

INNOVATIONS IN ONCOLOGY

Annual Report 2019



KNIGHT
CANCER
Institute



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► Brian Druker, M.D., revolutionized the treatment of cancer through research that resulted in the first drug (Gleevec) to target the molecular defect of a cancer while leaving healthy cells unharmed. Now he is applying key principles of precision medicine to early detection.



Message from the Chairman

Dear friends and colleagues,

We are happy to present the 2019 OHSU Cancer Committee Annual Report, a comprehensive look at the work we are doing at the OHSU Knight Cancer Institute.

At the Knight Cancer Institute, we envision a world freed from the burden of cancer. Our mission is to care for each person with individualized and specialized care, while researching new ways to identify cancer earlier and treat it even more effectively. Working collaboratively, our aim is to end cancer as we know it.

In this annual report, you'll learn about:

- The Strategic Plan for Innovation and Discovery, a roadmap for our research efforts at the Knight Cancer Institute.
- OHSU Health, now offering more patients expert care close to home through partnership with Tuality Healthcare and Adventist Portland.
- A melanoma public service campaign designed to help people identify skin cancers earlier, when we can treat them most effectively.
- SMMART Trials, our newest protocol that offers additional options and in-depth analysis for patients with advanced cancer.

At the Knight Cancer Institute, we recognize it will take a collective effort to solve the complexity of cancer. By sharing what we know and helping you care for your patients, we know that together, we can end cancer as we know it. We thank you for allowing us to partner with you.

Sincerely,



Brian Druker, M.D.

Director, OHSU Knight Cancer Institute
JELD-WEN Chair of Leukemia Research
Investigator, Howard Hughes Medical Institute

Blazing a trail to end cancer as we know it

Following a successful \$1 billion fundraising campaign, OHSU Knight Cancer Institute is excited to embark on pioneering new methods of precision oncology and early detection. A state-of-the-art cancer research facility, a new model of combining scientific disciplines, and expanded clinical trials will translate scientific discoveries into next-generation detection tests, tools and treatments. We've recruited some of the most renowned clinicians and scientists in the country to lead the effort.

OHSU is based in Portland, Oregon. We have more than 1 million patient visits each year, operate the top-ranked adult and children's hospitals in Oregon, and secure competitive research funding of \$485 million. As a public corporation serving the best interests of Oregon and the region, we also provide outreach that improves health in communities across the state and services to the most vulnerable Oregonians.





Nationally Recognized

OHSU Hospital is No. 1 in Oregon, according to U.S. News & World Report's Best Hospitals 2019-2020, and ranks among the best hospitals in the nation in seven specialties. Knight Cancer Institute ranked 46th in the nation.



Knight Cancer Institute accolades, accreditations and recognitions

- **Ranked as 46th cancer center in the nation** by U.S. News & World Report.
- **The first center in the Pacific Northwest** to offer the first FDA-approved CAR T-cell therapy (Novartis's Kymriah).
- **National Cancer Institute designation:** OHSU Knight Cancer Institute has been awarded Comprehensive Cancer Center status by the NCI. It's been an NCI-designated center since 1997.
- **Commission on Cancer accreditation:** OHSU has been accredited by the Commission on Cancer since 1940. OHSU has recently been reaccredited by the Commission on Cancer after the most recent survey found 100% compliance in all 34 standards. This continues OHSU's flawless score for the past three consecutive surveys, a span of nine years.
- **One of 12 NCI-designated centers** to receive NCI award to increase HPV vaccine coverage.
- **OHSU is one of five Drug Resistance and Sensitivity Centers** established by the NCI to explore how acute myeloid leukemia cells evolve and adapt.



Research

OHSU is among the top 25 cancer research centers in the U.S. in terms of funding from the National Cancer Institute. Cancer researchers at OHSU received \$47.4 million in competitive funding awarded by the National Cancer Institute in FY2019, up from \$38.4 million the previous year (\$38,407,254). OHSU now ranks No. 22 in NCI funding.

OHSU received \$279 million (\$278,961,288) in overall funding from the National Institutes of Health in FY 2019, up from \$246 million (\$245,621,424) in FY 2018.

Clinical Trials: 700



Facilities and employees

Knight Cancer employees: Since the Knight Cancer Challenge was announced in 2013, the OHSU Knight Cancer Institute has recruited more than 622 researchers, post-docs, clinicians and administrative staff.

OHSU Knight Cancer locations, including partners and collaborations: 15

OHSU KNIGHT CANCER INSTITUTE COMMUNITY PARTNERSHIP PROGRAM

\$3.2 million

Invested

119

Grants funded

36

Oregon counties reached

208

Evaluation consults

17

Tiered grants*

4

Community Action Model grants*

*Since 2019

Instituting a strategic plan for the OHSU Knight Cancer Institute

Our vision is: A world freed from the burden of cancer.

Our mission is: We will end cancer as we know it. Through innovative, collaborative research and education, we provide prevention, detection and care — one person at a time.

These words are a driving force behind everything we do for our community and our patients. That's why the OHSU Knight Cancer Institute has developed a strategic plan to focus on key areas to further reinforce our foundation and build on our strengths. With a key focus in precision early detection, led by Sadik Esener, Ph.D., we will work to understand why some tumors become malignant and others remain benign. This effort includes the detection of early as well as late stage cancer progression and evolution. Because the earlier we can anticipate change and interrupt it, the greater our patients' survival rates.

Another key focus area is precision oncology. As a world leader in this area — based on our pioneering work with Gleevec as a targeted cancer therapy — and with the expertise of Gordon Mills, M.D., Ph.D., we will continue to innovate and develop new approaches to personalized therapies specifically tailored to each patient.

With every discovery, we are making strides to end cancer as we know it for all patients in Oregon and around the world.

Four foundational pillars of research



Cancer systems
biology



Clinical
research



Community-
engaged research



Computational
biology



◀ An art installation at the Knight Cancer Research Building uses dots to represent the more than 10,000 donors who contributed to the Knight Cancer Challenge.

