. See you 11 a.m. July 18.”

“Mike is the first patient to send me a card that he is excited to see me in cancer clinic,” said Rom Leidner, M.D., assistant member and co-director, Providence Head and Neck Cancer Program.

Ritchey’s enthusiasm is well-founded. Dr. Leidner and colleagues saved his life. Ritchey, who lives part of the year in Portland and the rest in Gunnison, Colorado, was due for his postsurgical checkup. “It was really a stroke of luck how it happened,” Ritchey said.

With a referral from Dr. Cheng, Ritchey was the first patient to enroll in a new clinical trial at Providence Cancer Institute for patients with head and neck cancer.

“The next thing I know I’m in this clinical trial, meeting Dr. Leidner and Dr. Marka Crittenden. The surgery was the same, except for the beforehand treatments. I only had five light doses of radiation, and 10 immunotherapy treatments – about 15 minutes per treatment.”

A Better Therapy
Marka Crittenden, M.D., Ph.D., associate member and director, Translational Radiation Research, along with Dr. Leidner, Dr. Bell and Kristina Young, M.D., Ph.D., assistant member, Tumor Microenvironment Lab, had long believed a better therapy was needed for patients with head and neck cancer.

Although patients with early stages of this disease benefit from high survival rates, many suffer from lifelong, debilitating side effects. The standard course of treatment – surgery, chemotherapy and radiation – is known to cause dental decay, tooth loss and dry mouth, among other problems affecting quality of life. Many patients find they are unable to continue with everyday social events, like sharing a meal with friends or co-workers.

“We sought to design a trial that offers these patients the same survival outcomes as standard therapy while sparing them from the harmful side effects,” said Dr. Leidner. Together with Drs. Crittenden, Bell and Young, he devised a clinical trial combining immunotherapy and radiation therapy as a means of down-staging cancer before surgery. Dr. Crittenden and colleagues at Providence were among the first to demonstrate a
synergy between immunotherapy and radiation therapy in patients with melanoma.

The phase I study, known as NIRT: Neoadjuvant Immuno-RadioTherapy in Head and Neck Cancer, is the first study worldwide to evaluate the safety and effectiveness of radiation therapy and nivolumab, an anti-PD-1 immune checkpoint inhibitor approved for several cancers, given to patients with head and neck cancer before surgery. And, if needed, standard-of-care chemotherapy and radiation would be given following surgery to eliminate any residual microscopic disease.

“Instead of broadly radiating the neck and oral cavity – common procedure with standard care, we chose to focus the radiation to the precise location of the cancer,” said Dr. Crittenden. “Normal tissue is spared, such as healthy salivary glands needed to avoid tooth decay and dry mouth.”

Another benefit of radiation therapy is its immune-stimulating function. Radiation has potential to propagate an immune attack against cancer at the radiation treatment site and also against unknown microscopic disease located outside the treatment field.

When combined with a potent PD-1 inhibitor such as nivolumab, radiation is an effective treatment strategy for shrinking cancers before surgery.

OF PRIMARY IMPORTANCE
Eliminating cancer at the treatment site and priming an anticancer immune response against microscopic disease are essential to preventing cancer recurrence, particularly in patients whose primary sites of cancer are unknown.

Such was the case for Mike Ritchey. His ultrasound showed a malignant mass in his right neck and three affected lymph nodes, but the origin of his cancer was unidentified. That was until Dr. Cheng performed surgery.

Ritchey had completed his short course of radiation therapy to his right neck and lymph nodes, and received several intravenous immunotherapy treatments. Another presurgical scan indicated the immuno-radiotherapy combination shrunk the cancer in his neck.

But when Dr. Cheng began surgery, what he found was remarkable: Ritchey’s cancer had vanished. The mass on his neck and all affected lymph nodes were cleared of disease. And his right tonsil – which was confirmed...
There is no better place to run into cancer than Providence and its powerful squad of healers.

as the cancer’s origin – showed evidence of tumor regression despite having received no direct radiation.

Ritchey was cancer-free, thanks to immuno-radiotherapy, and he felt great. “I never experienced one single side effect, it was just lickety-split,” said Ritchey. “Even friends of mine are wide-eyed, in disbelief, that I’ve never felt bad.”

Through it all Susan was at his side. “We double-teamed it. She went to every session with me – visits with Dr. Leidner, Dr. Cheng, Dr. Crittenden – taking notes and asking questions. Even though we’ve been married 46 years, our relationship prospered further by the experience.”

With his treatments behind him, they could return to activities they loved, like treks to Mount Tabor Park or strolling along Hawthorne Street, stopping at Powell’s Books. “We’ve always been outdoorsy and active,” recalled Ritchey. “We started coming to Portland because our daughter Marianna went to Lewis and Clark College. She graduated in the late ‘90s, but we just kept coming, because we love Portland so much.”

