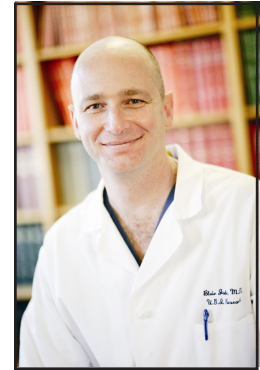


OHSU Esophageal Cancer Research Laboratory

Forging the Path to Prevention and Cure

A Commitment to Changing the World

Since 1970, the incidence of esophageal cancer has increased by 350% and its occurrence is rapidly rising, outpacing all other cancers. The National Cancer Institute estimates that this year 13,200 Americans will be diagnosed with esophageal cancer and approximately 12,500 will die of the malignancy. More than half of newly diagnosed patients have incurable disease at their first evaluation, and more than 90% of patients with esophageal cancer die within five years of diagnosis. At the Oregon Health & Science University Cancer Institute, Blair Jobe, M.D., and his colleagues are out to change these statistics.



Blair Jobe, M.D., FACS

Dr. Jobe and researchers in the Esophageal Cancer Research Laboratory are focused on understanding the clinical and molecular risk factors for esophageal cancer in order to develop better screening, preventative and curative treatment strategies. Their ultimate goal is to stop esophageal cancer from being a deadly disease, or better yet learn how to prevent it all together. Already their ground-breaking discoveries in developing novel screening methods and new treatment techniques are helping to change standards of care and bring new hope to people who encounter this disease. We invite you to be our partner in conquering esophageal cancer.

Our Vision

The Esophageal Cancer Research Laboratory is comprised of a multidisciplinary team of surgical oncologists, radiation oncologists, medical oncologists, and researchers who collaborate with pathologists, advanced imaging scientists, gastroenterologists, biostatisticians, epidemiologists, and otolaryngologists to move comprehensive and rigorous research from the bench to bedside. Our goals are to:

- Improve the identification of the risk factors and thus, enhance the prevention or early detection of esophageal cancer and related diseases
- Achieve a better understanding of the processes and mechanisms underlying the evolution of normal esophageal tissue to cancer
- Develop medical therapies that are directed at specific molecular targets
- Improve detection methods and endoscopic therapies
- Improve surgical techniques to treat esophageal cancer and related diseases
- Improve techniques in palliative care and patient-family psychosocial support
- Disseminate knowledge to both the medical profession and the public about esophageal cancer and related diseases

Giving New Hope through Innovative Research

While the OHSU Cancer Institute is one of the youngest designated centers of the National Cancer Institute, it has quickly evolved as a world leader in cancer research and care because of revolutionary discoveries such as Gleevec, the first targeted cancer therapy, now approved for seven cancers. Gleevec has saved tens of thousands of lives around the world and opened a new era in cancer research by proving if you understand what is broken at the molecular level, you can find a way to fix it. What we've accomplished with Gleevec needs to be replicated with every cancer. That requires a commitment to understanding the molecular basis of specific cancers and a commitment to moving laboratory discoveries into the clinics. Because Dr. Jobe is committed to these principles, our Esophageal Cancer Research Laboratory is poised to make discoveries that will change the face of esophageal cancer research and care.

Our strong history of accomplishments in the early detection, screening and surgical treatment of esophageal cancer and our strengths as a cancer institute in an academic medical setting provide a solid foundation for success.

Key Discoveries and Innovations

- **Pioneered Less Invasive Strategies for Treatment.** To help reduce the complication rate associated with the most common surgical treatment for esophageal cancer – the standard esophagectomy – Blair Jobe, M.D., and John Hunter, M.D., developed a new technique called minimally invasive inversion esophagectomy. Inspired by techniques used in removing varicose veins, in this method the end of the esophagus is inverted as the surgeon removes it, similar to the inversion that occurs when pulling a foot out of a sock. The surgeon then creates a replacement for the esophagus from a portion of the stomach. This technique eliminates several of the obstacles that plagued the original procedure. OHSU is the only place on the West Coast that offers this procedure.
- **Identified Procedure to Reduce Complications from Surgery.** Dr. Jobe developed a new strategy to address a significant complication related to esophagectomy known as anastomotic leak, which is a breakdown of the new connection between the remaining esophagus and the tubularized stomach. Ischemia, a lack of blood flow to the stomach, contributes to anastomotic leak. Dr. Jobe has shown how a procedure known as surgical delay allows the stomach to accommodate to the diminished blood supply that is required for esophageal replacement, leading to improved blood flow at the time of esophagectomy and normal healing without leakage. The *Annals of Surgery* recently published these study results and several centers around the county have adopted this technique.