Introducing OHSU Health

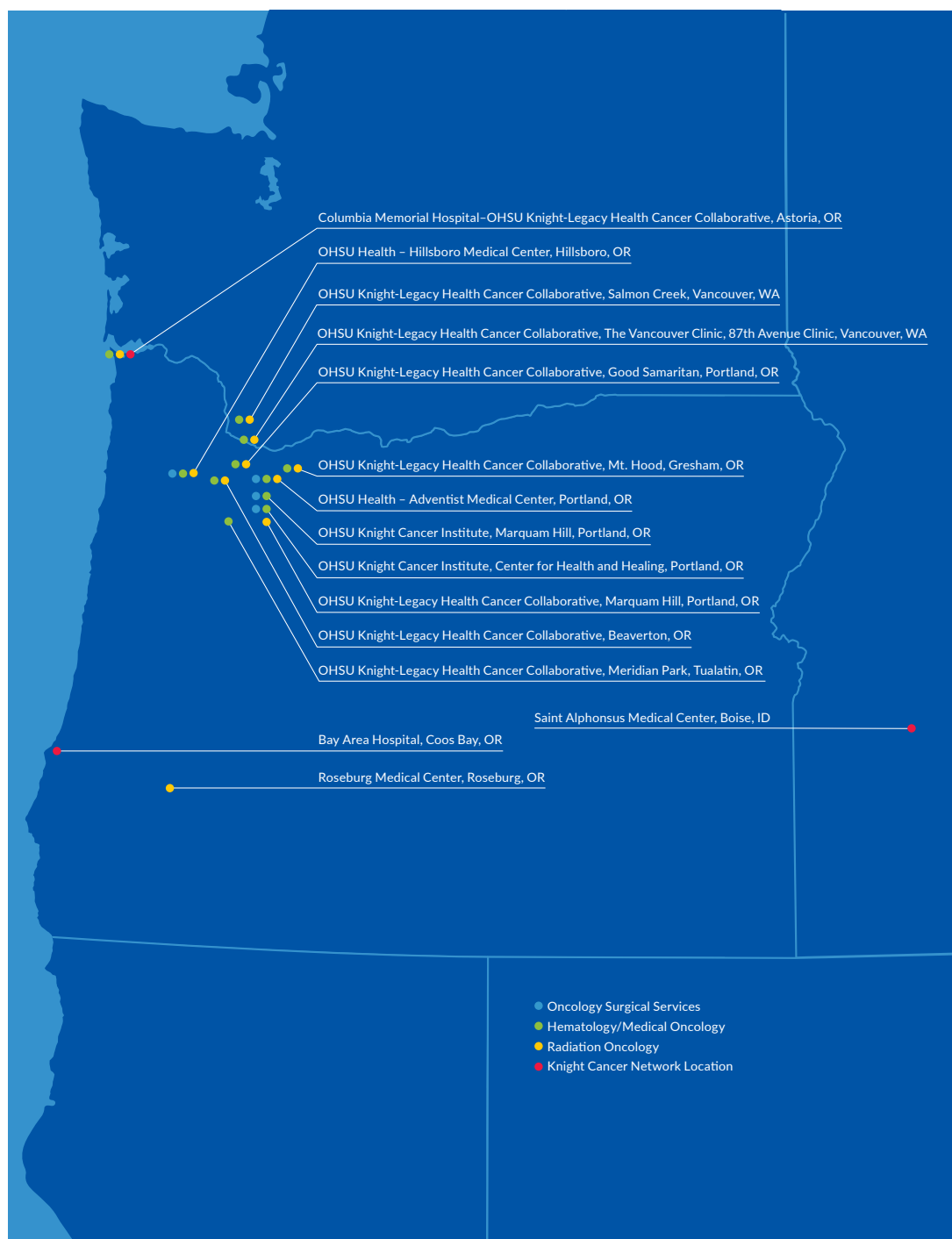
► OHSU Health includes 52 care locations in the Portland-metro area, with OHSU Doernbecher Children's Hospital and nearly 1,000 beds at the three adult hospitals.



In 2016, OHSU affiliated with two additional regional health systems, Adventist Health Portland and Tuality Healthcare. In 2019, all three are uniting under one banner: OHSU Health.

OHSU Health is the next step of an ongoing journey to integrate the leading-edge practices of an academic health center with the local knowledge of community hospitals. The system is a unique platform for innovation — bringing what happens in labs and classrooms to the bedside in communities throughout Oregon and beyond.

► Cancer clinic locations throughout Oregon, SW Washington and Idaho.



Reducing financial toxicity for cancer patients with new patient housing

Certain cancer treatments are a scarce resource in Oregon, such as radiation oncology and stem cell transplants. Though OHSU Knight Cancer Institute has the faculty expertise and state-of-the-art facilities, finding temporary housing in Portland, for treatments that can last several weeks, can be challenging and costly. The Gary and Christine Rood Family Pavilion guesthouse, which opened in 2019, meets a sizable demand for comfortable, affordable housing convenient for patients at OHSU.

► The Gary and Christine Rood Family Pavilion allows families to stay together during treatment. In the first year of operation, the guest house hosted more than 200 oncology patient stays averaging three weeks.



“For patients, knowing you can have advanced level care at OHSU without the housing struggles is huge,” said radiation oncologist Nima Nabavizadeh, M.D. “I know our multidisciplinary care here at the Knight Cancer Institute can make a meaningful difference to patients, and by reducing the financial toxicity, it allows us to treat patients how they should be treated.”

Nabavizadeh explained that radiation therapy can require less than an hour a day, but it is often a daily treatment necessary for several weeks that can cause exhaustion for patients. For example, lung cancer treatment may last six weeks, and some head and neck cancers may require seven weeks of radiation therapy.

The Rood Family Pavilion has 76 rooms on the top five floors and an urgent care on the ground floor. On-site amenities include communal kitchens, a fitness room, an expansive garden, and indoor and outdoor children’s play areas. The design and décor offer a comfortable homelike setting.

Bernard Brown, a 95-year-old World War II veteran, volunteers each week at the Rood Family Pavilion as a greeter. Many years ago, he had a child in the hospital for long-term treatment, and he is delighted to see families able to stay together now rather than endure separations.

“This building is a wonderful situation,” he said. “There’s a lot of sadness in the families. You have to be there for them and give support. It’s very gratifying to see the families getting all this care.”

Patients and families with limited resources who live 30 miles or more from OHSU receive priority at Rood Family Pavilion. The fee for adult patients is \$50 a night, with pediatric patients subsidized by Ronald McDonald House Charities.

“Having this resource available for patients absolutely increases access to lifesaving therapy,” Nabavizadeh said.



Gary and Christine Rood Family Pavilion's first year impact in oncology

274 days open

200+ oncology patient stays

3 weeks average length of stay

► The Rood Family

Pavilion has 76 rooms on the top five floors and an urgent care on the ground floor. On-site amenities include communal kitchens, a fitness room, an expansive garden, and indoor and outdoor children's play areas. The design and décor offer a homelike setting.



"This building is a wonderful situation. There's a lot of sadness in the families. You have to be there for them and give support. It's very gratifying to see the families getting all this care."

Bernard Brown, volunteer
and World War II veteran



New oncology clinic facilities offer convenience and comfort

The Knight Cancer Institute inhabits the upper six floors of the Center for Health & Healing Building 2 (CHH2) for oncology clinics, infusion services and clinical trials. The offices' design incorporates precision medicine in a patient-centered care environment. Knight Cancer Institute Women's Clinic provides spa-like amenities for mammography and ultrasound diagnostics. The 10th floor has a patient resource center for patients to obtain additional information about their diagnosis, try on wigs or learn about support classes such as meditation and yoga. A skybridge connects the new building to the Center for Health & Healing Building 1. CHH2 has a covered patient drop-off area, a new parking deck, a pharmacy, laboratory and an on-site café.