PERFECT 10

Ritchey is not the only patient to benefit from the innovative study. Ten patients with head and neck cancer were enrolled to the trial. All patients received radiation therapy and immunotherapy followed by surgical resection five weeks later. None experienced unplanned, treatment-related delays to surgery. At the time of surgery, nine patients were found to be cancer-free and one patient had less than 10 percent of cancer remaining, which was removed by surgery. None required chemotherapy or radiation after surgery.

“Our hope with this study was to deintensify treatment for better quality of life. The results have changed everything,” said Dr. Leidner. By changing both the treatment field and therapeutic modalities, Drs. Leidner, Crittenden, Bell and Young have introduced a potential alternative to standard care for patients with early-stage head and neck cancer, offering comparable survival and superior outcomes for tooth loss, dry mouth and other lifelong ailments.

Investigators across the world are taking notice. Dr. Crittenden reported early results at a joint meeting of the American Society of Clinical Oncology and Society for Immunotherapy of Cancer, and Dr. Bell presented the study to the American Head and Neck Society. At the 2019 annual meeting of the American Association for Cancer Research, Dr. Leidner gave an oral presentation at the Clinical Trials Plenary Session. “This study represents a major paradigm shift in the approach to treating locally advanced HPV-positive head and neck cancer,” Dr. Leidner said.

HPV – human papillomavirus – is associated with several cancers, including head and neck cancer. A new study cohort was added to evaluate the treatment strategy in patients with HPV-negative head and neck cancer. HPV-negative patients have the worst survival outcomes for this disease.

AN UPSIDE TO CANCER

Following their brush with cancer, Mike and Susan Ritchey are enjoying all that life has to offer. When not in Oregon or Colorado, they can be found in Massachusetts and Hawaii. Their daughter Marianna teaches musicology at the University of Massachusetts in Amherst, and their son Buck works in construction in Maui.

“I’m just on cloud nine here, riding a big wave, instead of something that could have been entirely different,” said Ritchey. “And don’t think for a minute I don’t realize it.” Ritchey returns to Providence Cancer Institute regularly for checkups with Drs. Leidner and Crittenden.

“I can’t honestly recommend it, but cancer can have an upside,” Ritchey said. “The opportunity to meet the doctors, nurses and staff – had I not gone through this fire, I would have been poorer for it. There is no better place to run into cancer than Providence and its powerful squad of healers. I am indebted to the entire system.”
Phase I progress

With the advent of personalized medicine, the need for more sophisticated early-phase clinical trials has emerged. Whereas classical models of phase I/II studies sought to determine the dose selection and safety profile of an investigational therapy, these studies have evolved to evaluate a bevy of clinical criteria including immune-based and genetic biomarkers.

Rachel Sanborn, M.D., associate member and director, Phase I Clinical Trials Program, oversees a robust early-phase clinical trials portfolio comprising immunotherapies, targeted therapies and other novel agents under investigation at Providence Cancer Institute. Together with Rom Leidner, M.D., assistant member and co-director, Providence Head and Neck Cancer Program, Brendan Curti, M.D., member and Franz Chair for Clinical Research, and a dedicated team of oncology nurses, research associates and coordinators, she leads one of the foremost programs of phase I cancer research on the West Coast.

Providence Cancer Institute offers the largest volume of phase I cancer studies in Oregon. Fifty phase I/II studies were open for enrollment in 2018, comprising more than 100 patient enrollments to trials for cancers of the lung, skin, breast, blood, head and neck, and several other malignancies. Half of the studies were open to patients with multiple tumor types.

Traditionally phase I/II studies were limited to patients with advanced disease. “More studies are now designed for patients with localized disease – before the cancer has spread,” said Dr. Sanborn. “And we are seeing more clinical activity and less toxicity in phase I studies.”

Other hallmarks of modern phase I studies are the early introduction of experimental treatments in
clinical care – whether in combination with standard care or as first-line treatment, and the incorporation of multiple patient cohorts. “Patients now have quicker access to investigational therapies. By designing studies with multiple cohorts, we have a process to fine-tune and adapt therapies to benefit the greatest number of patients,” Dr. Sanborn said.

The upshot: a lengthy regulatory approval process is compressed, and promising new therapies are brought to market more quickly.

PROVIDENCE SHARES IN ASCO SPOTLIGHT
At the 2018 annual meeting of the American Society of Clinical Oncology (ASCO), two of nine studies highlighted at the popular oral abstract session for Developmental Therapeutics – Immunotherapy were from the Providence phase I portfolio.

