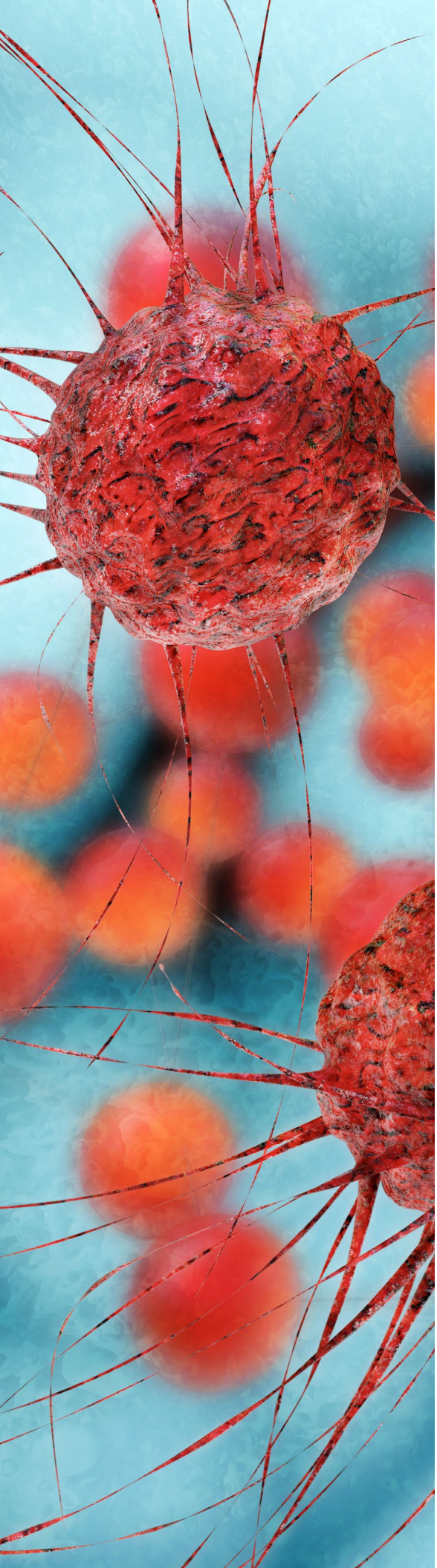

Stanford | MEDICINE

Stopping Cancer Before It Strikes

EARLY CANCER DETECTION AT THE CANARY CENTER

Twenty years ago, Grace Listwin was misdiagnosed twice with a bladder infection and given antibiotics. By the time her doctors discovered that she had advanced ovarian cancer, it was too late. Tragically, she died soon after.

"My mom was my best bud," says her son, former Cisco Systems executive Don Listwin. "She was always there for me." He wondered if his mother, and millions of others like her, would still be alive today if doctors had been able to identify the cancer early, when it was most treatable.

In response to his profound and potentially avoidable loss, Listwin channeled his prowess as an engineer and entrepreneur into answering this question, creating the Canary Foundation in 2004. Named after the bird that helped coal miners detect invisible, toxic gases before they turned deadly, the Canary Foundation supports innovative, early-cancer detection efforts at the world's premier research institutions.

Not content to stop there, he eventually brought his passion—and his expertise—to Stanford Medicine. In 2009, Listwin, who is an adjunct professor of radiology, partnered with the late Sanjiv "Sam" Gambhir, MD, PhD, the former Virginia and D.K. Ludwig Professor of Cancer Research and former chair of the Department of Radiology, to create the Canary Center at Stanford for Cancer Early Detection. With its multidisciplinary approach, this first-of-its-kind center aims to advance research discoveries to allow cancer to be caught early—and, ultimately, to stop it before it even starts.

The Canary Center at Stanford for Cancer Early Detection aims to foster discoveries that allow early cancer cells, like those illustrated here, to be detected sooner.

Addressing a Vital Need

While life-changing strides have been made in the diagnosis and treatment of many cancers, the Canary Center's goal is to take those successes even further. "We already have a lot of great therapies that would be much more effective if we could diagnose and treat every patient at a much earlier stage or even predict cancer before it starts," says Utkan Demirci, PhD, a professor of radiology and the Canary Center's interim director and division chief. "When diagnosed at stage 1, most cancers typically have fairly good survival rates. But those diagnosed at stage 4 have much worse odds. The Canary Center is working on cutting-edge approaches to get to stage 0—or even earlier, before the cancer is visible with our current technologies."

"We want to make early detection the rule rather than the exception, and to prevent cancer before it strikes," adds Ryan Spitler, PhD, deputy director of the Canary Center. "That's a paradigm shift that could save millions of lives and prevent so much suffering."

Despite the enormous potential of this vision, currently about 80 percent of federal funding is directed toward developing treatments for late-stage disease—not prevention. And industry alone cannot be expected to research and develop screening methods that could prevent many patients from needing expensive therapies. With its world-class clinicians and researchers, history of innovation, and global partnerships, the Canary Center is ideally positioned to make early discovery of cancer a reality within our lifetime.

Early Successes

In its first decade, the Canary Center has laid the groundwork for many exciting new approaches to early cancer detection. "We've made so many key discoveries," Dr. Demirci says, "and this field will only continue to expand in the next decade."

Here are just a few examples of how the Canary Center is applying its findings to develop concrete tools to catch cancer when it starts:

Tracing the roots of cancer | Tanya Stoyanova, PhD, assistant professor of radiology, and her colleagues identified Trop2, a biomarker that is associated with prostate cancer and potentially other types of cancer as well. Her team developed an imaging tracer that can be "welded" to Trop2 antibodies; now they're testing whether this targeted tracer can allow radiologists to see prostate cancer in its earliest stages, before tumors are visible on conventional images. It could also potentially help oncologists determine whether the cancer has metastasized and pinpoint the most strategic location to biopsy.