► This waiting area, in the Center for Health and Healing Building 2, was designed with patients in mind.

Raising awareness of melanoma

► Oregon consistently has one of the highest incidence rates of melanoma cases in the United States. Incidence for both sexes combined is 26.6 per 100,000 residents. This is more than 133% of the U.S. average for melanoma.



Spearheading a public health campaign to battle melanoma

OHSU Knight Cancer Institute is leading a War on Melanoma, a major clinical and research effort for education, prevention and early detection. Five years in the making and launched in May 2019, the campaign is an all-fronts effort to reduce melanoma-related deaths in Oregon. The primary goal is to encourage the public to look at their skin, and if they see something, do something. If melanoma is detected and treated in stages 1 and 2, the mortality rate from skin cancer could drop by as much as 50% in Oregon within five years. This test balloon effort will also help determine whether other early detection campaigns can have the desired impact and encourage preventative behaviors.



“Melanoma is a cancer that we can catch early because we have the necessary technology — our eyes,” said Sancy Leachman, M.D., Ph.D., who chairs the OHSU Department of Dermatology and is the principal investigator for the Melanoma Community Registry, an IRB-approved registry, officially named the War on Melanoma. “Our hypothesis is that this early detection campaign will increase melanoma literacy throughout Oregon, empowering individuals to seek help earlier, saving lives, and, eventually, reducing costs of medical care. At this point, we are focused on getting the word out to as many people as we can.”

◀ Sancy Leachman, M.D., Ph.D., who is leading the War on Melanoma, wants to make it as easy as possible for providers to use the resources however they fit in their practice.



Toolkits, education and resources for physicians

OHSU Knight Cancer Institute has assembled an information toolkit to help providers:

- Identify at-risk patients.
- Integrate skin screenings into everyday practice.
- Increase diagnostic accuracy.
- Educate their patients on self-exams.
- Free continuing medical education credit through a primary care/medical professional early detection curriculum available online. (3.0 AMA PRA Category 1 Credits)
- Every Thursday at 7 a.m., join a virtual melanoma tumor board that brings together specialists from many disciplines to review challenging cases. Any provider from around the state can sign in to present a patient for discussion.
- eConsults for dermatology will be available soon.

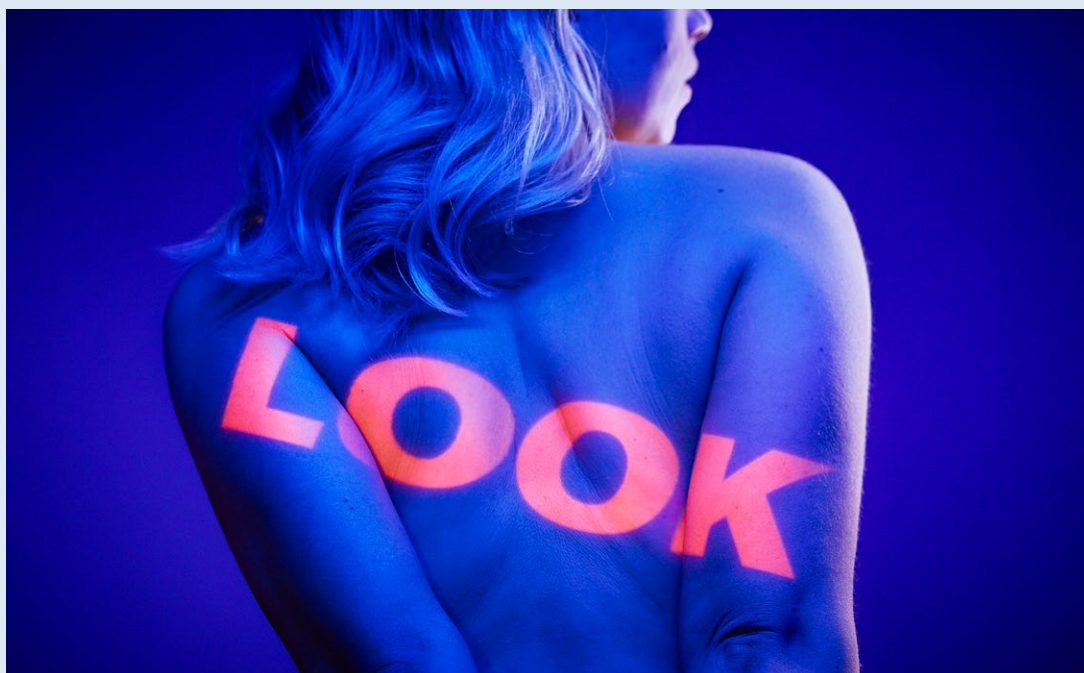


Self-help for the public

Through a large-scale media campaign, OHSU is directing people to look at their skin and to visit the website startseeingmelanoma.com.

“We are putting tools directly in the hands of the public to be informed and proactive about seeking medical advice if they see any suspicious lesion,” Leachman said.

- **Startseeingmelanoma.com:** Visitors can learn how to look at their skin, what to look for and what to do if something looks suspicious. They can learn about risk factors and see sample photos of benign and malignant lesions.
- **Melanoma Community Registry:** OHSU operates an IRB-approved research cohort for those with a history of melanoma, as well as family members and friends. By registering, participants receive direct information about research, education opportunities and ways they can volunteer in their communities to spread awareness.
- **Mole Mapper app:** A free, downloadable app available on iPhone. The app is a helpful tool to monitor changes in moles, a critical factor for detecting dangerous lesions early. Users can store photos to share with their providers and opt in to participate in machine-learning research.
- **Links to clinicians:** There is a link to the American Academy of Dermatology by ZIP code.
- **eVisits:** People can upload photos and information about a suspicious lesion to the OHSU Department of Dermatology to get a medical opinion about whether to get a biopsy. If needed, OHSU can refer them to local resources or schedule at OHSU. OHSU is charging \$75 for these eVisits.
- **Events:** OHSU is coordinating community outreach, screening events and patient symposia.



◀ As part of the public health awareness campaign, OHSU encouraged people to look at their skin.



