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CANARY CENTER  
AT STANFORD

FOR CANCER EARLY DETECTION

## Canary Center at Stanford for Cancer Early Detection

3155 Porter Drive  
Palo Alto, CA 94304

 @canarycenter  
<http://canarycenter.stanford.edu>

The Canary Center at Stanford is a world-class research facility dedicated to cancer early detection programs. Our mission is to discover and implement minimally invasive diagnostic and imaging strategies for the detection and prognostication of cancers at early, curable stages. The Canary Center is the first in the world to integrate research on both in vivo and in vitro diagnostics to deliver these tests, by housing state-of-the-art facilities and collaborative research programs in molecular imaging, proteomics, chemistry, cell and molecular biology, and bioinformatics. These initiatives have extensive links to the Stanford Cancer Institute, forming a direct pipeline for translation of early cancer detection research into clinical trials and practice. The Canary Center was established in 2009 through an alliance between Don Listwin, founder of the Canary Foundation, and Dr. Sanjiv Sam Gambhir, Professor of Radiology at Stanford University School of Medicine. The Canary Center is directed by Dr. Sanjiv Sam Gambhir, Virginia and D.K. Ludwig Professor in Cancer Research, and Chairman of the Department of Radiology at Stanford University School of Medicine.



### **Sanjiv Sam Gambhir, MD, PhD**

#### **Division Chief, Canary Center at Stanford for Cancer Early Detection**

Chair, Department of Radiology  
Virginia and D. K. Ludwig Professor of Cancer Research  
Professor by courtesy, Departments of Bioengineering  
and Materials Science & Engineering  
Division Chief, Molecular Imaging Program at Stanford (MIPS)  
Director, Precision Health and Integrated Diagnostics (PHIND) Center  
Stanford University School of Medicine



### **Stephanie van de Ven, MD, PhD**

#### **Deputy Director, Programs**

Canary Center at Stanford for Cancer Early Detection  
Department of Radiology

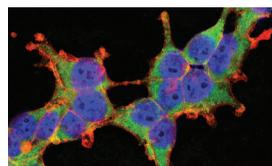


### **Mark Stolowitz, PhD**

#### **Deputy Director, Operations**

Canary Center at Stanford for Cancer Early Detection  
Department of Radiology

## Cover



Confocal image of prostate cancer cells expressing Trop2 oncogene and CD98 protein.

Courtesy of: Stoyanova Lab

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Antonieta “Toni” Benevento

## Saving Lives through Cancer Early Detection

The Canary Center at Stanford for Cancer Early Detection is committed to fundamental discovery and translation of novel early cancer detection and prognostication strategies. We have brought together scientists, physicians, and engineers to think outside the box to create new solutions for cancer early detection. We envision a two-stage diagnostic strategy to detect cancer at its earliest, most curable stage. This approach consists of a screening test as a first step, to identify individuals who are likely to have aggressive cancer (using biomarker tests in blood, urine, saliva, etc.), followed by a molecular imaging test as a second step, to localize and characterize the cancer. The Canary Center is the first in the world to integrate research on both in vivo and in vitro diagnostics to deliver these tests. A two-stage approach for early cancer diagnosis is critical to help avoid unnecessary invasive procedures, while still maintaining the sensitivity needed to identify as many instances of cancers as possible. We believe the merger of in vitro diagnostics with in vivo molecular imaging will be the way in which the cancer early detection problem will eventually be solved.

To support our integrated research strategy, the Canary Center houses four state-of-the-art shared resource facilities: (1) Proteomics, (2) Cell and Molecular Biology, (3) Chemistry, and (4) Preclinical Imaging. The Proteomics facility is designed to accommodate numerous technologies including several mass spectrometry platforms dedicated to the discovery, verification, and validation of biomarkers and imaging targets for early cancer detection. This core includes a Bioinformatics Resource devoted to developing solutions for collaborative translational research, including the implementation of software platforms for specimen tracking and cross-platform data analysis, sharing, and storage. The Cell and Molecular Biology facility is equipped with cutting-edge shared resources for cell culture, microscopy, and molecular biology. The Chemistry facility is dedicated to the development of molecular imaging agents for multiple modalities, including PET, ultrasound, MRI, photoacoustic, and optical imaging tests. The Preclinical Imaging facility develops infrastructure, expertise, and tools to perform multimodality in vivo imaging primarily for preclinical research.