Patients now have quicker access to investigational therapies.

Dr. Sanborn presented results of a phase I/II study investigating varlilumab, an immune-stimulating antibody, in combination with nivolumab, an anti-PD-1 checkpoint inhibitor approved for several cancers. The combination has been shown safe and effective in patients with advanced cancers that have resisted prior therapies, including melanoma and head and neck cancer. The trial expanded to include patients with colorectal and ovarian cancers.

“PD-1 inhibition combined with a potent T-cell activating agent broadens the number of patients that may benefit from checkpoint therapy, particularly those who are unlikely to respond to other therapies,” said Dr. Sanborn.

2018 PHASE I/II STUDIES AT PROVIDENCE CANCER INSTITUTE:
- 50 phase I/II studies totaling more than 100 patient enrollments for more than 10 tumor types

STUDIES BY TUMOR TYPE
- Lung 14%
- Skin 10%
- Breast 8%
- Other 18%

STUDIES BY SPONSOR
- Cooperative group or external reviewer: 4
- Industry-sponsored: 41
- Investigator-initiated: 5

FIGURES: Fifty phase I/II studies were open for enrollment at Providence Cancer Institute in 2018, comprising more than 100 patient enrollments for multiple types of cancer including lung, skin, breast, blood, head and neck, genitourinary and gastrointestinal cancers. Twenty-five of the studies were open to patients with multiple tumor types. Four studies were sponsored by cooperative groups or other external reviewers, 41 studies were sponsored by industry and five studies were initiated by investigators at Providence Cancer Institute.

PHASE I TEAM FROM TOP LEFT: Tara Foote, RN; Ashley Drokin; Mitch Clemens; Kate Tripp, RN; Melissa Pomeroy, RN; Mollie Fehribach; Kimberly Perry; Carlee Abel; Katrina Herz; Rachel Sanborn, M.D., Rom Leidner, M.D. Not pictured: Brendan Curti, M.D.; Kim Sutcliffe, RN.
FROM LEFT: Carlo Bifulco, M.D., member and medical director, Oncologic Molecular Pathology and Pathology Informatics; Brady Bernard, Ph.D., assistant member and associate director, Bioinformatics; Brian Piening, Ph.D., assistant member and technical director, Clinical Genomics; and Eric Tran, Ph.D., assistant member, Anti-Tumor T-cell Response Lab.
Precision immuno-oncology

Thanks to recent advances in genomics and cancer immunotherapy, the era of precision immuno-oncology has arrived. It is now possible for Providence oncologists to recommend highly personalized treatment plans – including approved and experimental immunotherapies – based on a patient’s unique genetic profile and the likelihood of treatment response.

Coupled with advances in experimental techniques, cloud computing and machine learning, our scientists are poised to develop predictive models for genomic biomarkers and new therapeutic targets deemed most effective for individual cancer patients.

GENOMICS EXPANSION

The Portland-based Providence St. Joseph Health Molecular Genomics Lab, led by Carlo Bifulco, M.D., member and medical director of Oncologic Molecular Pathology and Pathology Informatics, and Brian Piening, Ph.D., assistant member and technical director of Clinical Genomics, is one of the largest clinical genomics labs in the Pacific Northwest. Located within walking distance of the Robert W. Franz Cancer Center, the lab now serves cancer patients from all Providence locations in Alaska, Washington, Oregon, California, Montana, New Mexico and Texas.

While cancer treatment plans were once largely limited to surgery, chemotherapy and radiation, new classes of personalized therapies are targeted to genetic mutations – changes in the DNA sequence of a cancer cell. The lab identifies individual tumor mutations to guide development of customized treatment plans unique to each patient.

Drs. Bifulco and Piening use the latest in next generation sequencing technology to rapidly and simultaneously test many genomic biomarkers from small tumor tissue samples in a matter of days. By sequencing the tumor DNA and RNA, they can map out genetic mutations that are inherited from family, caused by environmental factors or both.

COMPUTATIONAL BIOINFORMATICS

The lab’s designation as the Providence systemwide genomics leader would not have been possible without the contributions of Brady Bernard, Ph.D., assistant member and associate director of Bioinformatics, and a team of bioinformatics scientists and software engineers.

In collaboration with Drs. Bifulco and Piening, the team developed custom-built bioinformatics pipelines and sophisticated computational models necessary for the generation and integrative analysis of high-throughput genomics data.

As the number of clinically significant biomarkers increases, genome sequencing and computational bioinformatics will play critical roles in customized cancer diagnosis and treatment.

GENOME-GUIDED ADOPTIVE IMMUNOTHERAPY

Genetic mutations make cancer cells different from normal cells, and some of these differences can be recognized and targeted by T cells in a patient with cancer.