2019 outreach connections

- More than 750 Oregon medical providers attended a melanoma CME lecture in 2019.
- More than 60 primary care providers completed Primary Care Melanoma Early Detection Training (3.0 CME hours) online.
- More than 100 licensed professionals in skin-centric professions attended "The Skinny on Skin" Early Detection Training (2.0 CE hours).
- Startseeingmelanoma.com attracted more than 30,000 users after the launch.
- Users in all 50 states (more than 1,000 users in Oregon) downloaded and used the Mole Mapper app since it launched.
- eVisits jumped to an average of 20 per week after launch.
- PDX Skincare Festival provided 250 free screenings, detected three melanoma cases and identified an additional 13 possible skin cancers.
- Medical students planned and will implement a high school curriculum to reach 50 teachers and potentially 6,000 students in 2020.
- Oregonian Melanoma Community Registry reached more than 3,500 participants.





Startseeingmelanoma.com

The website, the main resource for the public health campaign, is full of information for both individuals and physicians. Under the “For Medical Professionals” tab, learn more about:

- Online melanoma early detection CME training module designed for primary care.
- How to join the war (host events or screenings or distribute educational materials).
- Tools and materials for your patients.
- Continuing education events.
- The virtual melanoma tumor board for melanoma providers without access to a multidisciplinary team.

Home What is Melanoma? Get Involved Resources For Medical Professionals For Skincare Professionals About TAKE THE PLEDGE

MELANOMA IS THE CANCER YOU CAN STOP WITH YOUR EYES

HAVE YOU LOOKED AT YOUR SKIN LATELY?

You may just find something you've never seen before. Melanoma is the most deadly form of skin cancer. If it is caught early, survival rates are great —if it is left untreated over time, survival rates drastically decrease. Stop and look. Your eyes can be your best tool.

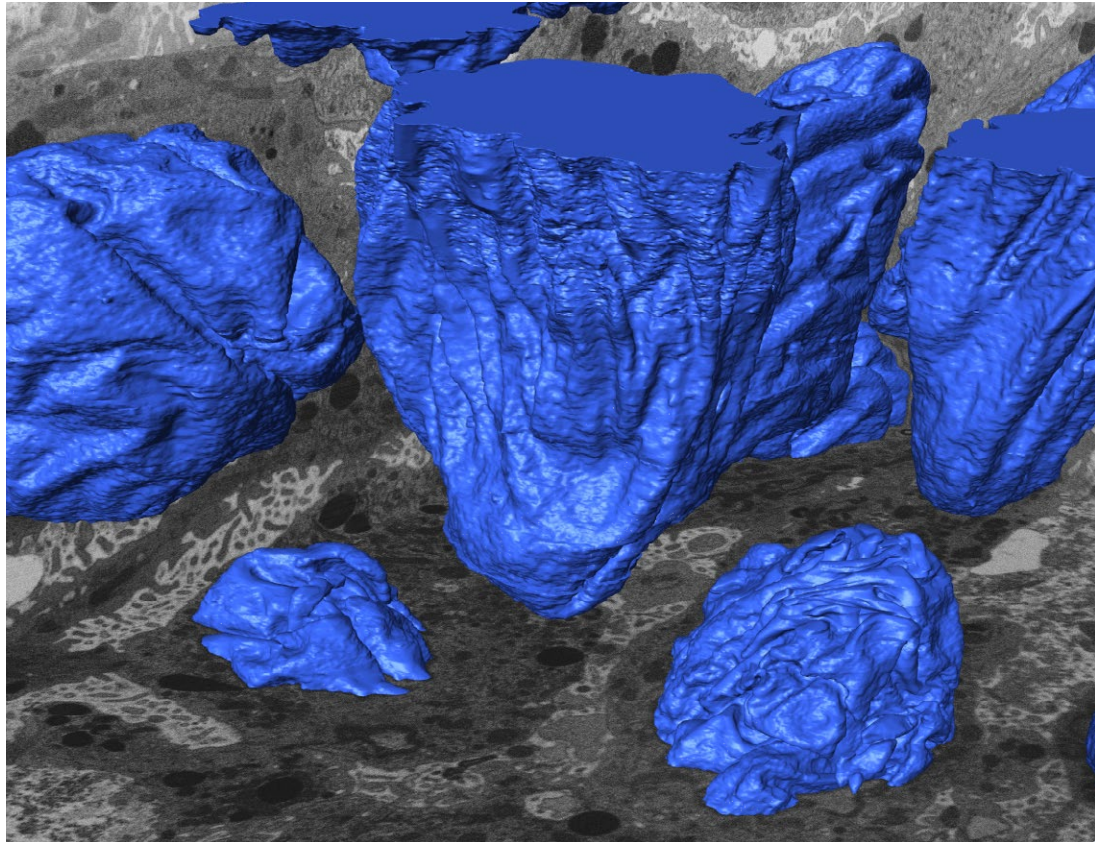
Check your skin. Check your partner's skin.
And if you see something. Do something about it. Get it checked out.

OK LOOK LOOK LO

◀ Visit the website startseeingmelanoma.com for more resources.

New advancements in clinical care

► Using 3-dimensional electron microscopy, cellular ultrastructure in a patient biopsy from metastatic breast cancer can be visualized with greater understanding of how cancer cells operate. In this image, nuclei from several cells are in 3D to show the deep invaginations of the nuclear membranes not observed in normal healthy cells.



Advancing SMMART® molecular medicine

Joe W. Gray, Ph.D., has been paving the way in breast cancer research for the past 30 years, inventing technologies that hone diagnosis and cut mortality rates. As a physicist and researcher, he spent more than four decades leading the field in genomics, cancer genetics and breast oncology at three top institutions before coming to OHSU in 2011. Today, he's focused on what could be his greatest life's work — precision oncology.

For Gray, the director of the OHSU Center for Spatial Systems Biomedicine and associate director for biophysical oncology at the Knight Cancer Institute, personalized treatment became less academic and more personal when his wife of 52 years, Jane, developed breast cancer. Jane's treatment in 2010 was initially a success. But in 2017, she learned that her cancer had metastasized, creating multiple tumors throughout her body. The five-year survival rate for her type of stage 4 metastatic breast cancer is 22%. Within a few days of the diagnosis, Jane became one of the first 50 patients in SMMART, a clinical trial to test a life-saving new approach for metastatic breast cancer. Today, Jane's cancer is nearly gone, except for three tiny lesions.



◀ Joe Gray and his wife Jane, of 52 years, who said, "I'm fortunate I'm alive. If my husband had taken a different path, I wouldn't be here today."

A SMMART approach to treating cancer

Gray began his work on SMMART, also known as Serial Measurements of Molecular and Architectural Responses to Therapy, when he arrived at OHSU. Today, SMMART is led by Gray, Gordon Mills, M.D., Ph.D., director of precision oncology at the OHSU Knight Cancer Institute, and Christopher Corless, M.D., Ph.D., executive director and chief medical officer of the OHSU Knight Diagnostic Laboratories, and supported by Zahi Mitri, M.D., assistant professor of medicine at OHSU, as well as a team of more than 150 dedicated individuals throughout multiple disciplines.