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>
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> *Deputy Director, Canary Center*

Dr. Stoyanova and her team are also investigating whether cancer-specific Trop2 antibodies could be welded to chemotherapy drugs that zero in on cancer cells, destroying tumors while minimizing collateral damage to healthy tissue.

Helping toilets detect cancer | Seung-min Park, PhD, an instructor in the Department of Urology, and his team have developed the Precision Health Toilet, a system that aims to use computer imaging and biochemical measurements to detect subtle changes in stool and urine that could indicate the presence of colon cancer, inflammatory bowel syndrome, and inflammatory bowel disease. Furthermore, as wastewater has become a critical tool in gauging the spread of COVID-19, Dr. Park believes his technology can play an important role in widespread testing for populations and individuals. Initially, this technology will function as a wellness device and, once clinical trials are conducted, as a diagnostic tool.

Isolating extracellular vesicles and exosomes for cancer research | Dr. Demirci's lab has developed an innovative tool that rapidly isolates extracellular vesicles and exosomes by size. Exosomes are nanosized vesicles that carry all the signatures of a cell, such as proteins, lipids, RNA, and DNA. Cancer cells produce and release these vesicles, as well as healthy cells, into their environments, into circulation, and into other bodily fluids.

Many cancers have biomarkers, or distinctive molecular signatures written in the language of proteins, that can serve as targets for both diagnosis and treatment. This new device is compatible with downstream omics analysis to better understand cancer and to be able to detect its biomarkers in various bodily fluids earlier. A new start-up company, Mercury Biosciences, is working to make the technology available globally.

Utkan Demirci, PhD

The interim director of the Canary Center, Dr. Demirci received his PhD in electrical engineering from Stanford University, where he also received MS degrees in electrical engineering and in management science and engineering. He is the holder of more than 25 pending or granted patents and is the recipient of several notable awards, including the National Science Foundation's CAREER Award and an Early Career Award from the IEEE Engineering in Medicine and Biology Society. Dr. Demirci is currently a fellow of the American Institute for Medical and Biological Engineering and a distinguished investigator of The Academy for Radiology & Biomedical Imaging Research.

A Multidisciplinary Team of Experts

One of the biggest challenges to this effort is detecting the very faint signals of early-stage cancer—the proverbial canary in the coal mine. Standard detection methods typically rely on cancer growing large enough to appear on imaging scans or for patients to develop symptoms. But the Canary Center is bringing us closer to being able to identify many types of cancer, including of the breast, prostate, lung, ovary, colon, and pancreas, in their very earliest stages. Employing innovative, minimally invasive diagnostic and imaging strategies, the center's experts aim to identify and target cancer when it is just a few rogue cells in the body.

Our multidisciplinary teams, which include experts in radiology, engineering, molecular biology, artificial intelligence (AI), and many other fields, have made breakthroughs in critical areas, including:

Identifying early cancer markers | Using proteomics, the Canary Center has discovered a number of new biomarkers that could be key to identifying cancer early and calculating how aggressive the cancer might be. Mining huge data sets to find clinically useful biomarkers requires tremendous computing power and expertise in bioinformatics, and Stanford University is a world leader in applying AI and mathematical modeling to help identify which biomarkers would be most detectable in early-stage cancer.

Using imaging to detect cancer when it starts | Stanford Medicine has long been a world leader in using tools such as CT, PET, ultrasound, and MRI to detect cancer. The Canary Center has taken this to the next level with molecular imaging. By developing imaging approaches that are designed to target cancer-specific biomarkers, radiologists are developing the ability to "see" cancer cells long before a tumor is detectable through conventional imaging.

Clinical trials | The Canary Center is testing and improving the efficacy of these novel diagnostic tools in patients through clinical trials. For instance, Alice Fan, MD, an assistant professor of medicine–oncology and a member of the Canary Center team, is conducting a study to identify molecular and imaging markers that can determine whether indeterminate pulmonary nodules are benign or malignant. She's also studying circulating DNA markers that can predict tumor recurrence. In addition, as a part of the Stand Up To Cancer project and with Department of Defense support, we are investigating early markers of lung cancer in small nodules and using this knowledge to improve image-based diagnostics.

▼ *Stanford Medicine has long been a leader in using imaging to detect cancer early.*

Help Bring the Promise to Life

"Early cancer detection is such a promising new field, and the Canary Center has been the first center of its kind and a leader in its field since the beginning," Dr. Demirci says. "Because many of these approaches are ahead of their time, philanthropy has really driven our ability to pursue the boldest ideas with the greatest potential."

With your support, the Canary Center will be able to recruit key faculty members, invest in state-of-the-art equipment, and fund more seed projects. "We want to accelerate our pace of discovery, expand collaborations, and translate promising discoveries all the way to the clinic so we can stop cancer right when it starts," he adds. "That way we can cure more patients and keep them healthy. This is a big challenge, and we need a strong, diverse team with every possible type of expertise to solve it."

"At the Canary Center, we work on the edge of what's possible," Dr. Spitler says. "We're passionate about using research not just to treat patients once they've been diagnosed, but to detect, cure, and ultimately prevent cancer before it ever develops."

In its first decade, the Canary Center has already made incredible discoveries that have the potential to fundamentally transform the way we diagnose cancer. Now we are poised to translate those discoveries into novel tests that could enable us to diagnose cancer at its very earliest stages.

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