Blair Jobe, M.D., visits
with patient Garrick Morse

- **Developed a Novel Screening Method.** The Esophageal Cancer Research Laboratory developed and validated a novel technique that will revolutionize the way physicians screen for esophageal cancer and its precursor. Currently, the cost and risk of conventional sedated endoscopy prevents large scale screening of at-risk populations. Researchers established the accuracy and patient acceptability of in-office unsedated small-caliber endoscopy, commonly referred to as the “skinny scope,” in the screening and surveillance of Barrett’s esophagus, the pre-malignant precursor of esophageal cancer. This technique will enable widespread screening in office settings since the esophagus can now be inspected as part of the physical examination. The results of this work were recently published in the *American Journal of Gastroenterology*.
- **Created an Esophageal Cancer and Related Diseases Tissue Bank.** The Esophageal Cancer Research Laboratory developed the Esophageal Cancer and Related Diseases (ECRD) tissue bank, funded by the National Cancer Institute, to provide the foundation for correlative investigations between clinical risk factors and genetic factors involved in malignant transformation and metastasis. The ultimate goal is to improve screening and identify high-risk populations prior to the development of incurable esophageal cancer. All esophageal cancer patients at OHSU and the Portland V.A. Medical Center provide questionnaire data, clinical history, esophageal tissue and peripheral blood, and tissue is collected endoscopically from a cross-section of patients with Barrett’s esophagus. The goal of this work is to develop a blood test that will predict the risk of cancer development based on genetic analysis.


- **Identified Risk Factor to Increase Early Detection.** At the time of diagnosis, more than 95% of patients who present with esophageal cancer seek medical attention for difficulty swallowing. This is a very “late sign,” and the majority of these patients are incurable. A recent discovery by the Esophageal Cancer Research Laboratory has identified patients with cough, regardless of whether they have typical symptoms of gastroesophageal reflux disease (heartburn or regurgitation), as being a clinical risk factor for the presence of esophageal cancer. They noted that unlike difficulty swallowing, the symptom of cough did not correlate exclusively with advanced disease. Therefore, using this risk factor as a trigger for unsedated screening endoscopy may lead to early detection and saved lives. The results of this work were published in the *Annals of Surgery*. This symptom is now used as a trigger for screening endoscopy by many centers across the nation. A large-scale clinical trial has recently been completed at OHSU and supports these initial observations. This work has been submitted to *Gastroenterology*.

Current and Future Research Projects

Esophageal cancer researchers have many other promising studies planned or underway to:

- Examine how gene therapy can induce the stomach to grow more new microvessels to limit ischemia and reduce the risk for leak after esophagectomy.

Current and Future Research Projects, *continued*

- Work with Charles Springer, Ph.D., director of the OHSU Advanced Imaging Research Center, to develop new noninvasive methods to acquire images of the esophagus in patients with esophageal cancer. This method, known as dynamic contrast-enhanced magnetic resonance imaging, provides high-resolution three-dimensional images that can identify locations of residual tumor after treatment with chemotherapy and radiation. This technology will help physicians monitor a patient's response to chemoradiation and identify patients in whom the tumor has been completely eradicated or for whom the therapy is not effective. Physicians may then better tailor a patient's treatment, potentially avoiding operations or chemoradiation treatment. This form of imaging, which has recently been validated by Jobe and colleagues will enable providers to directly gauge tumor response to therapy and thus will serve as a direct measure of tumor biology on patient-by-patient basis. This preliminary work was recently presented in Rome, Italy and has been accepted for publication in the *Journal of Gastrointestinal Surgery*.