As part of the SMMART trials, doctors use a combination of targeted therapy drugs to stop tumors before they can adapt and become drug-resistant. The purpose is to find the best possible treatment in real time by using cutting-edge molecular analysis to inform treatment decisions. By analyzing the micro-environment characterizing the tumor ecosystem over time, tumor response can inform which drug combination is likely to be beneficial. The goals are to increase the spectrum of patients who benefit, decrease toxicity of therapy and increase the depth and durability of response.

So far, it's working. In early results, over half of participants responded exceptionally well to treatment, well beyond the 30% response rate the team hoped to achieve and roughly double the response rate achieved in studies using single drugs.

Mills is using breast cancer for proof of concept trials, but he anticipates extending these concepts to additional diseases, with programs already in development for pancreatic cancer, prostate cancer and leukemia.

► Jacqueline Vuky, M.D. consults with Joy Bachman, whose metastasized melanoma cancer tested positive for BRAF gene mutation and responded to dabrafenib.



For more about the SMMART trial efforts to end cancer as we know it, see the video at: www.greatbigstory.com/stories/precision-oncology-fighting-against-cancer



Two competitive advantages make OHSU the right place for SMMART

The Knight Diagnostic Laboratories and the OHSU Center for Spatial Systems Biomedicine provide the perfect toolkit to initiate an effort like the SMMART trials. The Knight Diagnostic Laboratories offer an extensive menu of molecular and genetic tests for oncology, further supported through a BioLibrary and Histopathology Shared Resource. The Center for Spatial Systems Biomedicine hosts an enviable array of world-class research capabilities through the Multiscale Microscopy Core, OHSU's state-of-the-art electron microscopy core.



Existing SMMART trials and expansion for 2020

Thus far, OHSU Knight Cancer Institute has enrolled approximately 60 patients in the SMMART Treatment Program. There are several trials underway and some that will be expanding in 2020.

- The SMMART Treatment Program has two off-label drug use clinical trials underway, currently enrolling a breast cancer cohort but with the ability to enroll patients with prostate cancer, pancreatic cancer and acute myeloid leukemia.
- In January 2019, the program opened a clinical trial specific to the triple negative breast cancer population. The trial is nearing its interim analysis timepoint and demonstrates positive response in a majority of enrolled patients. The trial currently enrolls patients at the OHSU main campus and Knight Cancer Institute Community Hematology Oncology clinics throughout the greater Portland-metro region. In 2020, the TNBC trial has plans to expand to sites beyond the Portland metro area, including Salem, Oregon and across state lines. The goal of the program is to have the data and sample travel, while allowing patients to stay with their local oncologist and care team. The program expects to open a neoadjuvant clinical trial in 2020.
- The SMMART Treatment program opened a clinical trial for patients with pancreatic cancer in late 2019. The program has plans to expand its clinical trial portfolio to include additional diseases within capacity.

► Susan Slater, F.N.P., Sarah Nagle, M.D. and Brandon Hayes-Lattin, M.D., all with the Knight Cancer Institute collaborate on patient care.



Expanding precision immunotherapy with new CAR-T clinical trials for additional cancers

An early adopter and one of the few certified treatment centers in the nation to offer chimeric antigen receptor T-cell immunotherapy, OHSU and OHSU Doernbecher have now treated dozens of adults with relapsed, refractory diffuse large B-cell lymphoma and children and young adults with acute lymphoblastic leukemia and lymphoma.

“We’ve gained enormous expertise with this new and complicated therapy,” said Brandon Hayes-Lattin, M.D., medical director in the Division of Hematology and Medical Oncology at OHSU and of the OHSU Knight Cancer Institute’s Adolescent and Young Adult Oncology Program. “We’ve assembled a strong team within hematology/oncology, but also partnered with our neurology colleagues to safely manage some of the unique toxicities. We are seeing responses in patients who didn’t have any standard of care options. Many

have gone into remission using this non-chemotherapy, cellular-based therapy.”

OHSU now has open studies that offer CAR-T to adult lymphoma patients earlier in their disease course than commercially available. The intervention can come as a first-line treatment for patients with relapsed or refractory disease, and it investigates whether CAR-T could replace current standards in early treatment. Hayes-Lattin said this will also apply to childhood ALL soon.

“It will be exciting to bring these treatment options in earlier and earlier to fend off some of the detrimental effects

on the body from these diseases and repeated cycles of chemotherapy currently used to treat them,” Dr. Hayes-Lattin said.

In 2020, OHSU will expand CAR-T therapy to other patient populations and cancers that have no other curative treatment, possibly providing a game changer in these diseases.

“We plan to open a clinical trial for older adults with ALL in 2020, because the current FDA-approved CAR-T treatment is only for patients up to age 25,” Hayes-Lattin said. “We will also have trials planned for multiple myeloma and sarcoma, our first non-hematological cancer to use CAR-T therapy.”

“We are seeing responses in patients who didn’t have any standard of care options. Many have gone into remission using this non-chemotherapy, cellular-based therapy.”

Brandon Hayes-Lattin, M.D.