We now know that adoptive immunotherapy can mediate durable responses, and sometimes cures, in these otherwise incurable cases.

Since his arrival in 2017, Eric Tran, Ph.D., assistant member, Anti-Tumor T-cell Response Lab, continues to build his adoptive immunotherapy program focused on harnessing these mutation-reactive T cells for patient therapy.

With few exceptions, the mainstays of cancer therapy – surgery, chemotherapy and radiation – are not curative for patients with metastatic cancers, especially solid-tissue cancers. “We now know that adoptive immunotherapy can mediate durable responses, and sometimes cures, in these otherwise incurable cases,” said Dr. Tran.

This approach entails identifying mutation-reactive T cells from a patient with cancer and then amplifying them to large numbers in the lab, followed by infusion of the cells back into the patient. Since each cancer has a completely unique mutation profile, each patient will have a unique repertoire of mutation-reactive T cells, making this therapy highly personalized.

In collaboration with his colleagues in medical and surgical oncology, Dr. Tran is developing clinical trials for patients with epithelial cancers – cancers of the skin and tissues lining the organs and cavities inside the body – whose cancers are predicted to recur within three years. These include pancreatic cancer and cholangiocarcinoma, cancers with some of the worst survival outcomes.

Dr. Tran worked closely with Drs. Bifulco, Piening and Bernard to develop the bioinformatics pipeline necessary to identify genetic mutations associated with epithelial cancers. “We are working toward enhancing the pipeline to identify other types of genetic alterations in cancer that might be targetable with adoptive T-cell therapy,” said Dr. Tran. “We hope to offer patients therapy with mutation-reactive T cells in the next year.”

Learn more about adoptive T-cell therapy on Page 14.
A PROMISING OUTPATIENT THERAPY

Nearly a decade has passed since the first patient with B-cell lymphoma, a type of Non-Hodgkin lymphoma, received an infusion of T cells engineered to express a synthetic chimeric antigen receptor (CAR) targeting the CD19 antigen – a protein expressed on the surfaces of normal and malignant B cells. Like other T cells, CAR T cells are also endowed with an immune-activating receptor.

Named for the mythological hybrid creature Chimera, it is this dual-purpose function of antigen targeting and immune activation that gives CAR T cells their anticancer potency. Subsequent studies of CD19-targeted CAR T-cell therapy showed a complete response in patients with relapsed or chemotherapy-refractory lymphomas for whom there were no effective therapies.

Because of the complexity of CAR T-cell therapy and its challenging side effects – including fever, low blood pressure, anemia and even seizures, it had been limited to inpatient treatment at university medical centers.

Yet most patients with relapsed or refractory large B-cell lymphoma receive therapy at community medical centers in the outpatient setting. And thanks to a new clinical trial, some of these patients can now receive CAR T-cell therapy.

A BRIGHT FUTURE FOR BILL RICHARDSON

Bill Richardson went from planning his funeral to planning his future. He was given six weeks to live after several chemotherapy treatments proved unsuccessful against his large B-cell lymphoma.
“I met with a funeral director. I worked on my life history, worked on my obituary,” said Richardson, a 71-year-old husband, father and grandfather. Then his Providence medical oncologist, Stacy Lewis, M.D., suggested he consider a new CAR T-cell clinical trial led by John Godwin, M.D., MS, member and program leader, Hematologic Malignancies. Providence Cancer Institute is one of 11 centers in the U.S. to offer the phase II trial.

We are at the beginning of a potential revolution with this treatment.

This personalized therapeutic approach entails the removal of peripheral-blood T cells from a patient, followed by in vitro activation, genetic modification and expansion of the T cells in a production facility before they are rein infused back into the patient.

“For me, it was an easy decision. I was either going to check out really soon or I was going to check out a little later. So I signed the paper,” Richardson said. After receiving the treatment, he felt immediate relief.

“We examined him at 30 days, but he could feel the difference overnight,” said Dr. Godwin. Four weeks after receiving his CAR T-cell infusion, Richardson underwent a PET scan. His tumors had disappeared. And he experienced none of the debilitating side effects.

Dr. Godwin is thrilled with Richardson’s results and continues working with other patients in the trial. “This is so new. We are at the beginning of a potential revolution with this treatment,” he said.

“Every day I’m feeling better,” said Richardson. “There are lots of things I have left to do in this life.”
RESEARCH FACILITIES AND SERVICES

The Earle A. Chiles Research Institute was built and designed specifically for translational research, with 45,000 square feet dedicated to cancer research. Basic science laboratories are located in close proximity to medical and radiation oncology clinics, operating suites and patient rooms. This environment is ideal for translating the most promising preclinical discoveries into novel treatments for patients with cancer.