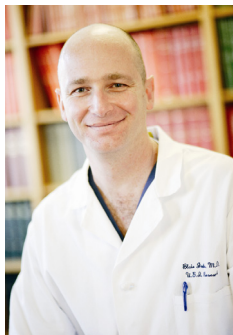
- Define molecular genetic markers of cancer progression and use these markers to identify small molecules that may be of value in preventing esophageal cancer.
- Develop a predictive model to help physicians identify people who are at risk of developing esophageal cancer. Prostate cancer researchers at OHSU have developed a similar model – a nomogram – to help physicians and patients identify which men might be at risk for prostate cancer and whether aggressive cancer is present, as these men are by far the most likely to benefit from treatment. The nomogram itself is a graphic made up of lines representing individual risk factors marked off to a scale and arranged in such a way that a numeric representation of the likelihood of cancer can be easily calculated. In developing the nomogram, researchers identified risk factors associated with malignant biopsies, which reveal four independent predictors of a positive biopsy. This can be used in the clinic setting to identify who is actually at risk for cancer based on easily determined clinical factors.
- Dr. Jobe has assembled the Barrett's Esophagus Risk Consortium (BERC) which is a national consortium centered on improving risk stratification for esophageal cancer which will be translated into clinically applicable mechanisms for the prevention and early detection of malignancy and a resultant survival advantage. BERC is composed of 11 sites which are strategically distributed across the entire geographic United States. Consortium members represent the Nation's foremost experts in esophageal cancer research. This work serves to unify the vision for esophageal cancer research in the Nations and avoid parallel lines of investigation, duplicated efforts, missed opportunity, and an ineffective use of talent.

People, Resources, and Infrastructure:

What Gives OHSU the Leading Edge in Cancer Discovery?

As part of Oregon’s only academic medical center, the OHSU Cancer Institute is able to quickly translate basic research into clinical research and then into new standards of care. Because of the institute’s exemplary basic and clinical research, in 1997, it achieved recognition as a designated center of the National Cancer Institute. The institute manages more than 1,000 research projects and at any given time has more than 120 open clinical trials. The institute is recognized worldwide for leadership in molecularly targeted therapies. Brian Druker, M.D., JELD-WEN Chair of Leukemia Research, with his development of Gleevec, was the first to prove that molecularly targeted cancer therapies work. Approved by the FDA for treating seven types of cancer, Gleevec has opened a new era in cancer research. Tens of thousands of people around the world are alive today because of this and other research discoveries made at the OHSU Cancer Institute.

The team of physicians and scientists who have come together to advance the progress in esophageal cancer research and care brings talents that are based in a passion for their work, which leads to excellence and a quest for new answers. This team of investigators is linked to clinical care through the Esophageal Care Team and its multidisciplinary conference. Below are key leaders who are working diligently to further esophageal cancer research and care (full bios are available upon request):



Blair Jobe, M.D., FACS, is the principal investigator for the Esophageal Cancer Research Laboratory and director of Foregut Research in the OHSU Digestive Health Center. Since joining the OHSU Department of Surgery in 2001, Dr. Jobe has developed the research program in esophageal cancer and related diseases. He is internationally recognized as a leader in his field. Under his direction, the laboratory has received several grants and produced more than 45 peer-reviewed publications. Dr. Jobe has received two NIH grants and has mentored five research fellows, who have received awards for their research achievements. The Society of Gastrointestinal Endoscopic Surgeons named Dr. Jobe as the Outstanding Young Researcher in 2005.



John Hunter, M.D., is professor and chairman for the OHSU Department of Surgery and director of the OHSU Digestive Health Center. He is a pioneer in minimally invasive surgical techniques and provides extensive expertise in the surgical treatment of esophageal cancer. Dr. Hunter has been instrumental in developing new techniques for removing the esophagus in patients with cancer and promoting healing at the site following removal. He has published more than 65 articles on esophageal surgery in peer-reviewed journals.



Grover Bagby, M.D., is founding director of the OHSU Cancer Institute and specializes and conducts research in hematopoiesis, leukemia and myelodysplasia, and Fanconi anemia. It is in large part because of Dr. Bagby’s efforts as founding director that the institute was designated as a center of the National Cancer Institute. Dr. Bagby is associate editor of the journal *Blood*, past president of the International Society of Experimental Hematology and member of the Association of American Physicians.

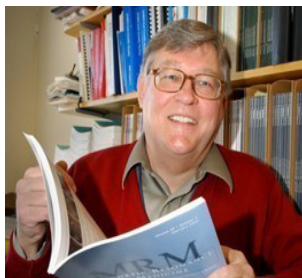
Eugene Chang, M.D., is a research fellow in the Esophageal Cancer Research Laboratory and is a promising physician-researcher with expertise in advanced statistical methods and computer science. He has taken the lead on developing new Magnetic Resonance Imaging (MRI) techniques to more accurately assess response to chemoradiation without the need for surgery. Dr. Chang has received funding for this work through the Society of Gastrointestinal Endoscopic Surgeons and is the recipient of an Early Clinical Investigator Award with Dr. Jobe as his mentor.