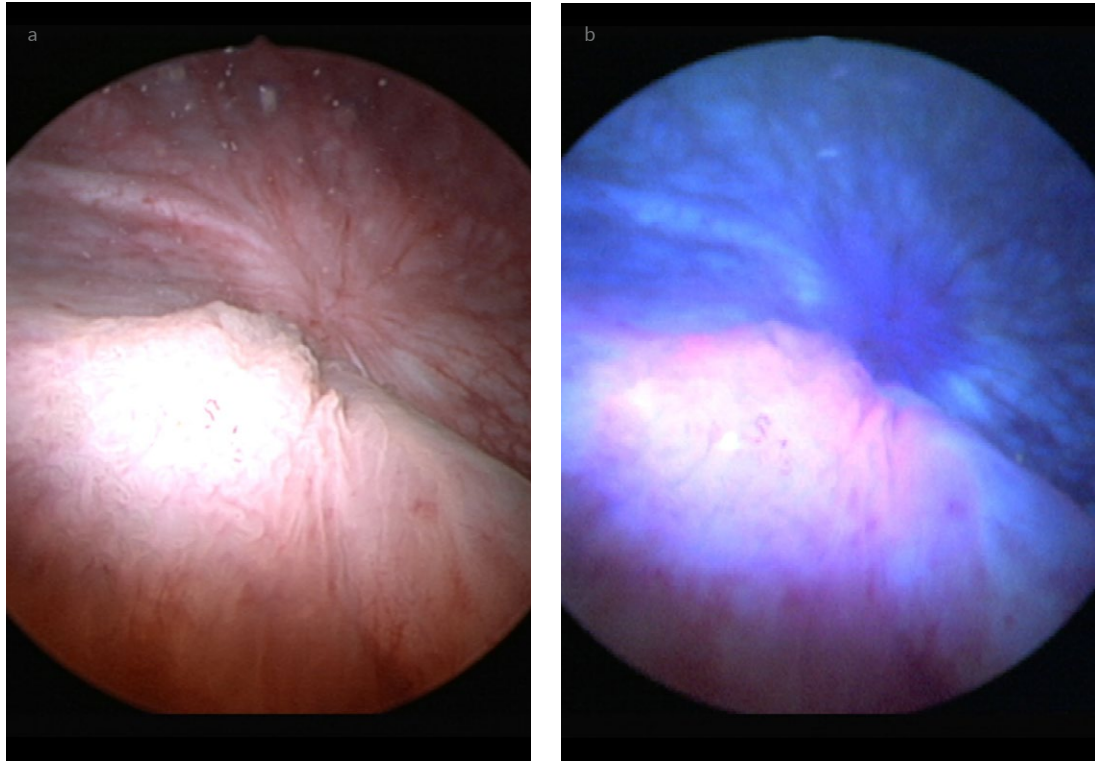


Evaluation before treatment key to inclusion

A critical point for inclusion in the CAR-T trials is identifying patients before any second-line treatments begin, Hayes-Lattin explained, which is not the typical pattern.

“The Knight Cancer Institute would love to be involved in the care of those patients, so we can capture when they are eligible for these trials,” he said.

► a) Image seen under white light with standard cystoscopy. b) Image seen with blue light cystoscopy. The cancerous areas appear hot pink.



Enhancing bladder cancer diagnosis with blue light cystoscopy

OHSU Knight Cancer Center is the first and only center in Oregon to offer blue light cystoscopy for bladder cancer diagnosis. Urologic oncologists utilize BLC using hexaminolevulinate to detect bladder cancer with improved sensitivity over traditional cystoscopy. The American Urological Association and the Society of Urologic Oncology guidelines recommend offering BLC to patients with nonmuscle-invasive bladder cancer, particularly for tumors that are hard to visualize with traditional methods. OHSU urology oncologist Jen-Jane Liu, M.D. said BLC is superior for detecting cancer in complex cases of flat aggressive cancers.

“It’s exciting to have this technology available now at OHSU for our bladder cancer patients,” Liu said. “The usage of blue light during bladder tumor resection can also facilitate more complete resection and reduce the rate of cancer recurrence.”

Improving recovery for CRS/HIPEC through ERAS protocols

With cytoreductive surgery and hyperthermic intraperitoneal chemotherapy, there is a high incidence of postoperative ileus resulting in extended hospital stays. In an innovative approach to this patient population, OHSU surgeons V. Liana Tsikitis M.D., M.C.R., M.B.A., F.A.C.S., F.A.S.C.R.S. and Erin W. Gilbert M.D., M.C.R., F.A.C.S. incorporated an enhanced recovery after surgery protocol last year in a single institution study with the intent of reducing length of stay.

“Our results showed an earlier return of bowel function and shortened length of stay by four days with no difference in mortality or morbidity,” Gilbert said. “The ERAS protocols are the same as the standard for many GI surgeries, including minimizing opioid use, early ambulation and other strategies to maximize the gut’s ability to digest.”

OHSU Knight Cancer Institute began offering CRS/HIPEC in 2016 to provide more treatment options for stage 4 gastrointestinal cancers, particularly appendiceal mucinous neoplasms.



“As a tertiary center, we saw a need at OHSU in this patient population and wanted to better serve our patients.”

V. Liana Tsikitis M.D., M.C.R.,
M.B.A., F.A.C.S., F.A.S.C.R.S.

◀ V. Liana Tsikitis,
professor and division
head of Gastrointestinal
and General Surgery

OHSU is the only academic center offering this treatment in the Pacific Northwest. Though CRS/HIPEC has been available for about 20 years, many centers haven't been willing to offer this complex alternative for late-stage cancers.

"As a tertiary center, we saw a need at OHSU in this patient population and wanted to better serve our patients,"

said Tsikitis, who is the division head of Gastrointestinal and General Surgery.

Over the last four years, OHSU surgeons have operated on 66 patients with intent to treat. Of those, 48 received HIPEC. Currently, OHSU surgeons perform about two CRS/HIPEC procedures a month, working closely with a multidisciplinary GI tumor board for patient selection.

Results before and after implementation of ERAS protocol for CRS/HIPEC patients:
Data reported as medians and range as appropriate. Non-parametric testing was performed to determine significance.

	BEFORE ERAS	AFTER ERAS	
NUMBER OF PATIENTS	16	15	
AGE	57 (31-72) YEARS	60 (36-73) YEARS	NS
OPERATION LENGTH	452 (278-780) MIN	418 (270-590) MIN	NS
PERITONEAL CARCINOMA INDEX (PCI)	6 (0-18)	3 (0-26)	NS
RETURN OF BOWEL FUNCTION	5.5 (4-8) DAYS	4 (3-10) DAYS	P<0.05
LENGTH OF STAY (LOS)	11 (5-20) DAYS	7 (5-27) DAYS	P<0.05
COMPLICATION (CLAVIEN DINDO ≥3)	25%	20%	NS



◀ Surgeon performs procedure on patient.



HIPEC treatment

After the surgeon removes all visible tumors, HIPEC involves heating mitomycin C and then pumping it into the abdominal cavity. The patient lies on a special cooling blanket to keep body temperature at safe levels. Surgeons physically rock the patient back and forth on the operating table for about two hours to ensure that the drug reaches all areas of the abdomen, killing any cancer cells that may remain after cytoreductive surgery and reducing the risk for cancer recurrence using a single dose of chemotherapy.