Our investigators and collaborators benefit from several core facilities specializing in state-of-the-art cancer research technology and services, including:

- Biospecimen Repository
- Flow Cytometry Lab
- Human Applications Lab
- Immune Monitoring Lab
- Immuno-Histology Core
- Molecular Pathology Core

Our longstanding collaboration with the Medical Data Research Center at Providence St. Vincent Medical Center ensures our researchers receive robust biostatistical analysis and support. Several other shared facilities are accessible through faculty appointments at Oregon Health & Science University.

SPOTLIGHT ON HUMAN APPLICATIONS LAB

Our Human Applications Lab (HAL) is a therapeutic manufacturing facility with Good Manufacturing Practice designation. This ultrastereile environment makes HAL essential to our translational research, allowing for the processing of autologous and allogeneic products administered to patients participating in clinical trials at Providence Cancer Institute. HAL is also key to the development of tumor cell lines and tumor-infiltrating lymphocytes from patient specimens, and the processing of apheresis products for reinfusion.

These services are vital to our Anti-Tumor T-cell Response Lab, led by Assistant Member Eric Tran, Ph.D. Dr. Tran is an expert in adoptive immunotherapy – a process in which a patient’s tumor-reactive T cells are expanded in culture, and reinfused to the patient in greater numbers. The identification, selection and isolation of a patient’s tumor-reactive T cells from thousands of other T cells is a critical component of adoptive immunotherapy.

Dr. Tran and his lab work closely with Miranda Gilchrist, manager, Flow Cytometry Lab, to purify the tumor-reactive T cells using flow cytometry-based cell sorting. Thanks to a gift from the late Elsie Franz Finely, a new Sony FX500 cell sorter was installed. "Purity and sterility were the highest priority when considering a cell sorter to be used for therapies in patients,” said Gilchrist. “We are grateful to donors like Elsie for their generous support.”

Miranda Gilchrist, manager of the Flow Cytometry Lab, uses the Sony FX500 cell sorter to purify patients’ tumor-reactive T cells. Through philanthropic support, the cell sorter was installed in our Human Applications Lab to enhance our translational research capabilities.
TRAINING PROGRAMS

As part of our mission to train the next generation of immunologists, the Earle A. Chiles Research Institute offers a rich training environment spanning the continuum of higher education, from undergraduates to postdoctoral fellows:

- Graduate education
- Immuno-Oncology Fellowship
- Postdoctoral training
- Summer Research Program

Past trainees continued their education at the National Cancer Institute, Mayo Clinic Graduate School of Biomedical Sciences and Northwestern University School of Medicine, among others, and received funding from the NIH Pathway to Independence Award, American Cancer Society, Prostate Cancer Foundation and Susan G. Komen.

SPOTLIGHT ON SUMMER RESEARCH PROGRAM

An intensive nine-week internship for undergraduate students, this program provides hands-on research experience and mentoring for students pursuing careers in biomedical sciences.

No matter what path I take, research will always be the cutting edge of medicine, and I want to be a part of that to support discovery.

Students complete an independent research project and present their results at a capstone poster symposium. As one student described, “I really appreciated that my lab had a full project ready for me to conduct pseudo-independently; this allowed me to complete a full project start to finish.”

They also receive training in bioinformatics and attend department seminars and meetings where recent journal articles are reviewed and discussed. “The academics behind the work were very fascinating to me,” said another student. “I had never learned of my research topic before this, and I have a lot of respect for researchers in this field now.”

In summing up the experience, another student shared, “I certainly see that no matter what path I take, research will always be the cutting edge of medicine, and I want to be a part of that to support discovery.”
Excellence in gastrointestinal cancers

Gastrointestinal (GI) cancers, when considered together, account for the highest incidence of cancer in the U.S. These include cancers of the GI tract – from the esophagus and stomach to the small intestine, colon and rectum; and hepatobiliary cancer – cancers of the liver, pancreas, bile ducts and gallbladder. Providence Cancer Institute is home to several clinics and programs specializing in the latest treatments, technology and research for patients with GI cancers, including:

- **Providence Colorectal Cancer Program and Anal Dysplasia Clinic** led by Medical Director Mark Whiteford, M.D., FACS, FACRS, colon and rectal surgeon.
- **Providence Hepatobiliary and Pancreas Cancer Program** led by Medical Director Paul Hansen, M.D., FACS, liver and pancreas surgeon.
- **Providence Liver Cancer Clinic** led by Medical Director Pippa Newell, M.D., assistant member and liver and pancreas surgeon.