The Canary Center's main research areas currently include: cancer biomarker discovery and validation, development of novel technologies and point-of-care diagnostics, mathematical modeling of cancer, development of new imaging techniques and molecular imaging probes, and translation of new diagnostic approaches into clinical trials. Our world-class research facilities will continue to expand over the next few years as we continue to grow our program and build new partnerships with companies and institutions worldwide. Solving the cancer early detection problem may take many years and we remain committed to making a difference in helping generations yet to come in leading healthier and more fulfilling lives.

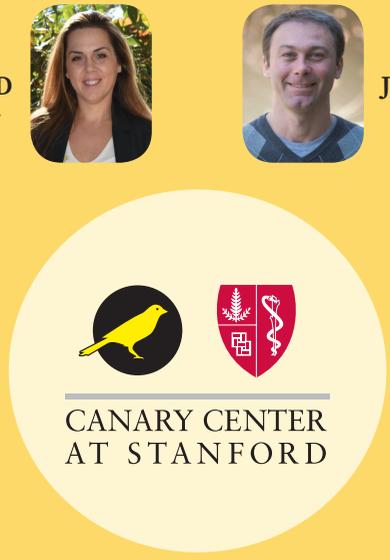


Don Listwin and his mother Grace Listwin

The Canary Foundation is the world's first non-profit organization dedicated solely to cancer early detection research. Canary's founder, Don Listwin, decided something needed to be done about the way cancer is detected after his mother was twice misdiagnosed with a bladder infection, and by the time they discovered late-stage ovarian cancer, it was too late. Soon after this tragedy, Don met Dr. Lee Hartwell, former president of the Fred Hutchinson Cancer Research Center, who shared his passion for finding ways to detect cancer in its earliest stages. They put together the first Canary research team, which included Dr. Sanjiv Sam Gambhir at Stanford University School of Medicine. This initial team became the beginning of the Canary Foundation, officially established in 2004.

Since then, the foundation has partnered with Stanford University to create the Canary Center at Stanford and has funded the university's first faculty members dedicated 100% to cancer early detection. The foundation also works with partners across the globe to form multidisciplinary research teams and fund innovative projects, often bridging the gap between academia and industry. Additionally, the Canary Foundation hosts multiple events throughout the year to assist with fundraising. The largest of these, the Canary Challenge, is a cycling and walking event bringing hundreds of participants together each year to support Canary's mission of stopping cancer early.

<http://www.canaryfoundation.org>



Tanya Stoyanova, PhD  
Assistant Professor



Jeremy Dahl, PhD  
Associate Professor



Tom Soh, PhD  
Professor



Utkan Demirci, PhD  
Professor



Sharon Pitteri, PhD  
Associate Professor



Alice Fan, MD  
Assistant Professor



Parag Mallick, PhD  
Associate Professor



Sanjiv Sam Gambhir, MD, PhD  
Division Chief



## Associate Members

 J Brooks, MD Urology	 Z Cheng, PhD Radiology	 C Curtis, PhD Oncology, Genetics	 B Daniel, MD Radiology	 A de la Zerda, PhD Structural Biology	 M Diehn, MD, PhD Radiation Oncology	 D Felsher, MD, PhD Oncology, Pathology	 J Ford, MD Oncology	
 O Gevaert, PhD Biomedical Informatics	 J Harris, PhD Engineering	 S Hori, PhD Radiology	 A Iagaru, MD Nuclear Medicine	 H Itakura, MD, PhD Oncology	 B Jeffrey, MD Radiology	 H Ji, MD Oncology	 P Khuri-Yakub, PhD Electrical Engineering	
 A Kurian, MD Oncology	 A Leung, MD Radiology	 J Liphardt, PhD Bioengineering	 J Lipson, MD Radiology	 S Malhotra, PhD Radiation Oncology	 I Oakley-Girvan, PhD, MPH Health Research & Policy	 R Paulmurugan, PhD Radiology	 S Plevritis, PhD Radiology	 J Reiter, PhD Radiology
 N Scholler, MD, PhD SRI International	 J Siddhartha, MD, PhD Pathology	 O Solgaard, PhD Electrical Engineering	 G Sonn, MD Urology	 M Stefanick, PhD Obstetrics & Gynecology	 S Wang, PhD Radiology	 R West, MD, PhD Pathology	 J Wu, MD, PhD Endocrinology	 J Ye, PhD Radiation Oncology