Offering a novel treatment for patients with advanced liver cancers

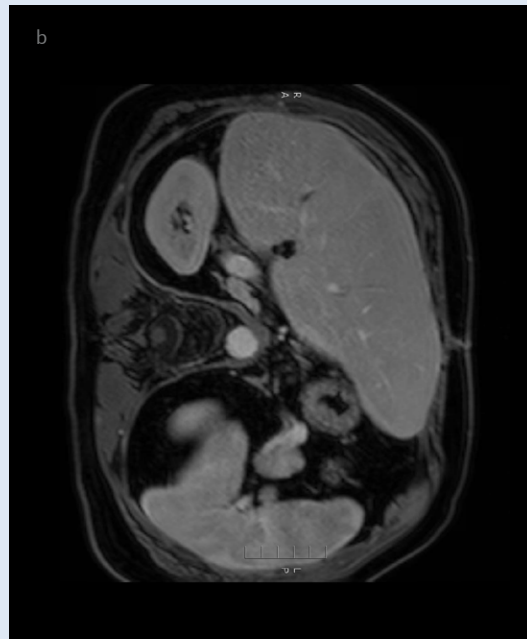
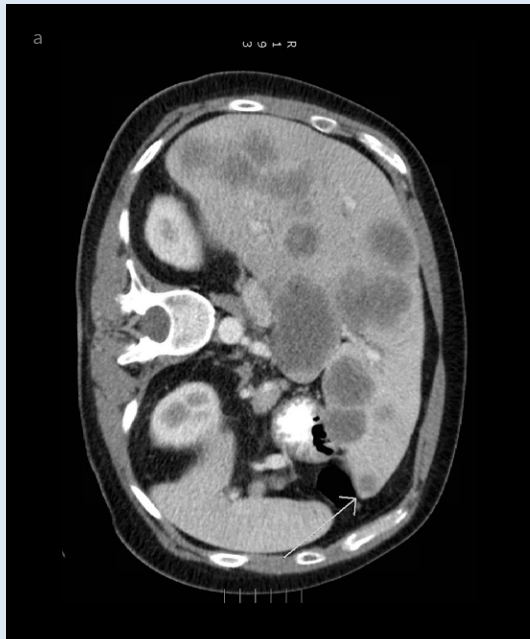
The OHSU Knight Cancer Institute is the only center west of the Mississippi River offering hepatic artery infusion chemotherapy. HAI has been an accepted treatment for patients with colorectal liver metastases for decades (and recently for patients with advanced intrahepatic cholangiocarcinoma), but only a handful of centers in the country offer this treatment due to the complexity of building and maintaining the necessary interdisciplinary program.

“We believe it is important to have this option as part of the full spectrum of care for patients with colorectal cancer and for other cancers in the liver,” said Skye C. Mayo, M.D., M.P.H., F.A.C.S., a hepatopancreaticobiliary surgical oncologist and the director of Hepatic Arterial Infusion for Advanced Liver Malignancies at OHSU Knight Cancer Institute. “Over the past decade, I’ve seen the tremendous benefit it can have for patients with advanced liver cancers, especially as an option for people running out of options.”

Since 2016, OHSU has performed nine to 10 HAI operations per year with good success and safety results. Mayo anticipates that the number of patients offered HAI treatment at OHSU will continue to grow, approaching 15-25 a year.

“Oncologically, what’s amazing about this treatment is that it takes advantage of the liver’s first-pass metabolism,” Mayo said. “Patients can get 400 times the dose of chemotherapy compared to what they could tolerate systemically. Because 95% of it stays in the liver, they don’t feel the side effects associated with traditional systemic chemotherapy.”

When HAI treatment is combined with traditional chemotherapy, the synergy can convert patients with initially non-resectable CRLM to resectable disease, improving patient survival and quality of life. When the patient’s cancer responds well to treatment, Mayo can perform additional liver resections to ultimately clear the cancer from the liver. Over the past several years, Mayo’s team has converted almost 30% of patients with initially unresectable disease to complete clearance of the cancer from their liver.



◀ Images are from a 40-year-old female with rectal cancer widely metastatic to her liver. Image (a) is pretreatment showing disease in all liver segments, image (b) shows no evidence of disease in the two segments of liver remaining after completed treatment.

“HAI requires an exceedingly complex, multidisciplinary program because it touches a large number of medical specialties and requires aligning all of these experts to deliver this intensive treatment,” Mayo said. “Building and maintaining a program like this takes dedication and passion to lead the sequencing of this care. Also, a team is essential for appropriately selecting patients most likely to benefit from HAI.”

The HAI program also offers a unique area of research opportunity.

“At OHSU, we have an eye on discovery and innovation, and we see this as an incredible opportunity,” Mayo said. “We’ve been using the same therapeutic agent, floxuridine, delivered by the same pump for years. Our research goal is to explore and discover novel therapeutics directly delivered to target the liver, taking advantage of the unique metabolism in the liver, so patients experience minimal side effects and maximal impact upon their liver cancer.”

“Over the past decade, I’ve seen the tremendous benefit it can have for patients with advanced liver cancers, especially as an option for people running out of options.”

Skye C. Mayo, M.D., M.P.H., F.A.C.S.

Research advancements

Engineering bone tissue of unprecedented precision

Replicating the complexity of bone tissue has been elusive until a breakthrough at OHSU in 2019.

“We can now engineer bone-like tissue in the lab with the same complexity that nature does,” said biomedical engineer Luiz Bertassoni, D.D.S., Ph.D., an assistant professor in the OHSU School of Dentistry and a member of CEDAR, the Cancer Early Detection Advanced Research Center in the OHSU Knight Cancer Institute. “This is the first time anyone has been able to embed cells in minerals, which is what characterizes bone tissue. Now we can address all the questions we couldn’t before about how bone develops or interacts with disease in the context it happens in nature.”

The new discovery replicates human bone tissue with an unprecedented level of precision, from its microscopic crystal structure to its biological activity. Like real bone, the material has a 3D mineral structure populated with bone cells, nerve cells and endothelial cells that self-organize into functioning blood vessels. It takes 72 hours or less to create the material in a lab.

“We can reproduce the architecture of bone down to a nanometer scale,” Bertassoni said. “Our model goes through the same biophysical process of formation that bone does.”

This “bone in a dish” offers exciting implications for both basic and clinical research, providing a unique model to study bone function, diseases and regeneration.

“Now we can address all the questions we couldn’t before about how bone develops or interacts with disease, in the context it happens in nature.”

Luiz Bertassoni, D.D.S., PH.D.



◀ Luiz Bertassoni, D.D.S., Ph.D. leads a multidisciplinary research group working on various aspects of biomaterials and tissue engineering.

New formula cracks imitation bone

Bone is a unique organ in the body, being an organic and inorganic nanocomposite, making it difficult to replicate. In this new method, Bertassoni and his team combine human stem cells and collagen, then expose the material to a cocktail of calcium and phosphate, along with the protein osteopontin. In this calcified environment, stem cells develop into functioning bone cells, osteoblasts and osteocytes. When the OHSU scientists add nerve cells and endothelial cells to the mixture, they form interconnected networks that persist after mineralization.

“With this model system, you can start asking questions about how bone cells attract different types of cancers, how cancer cells move into bone, how bone takes part in the regulation of marrow function,” Bertassoni said. “It can even be relevant to dissect the mechanisms that are leading to diseases such as leukemia.”

The discovery is the first step in the development of a platform with multiple potential applications. Bertassoni and his team are now working to optimize the material for bone regeneration. They have tested the material as a replacement for injured bone in animal models with positive results that they expect to report soon. OHSU is working with the Food and Drug Administration to get the material cleared for use in humans.

Care for the whole patient

Specializing in the psychosocial needs of cancer patients

While physicians engage with the patients' diseases, OHSU Knight Cancer Institute's team of 16 oncology-specialized social workers help patients contend with the ripple effects from cancer that touch mental health, finances, caregiver and family relationships and much more.