Providence patients benefit from innovative and personalized care, from screening and diagnostic procedures to cancer treatment and surveillance. Our clinicians work in collaboration with multiple specialists including gastroenterologists, surgeons, pathologists, radiation and medical oncologists, immunologists, cancer genetics experts, oncology social workers and nurse navigators. Patient cases are presented at weekly conferences for expert consultation from a multidisciplinary care team.

PROVIDENCE EXCEEDS COLORECTAL CANCER BENCHMARKS

Patients treated according to national guidelines for cancer care have the best survival rates and quality of life. Providence Cancer Institute meets or exceeds the targets for colorectal cancer set by the Commission on Cancer, and survival outcomes of our colorectal patients surpass the national average.

**Colorectal cancer performance measures**

- **Panel A:** At least 12 regional lymph nodes are removed and pathologically examined for colon cancer (CoC benchmark).
- **Panel B:** Preoperative chemo and radiation are administered for clinical AJCC T3N0, T4N0, or stage III; or postoperative chemo and radiation are administered within 180 days of diagnosis for clinical AJCC T1-2N0 with pathologic AJCC T3N0, T4N0, or stage III; or treatment is recommended for patients under the age of 80 receiving resection for rectal cancer (CoC benchmark).
- **Panel C:** Adjuvant chemotherapy is recommended or administered within 120 days of diagnosis for patients under the age of 80 with AJCC stage III, lymph-node-positive colon cancer.

Commission on Cancer (CoC) guidelines compared to Providence performance for 2018:

- (a) At least 12 regional lymph nodes are removed and pathologically examined for colon cancer (CoC benchmark); (b) Preoperative chemo and radiation are administered for clinical AJCC T3N0, T4N0, or stage III; or postoperative chemo and radiation are administered within 180 days of diagnosis for clinical AJCC T1-2N0 with pathologic AJCC T3N0, T4N0, or stage III; or treatment is recommended for patients under the age of 80 receiving resection for rectal cancer (CoC benchmark); (c) Adjuvant chemotherapy is recommended or administered within 120 days of diagnosis for patients under the age of 80 with AJCC stage III, lymph-node-positive colon cancer. In the absence of CoC benchmark, outcomes are compared to internal quality standards.

**Five-year relative survival rates: colorectal cancer**

The five-year relative survival rates for Providence patients diagnosed with colorectal cancer in years 2008 to 2014, compared to national averages provided by the National Cancer Institute Surveillance, Epidemiology and End Results (SEER) Program.
PROVIDENCE WELCOMES GI PHYSICIAN RESEARCHER

Medical oncologist Gina Vaccaro, M.D., joined the GI care team at Providence Cancer Institute in 2018. Dr. Vaccaro specializes in the evaluation and treatment of cancers of the GI tract. She works closely with all members of our care team, including Drs. Hansen, Newell and Whiteford, to offer patients the highest quality of care.

Dr. Vaccaro is an active clinical investigator with experience leading studies of novel therapies, such as experimental targeted therapies, immunotherapies and combination therapies. Several studies led by Dr. Vaccaro are underway, including a phase III multicenter study for patients with unresectable or metastatic bile duct cancer, also known as cholangiocarcinoma. Although cholangiocarcinoma is a rare cancer, few treatment options exist for patients whose cancers have progressed after first-line chemotherapy.

The study, known as FIGHT-302, compares the safety and effectiveness of standard chemotherapy to pemigatinib – an experimental therapy targeting gene alterations of fibroblast growth factor receptor 2. Pemigatinib has shown anticancer potency in cholangiocarcinoma patients whose tumors express this gene alteration.

“Our hope is to offer effective targeted therapy with fewer side effects than chemotherapy, resulting in improved quality of life,” said Dr. Vaccaro.

ABOVE: Gina Vaccaro, M.D., medical oncologist, Providence Cancer Institute.
AT RIGHT: Paul Hansen, M.D., FACS, liver and pancreas surgeon; Pippa Newell, M.D., assistant member and liver and pancreas surgeon; and Mark Whiteford, M.D., FACS, FACRS, colon and rectal surgeon. Drs. Hansen, Newell and Whiteford are medical directors of Providence Cancer Institute and specialists of The Oregon Clinic.
Providence remembers Elsie Franz Finley

Elsie Franz Finley will be forever remembered as a pioneering business woman, loving wife and sister, friend, community leader and philanthropist. She generously gave her time, talents and treasure to the community she loved. Providence was blessed to have been one of Elsie’s favorite organizations and the place she trusted with her health care.

Elsie was born in Portland and was a longtime resident of Vancouver, Washington. She was preceded in death by her husband, Don Finley, her brother Robert W. (Bob) Franz, and her parents Joseph Franz and Elizabeth Streib Franz. Together, Elsie and her brother had an enormous impact throughout Oregon and Washington, especially at the University of Portland and Providence Cancer Institute.