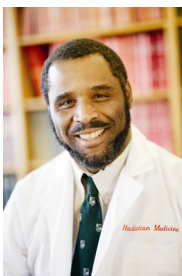
David Lieberman, M.D., is co-director of the OHSU Digestive Health Center and is interested in esophageal diseases, colon cancer screening and outcomes in endoscopy. He is internationally recognized for his work in screening endoscopy and has been continuously funded by the NIH for over 15 years. He is the former president of the American Society of Gastrointestinal Endoscopy. Board-certified in Internal Medicine and Gastroenterology, he heads the OHSU Division of Gastroenterology. He serves on the Advisory Board of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).



Cynthia Morris, Ph.D., M.P.H., is professor and vice chair of the OHSU Department of Medical Informatics and Clinical Epidemiology and Deputy Director for the National Endoscopic Databases. She is an experienced clinical researcher with more than 100 peer-reviewed publications and a record of continuous NIH grant funding throughout the majority of her career.



Charles Springer, Ph.D., is the director of the OHSU Advanced Imaging Resource Center (AIRC). Previously, he was a senior chemist at Brookhaven National Laboratory. For more than 35 years, the Springer Research Group has pursued and become widely recognized for its investigations into fundamental magnetic resonance principles. The OHSU AIRC, housed in the Biomedical Research Building, is one of the most sophisticated imaging centers in the country and houses 12-, 7- and 3-Tesla magnets.



Charles Thomas, Jr. M.D., is professor and chairman of the Department of Radiation Medicine and professor in the Division of Hematology and Medical Oncology in the OHSU School of Medicine. His academic and clinical areas of focus are in thoracic and gastrointestinal cancers. Dr. Thomas is principal investigator on multiple esophageal cancer trials sanctioned by the South Western Oncology Group (SWOG). He and Dr. Jobe co-direct the Esophageal Care Conference.



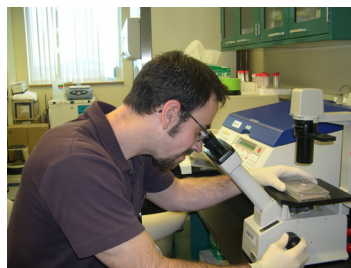
A tram connects OHSU's Marquam Hill Campus to the Center for Health & Healing on the Southwest Waterfront.

Access to the latest technologies and several core resources at the OHSU Cancer Institute provide cancer researchers with unique opportunities to conduct innovative research projects. For example, core resources such as the Gene Microarray Resource and the Proteomics Shared Resource give scientists the ability to compare cancerous tissue to normal tissue to better understand at the molecular level the pathways that lead to cancer. The Bioinformatics and Biostatistics Shared Resources are core to our ability to analyze statistical data of functional genomics data pathway modeling and data integration. Bioinformatics staff members work with researchers in the design and analysis of microarray studies. The Advanced Imaging

Center, the Pharmacokinetics Shared Resource, and the Clinical Research Management team also provide critical resources and expertise in designing and conducting studies.

In the past two years, OHSU's campus has significantly expanded providing much needed space for ongoing research, patient care and new collaborations. The new Center for Health and Healing on the South Waterfront houses the Esophageal Cancer Research Laboratory on the 14th floor and patients receive their care on the 6th floor. This innovative 16-story structure, which features solar panels, eco-roofs, and amazing advances in wastewater treatment, is the first medical and research building in the nation to receive a platinum LEED rating by the U.S. Green Building Council.

The Need: An Investment in the Future



With the incidence of esophageal cancer on the rise, we must find answers to stop this devastating disease. To make esophageal cancer a disease of the past, it is critical we invest in translational research and in outstanding physician-scientists who will lead the way with groundbreaking research that will translate to better care for patients and more reliable strategies for early diagnosis and cancer prevention. Our measures of success will be the number of new discoveries and the numbers of people healed and lives saved because of breakthroughs in cancer

prevention, detection and treatment. The OHSU Cancer Institute and Esophageal Cancer Research Laboratory is poised to make many more promising discoveries. We invite you to be our partner in achieving these goals. The investment in lives saved will be priceless.

To accelerate the pace of discovery and innovation, we have identified the following top priorities that will further our pioneering efforts to bring new hope to patients and their families. Investment in these priorities will help build the infrastructure necessary to achieve our vision.