“We don't want people to just survive; we want people to thrive. And integrative medicine adds to that possibility.”

Susan Hedlund, M.S.W.,
L.C.S.W., O.S.W.-C.

◀ Susan Hedlund is a national speaker on issues ranging from caring for caregivers to end of life and represents oncology social workers nationally at the Commission on Cancer. She is also a past president of the Association of Oncology Social Work.

“Our team is highly specialized to oncology; almost all of us have oncology service certification beyond our master’s degrees,” said Susan Hedlund, M.S.W., L.C.S.W., O.S.W.-C., the director of Patient/Family Support Services. “The majority of our team also have in-depth knowledge of palliative care and navigating advance care and end-of-life decisions.”

Caroline Macuiba, L.C.S.W., O.S.W.-C. said there are uniquely complex factors for cancer patients that require context, which may not translate easily to an outside mental health provider. The oncology social work team provides a continuum of care from counseling to logistical hurdles such as transportation and housing. The team also leads robust support groups for prostate cancer, brain tumor, rare blood disorders and young

adult survivors of childhood cancer. They hosted conferences for sarcoma patients and bone marrow transplant survivors last year, all free for patients.

Additionally, Knight Cancer Institute has 15 contractors providing integrative medicine services. Through philanthropic support, nearly all of these services are free to the patients, with the exception of acupuncture.

“We don't want people to just survive; we want people to thrive. And integrative medicine adds to that possibility,” Hedlund said. “We added these services because our patients want them. If we didn’t have them on-site, we assume they would pursue these services outside of the medical system. This way, we have embedded that care at our clinics and work closely with the providers.”

For example, Hedlund's team has hired seven massage therapists to offer massage for inpatients units and the infusion clinic. Each of the massage therapists has advanced levels of certification in oncology massage. Other contractor-led activities include three writing groups, mindfulness and yoga classes for patients and survivors. Another resource, a naturopath/acupuncturist, is a former oncology nurse.

"We wanted to ensure that the people we hired in integrative oncology understood both worlds of traditional cancer treatment and integrative care," Hedlund said.

One patient who took advantage of the integrative services commented, "It was remarkable to me how much acupuncture helped. I went in with debilitating neuropathies in my hands and feet from chemotherapy; I came out of my session feeling 90% of my neuropathies relieved!"

Hedlund said, "Patients love these options. From the writing groups, people say they are so grateful for a safe place to write about their cancer experience, because they wouldn't go to a traditional support group or therapist."

Macuiba said they get similar responses from the yoga and mindfulness classes, where people say they appreciate the social support of shared experience.

"We know the earlier we are involved, the more likely we can help patients cope and get the resources they need," Hedlund said. "We are always looking for best practices relevant to oncology. There is a lot of research that this intervention prevents emergency room visits and hospitalizations and helps with compliance with treatment follow-through."

"We know the earlier we are involved, the more likely we can help patients cope and get the resources they need."

Susan Hedlund, M.S.W., L.C.S.W., O.S.W.-C.



Participation by patients, survivors and caregivers in integrated support services

- **Integrative Oncology Conference at OHSU:** 50 patients and caregivers attended the free conference to introduce the available services. The next event will be in April, 2020.
- **Massage:** In 2018, the cancer massage therapists provided 1,683 massages to lessen anxiety and pain.
- **Writing groups:** Three separate writing groups (for women, men and adolescents and young adults) each met 35 times in 2019.
- **Mindfulness-based stress reduction course:** 20 patients and caregivers completed the eight-week class.
- **"Breath by Breath" class:** 80 patients attended the drop-in class aimed at teaching relaxation and stress reduction techniques. Additionally, 35 patients on the inpatient Bone Marrow Transplant Unit received bedside teaching of this technique.
- **Yoga classes for cancer patients:** More than 300 visits in 2018.



◀ There are various classes, conferences and writing groups offered to patients through support services.

OHSU Knight Cancer Institute locations

Key

- Oncology Surgical Services
- Hematology/Medical Oncology
- Radiation Oncology
- Knight Cancer Network Location

Astoria, OR

Columbia Memorial Hospital-OHSU Knight Cancer Collaborative ●●●●
2111 Exchange Street
Astoria, Oregon 97103

Coos Bay, OR

Bay Area Hospital ●
1775 Thompson Road
Coos Bay, Oregon 97420

Portland

OHSU Knight Cancer Institute, Marquam Hill ●●
3181 SW Sam Jackson Park Road
Portland, Oregon 97239

OHSU Knight-Legacy Health Cancer Collaborative, Marquam Hill ●
Kohler Pavilion
808 SW Campus Drive
Portland, Oregon 97239

OHSU Knight Cancer Institute, Center for Health and Healing, Buildings 1 and 2 ●●
3303 S Bond Avenue / 2485 S Bond Avenue
Portland, Oregon 97239

OHSU Knight Cancer Research Building
2720 S Moody Avenue
Portland, Oregon 97201

OHSU Knight-Legacy Health Cancer Collaborative, Good Samaritan ●●
1130 NW 22nd Avenue
Good Samaritan Hospital Building Suite 100
Portland, Oregon 97210

East Portland

OHSU Health – Adventist Medical Center ●●●●
10000 SE Main Street, Suite 350
Portland, Oregon 97216

Beaverton

**OHSU Knight-Legacy Health
Cancer Collaborative, Beaverton** ●●
15700 SW Greystone Court
Beaverton, Oregon 97006

Gresham

**OHSU Knight-Legacy Health
Cancer Collaborative, Mt. Hood** ●●
24988 SE Stark Street
Legacy Mount Hood Medical Center
Building #3, Suite 140
Gresham, Oregon 97030

Hillsboro

**OHSU Health -
Hillsboro Medical Center** ●●●
335 SE 8th Avenue
Hillsboro, Oregon 97123

Roseburg

Roseburg Medical Center ●
2880 NW Stewart Parkway #100
Roseburg, Oregon 97471

Tualatin

**OHSU Knight-Legacy Health Cancer
Collaborative, Meridian Park** ●
19260 SW 65th Avenue
Medical Plaza Office Building 2, Suite 140
Tualatin, Oregon 97062

Boise, Idaho

Saint Alphonsus Cancer Institute ●
1055 N. Curtis Road
Boise, Idaho 83706

Vancouver, Washington

**OHSU Knight-Legacy Health Cancer
Collaborative, Salmon Creek** ●●
2211 NE 139th Street
Vancouver, Washington 98686

**OHSU Knight-Legacy
Health Cancer Collaborative,
The Vancouver Clinic,
87th Avenue Clinic** ●●
700 NE 87th Ave #110
Vancouver, Washington 98664

For questions about a referral or to seek advice from an OHSU provider, please contact us:
Call 800-245-6478 or visit www.ohsu.edu/health/physician-advice-and-referrals