Elsie grew up in the Laurelhurst neighborhood, attending church at All Saints Parish. She went to college at the University of Oregon graduating in 1943 with a degree in business administration. After graduating, she went to work for the family-owned First State Bank of Milwaukie – marking the beginning of a long career in banking alongside her husband, Don Finley, and her brother, Bob Franz. Many of Elsie’s colleagues recall her outstanding acumen, work ethic and the overall example of leadership she set in an era where female leaders were a rarity.

Elsie and her brother Bob were a major philanthropic and visionary force within Providence for more than 30 years. They were instrumental in the recruitment of Walter J. Urba, M.D., Ph.D., director and endowed chair of Cancer Research, to found a cancer program at Providence in 1993. And their continued support helped established Providence Cancer Institute as a worldwide leader in cancer immunotherapy.

After Bob’s death in 2016, Elsie was deeply involved with the renaming of Providence’s 11-story cancer tower to the Robert W. Franz Cancer Center to honor their unmatched generosity and leadership. Although many at Providence suggested she also be included in the naming, she insisted that only her brother be recognized.

Within Providence, Elsie’s legacy will live on through the thousands of health care providers, patients and families who will benefit from her tremendous generosity. “Elsie and Bob were incredibly generous and humble philanthropists. They never sought the spotlight,” said Dr. Urba.
Becky Roth is unstoppable. Cancer tried but it couldn’t stop Becky Roth. An avid runner, Becky wasn’t going to give up running because of cancer. “I am stronger now than I ever was,” Roth said. In 2010, Bryan Bell, M.D., D.D.S., FACS, associate member and head and neck surgeon at Providence Cancer Institute, discovered a tumor at the base of her tongue and jaw.

It was oral cancer. Patients with oral cancer undergo some of the most intense treatment of any form of cancer. Roth had multiple surgeries, chemotherapy and radiation. “In Becky’s case, treatment was particularly complex,” said Dr. Bell. “Your ability to speak, to taste, to swallow, to smell, see and hear; your facial appearance – all of these are affected.”

She had her jaw rebuilt using the fibula from one of her legs. A year later, the cancer returned and more of her jaw was replaced with the fibula from the other leg. “She is actually missing about two-thirds of her jaw and half her tongue,” he said.

Other doctors told her she’d never run again. That was not part of her plan. Since having her fibulas removed, she has completed several races including a half-marathon and a marathon. In 2018, she ran in the Providence Hood to Coast relay with a team made up of other cancer survivors and Providence caregivers. Their team name: the “Cancer Crushers.” More than $850,000 was raised by teams participating in Hood to Coast to support research at Providence Cancer Institute.

“I am a mom first and foremost,” said Roth. “I think this is why in the deepest part of my being, I needed to be here for my son and daughter. I don’t consider myself a hero. I am a wife and mom and I fought for them.”

Roth was a featured speaker at the 20th annual Creating Hope Dinner held May 23, 2018, at the Portland Art Museum. With her husband Chris at her side, she inspired guests to give a record-breaking $964,025 in support of Providence Head and Neck Cancer Program and Clinic, located within the newly opened Franz Clinic on the 11th floor of the Robert W. Franz Cancer Center.

“Patients are at the heart of everything we do,” said Dr. Bell. “Expanding our services on the 11th floor benefits our patients by bringing their care all together in one location. That makes a difference for those we serve, including Becky Roth.”

“Cancer Crushers” is the name of the team consisting of other cancer survivors and Providence caregivers who participated in the 2018 Hood to Coast Relay. The team was led by Becky Roth and raised more than $850,000 for cancer research.

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SELECT PUBLICATIONS


Chesney J et al. Phase IIIb safety results from an expanded-access protocol of talimogene laherparepvec for patients with unresected, stage IIIB-IVM1c melanoma. Melanoma Res. 2018;28(1):44.


Yossef R et al. Enhanced detection of neoantigen-reactive T cells targeting unique and shared oncogenes for personalized cancer immunotherapy. JCI Insight. 2018;3(19).

**BY THE NUMBERS: 2018 FACTS AND FIGURES**

**Investigators & Personnel**
- More than **150** researchers, including
  - 22 faculty members
  - 50 clinical researchers
  - 78 lab researchers

**Institute Publications**
- **133** total publications:
  - **59** journal articles
  - **3** books and book chapters
  - **71** conference abstracts

**Grant Funding, Sponsored Research & Philanthropy**
- **$4.5 million** annually in federal, private and sponsored research funding
- **$44.8 million** raised by Providence Foundations in Oregon for Providence Cancer Institute

**Cancer Clinical Trials**
- **1,949** total patient enrollments, including more than
  - **100** enrollments to phase I and II trials, and **44** enrollments to investigator-initiated therapeutic trials

**Memberships & Collaborations**
- American Association for Cancer Research Project GENIE
- Bristol Myers-Squibb International Immuno-Oncology Network
- NCI Community Oncology Research Program via Pacific Cancer Research Consortium
- NCI Cancer Immunotherapy Trials Network
- Partnership with MedImmune/AstraZeneca for clinical development of anti-OX40

**INVITED SEMINARS**
- 16 visiting professor seminars
- 104 faculty extramural seminars
FACULTY MEMBERS

R. Bryan Bell, M.D., D.D.S., FACS
Associate member and medical director, Providence Head and Neck Cancer Program and Clinic
Head and Neck Oncologic Surgery

Brady M. Bernard, Ph.D.
Assistant member, Computational Immuno-Oncology Laboratory
Associate director, Bioinformatics

Carlo B. Bifulco, M.D.
Member, Molecular Genomics Laboratory
Medical director, Oncologic Molecular Pathology and Pathology Informatics
Anatomic and Molecular Pathology

Alison K. Conlin, M.D., MPH
Associate member and medical director, Providence Breast Cancer Medical Program and High-Risk Breast Clinic
Medical Oncology

Marka R. Crittenden, M.D., Ph.D.
Associate member, Integrated Therapies Laboratory
Director, Translational Radiation Research Radiation Oncology

Brendan D. Curti, M.D.
Member and Robert W. Franz Endowed Chair for Clinical Research
Director, Cytokine and Adoptive Immunotherapy Program, Genitourinary Oncology Research and Melanoma Program
Medical Oncology

Thomas M. Duhen, Ph.D.
Assistant member, Anti-Cancer Immune Response Laboratory

Bernard A. Fox, Ph.D.
Member and Harder Family Endowed Chair for Cancer Research, Molecular and Tumor Immunology Laboratory

John E. Godwin, M.D., MS
Member and program leader, Hematologic Malignancies Medical Oncology

Michael J. Gough, Ph.D.
Associate member, Integrated Therapies Laboratory

Hong-Ming Hu, Ph.D.
Associate member, Cancer Immunobiology Laboratory

Rom S. Leidner, M.D.
Assistant member and co-director, Providence Head and Neck Cancer Program
Medical Oncology

Pippa H. Newell, M.D.
Assistant member and medical director, Providence Liver Cancer Clinic Liver and Pancreas Surgery

David B. Page, M.D.
Assistant member, Breast Cancer Immunotherapy Medical Oncology

Brian D. Piening, Ph.D.
Assistant member, Cancer Immuno-Genomics Laboratory Technical director, Clinical Genomics

William L. Redmond, Ph.D.
Associate member, Cancer Immunotherapy Laboratory
Director, Immune Monitoring Laboratory

Rachel E. Sanborn, M.D.
Associate member,
Phase I Clinical Trials Program
Co-director, Providence Thoracic Oncology Program
Medical Oncology

Eric Tran, Ph.D.
Assistant member,
Anti-Tumor T-cell Response Laboratory

Walter J. Urba, M.D., Ph.D.
Member, director and endowed chair of Cancer Research Medical Oncology

Andrew D. Weinberg, Ph.D.
Member and Judith Ann Hartmann Endowed Chair for the Laboratory of Basic Immunology

Kristina H. Young, M.D., Ph.D.
Assistant member,
Tumor Microenvironment Laboratory Radiation Oncology

ADMINISTRATION

Julie Cramer, MA, CCRP
Director, Cancer Clinical Research and Tumor Registry

Samantha Kaiser
Director, Cancer Research Operations

FRANZ LEADERSHIP CABINET

The Robert W. Franz Cancer Leadership Cabinet comprises men and women with a desire to connect community members with the dedicated teams of researchers working to finish cancer at the Earle A. Chiles Research Institute. Founded in 2001, the leadership cabinet has a strong and loyal membership representing a broad spectrum of the community.

2018 CABINET MEMBERS

Tyler Johnson, chair
Flo Atkinson
Stephen Bader, M.D.
Mark Beckius
Walter C. Bowen
Kay Carlisle
Charlie Engelberg
Dan Floyd
Pedro Garcia
Diana Hall
Cindy Harder
Robert “Rob” Hernandez
Dan Kinney
Sheryl Langerman Rosenfeld
Michael J. Larson
Lynn Loacker
Patricia Markesino
Jill McGinnis
Nicole McIntyre
Jooyon K. “Julieann” Park
Linda Read
James F. Robb, Ph.D.
Linda Smiley
Mark Williams
Linda Yoshida
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

chilesresearch.org