**Canary Center researchers continue to work tirelessly on novel strategies to detect aggressive cancers early, at a time that they can be cured. Some of their most recent innovations are described here:**

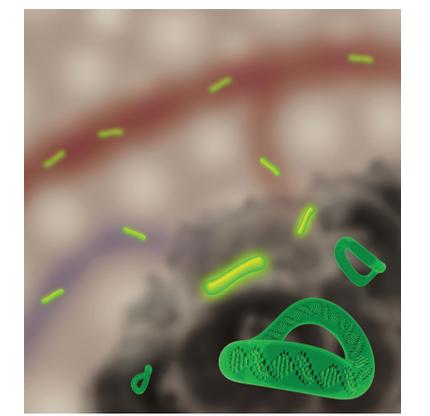
### High-throughput screening for cancer biomarker-specific aptamers

Aptamers are a promising class of affinity reagents because they are chemically synthesized, making them highly reproducible and distributable as sequence information rather than a physical entity. It is difficult to routinely generate aptamers that possess both high affinity and specificity because conventional aptamer selection can only be performed either for affinity (positive selection) or for specificity (negative selection), but not both simultaneously. Canary Center researchers have developed a method to quantitatively screen aptamers for affinity and specificity at high-throughput, called Multiparameter Particle Display. They have shown that these aptamers can outperform high-quality monoclonal antibodies in capturing cancer biomarkers.

Wang J, Yu J, Yang Q, et al. Multiparameter Particle Display (MPPD): A Quantitative Screening Method for the Discovery of Highly Specific Aptamers. *Angewandte Chemie International Edition* 2017;56:744-7.

### Using tumor-activatable minicircles to reveal early cancers in blood

Blood-based cancer biomarker screening is an attractive noninvasive approach to detect cancer. However, measuring endogenous molecules in early cancers is extremely challenging because there are typically very few cancer cells compared to the numerous healthy cells that produce those endogenous molecules. To overcome this challenge, Canary Center researchers have come up with an alternate strategy in which nonviral safe vectors, called “tumor-activatable minicircles” are administered. These minicircles make cancer cells produce a specific reporter (for example a protein) that is then shed into the blood stream, while healthy cells do not produce this reporter. Measuring such an “artificial biomarker” is a novel way to improve early cancer detection and potentially enable more timely interventions. Researchers are further optimizing these minicircles and also creating different versions for artificial biomarker detection in urine and breath.



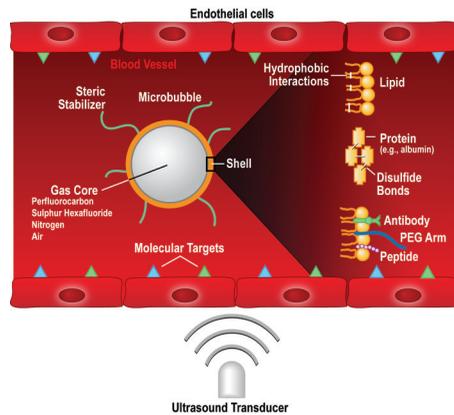
Ronald JA, Chuang HY, Dragulescu-Andrasi A, Hori SS, Gambhir SS. Detecting cancers through tumor-activatable minicircles that lead to a detectable blood biomarker. *Proc Natl Acad Sci USA* 2015;112:3068-73.

### Improving the sensitivity of ultrasound molecular imaging with coherence-based beamforming

Ultrasound imaging using molecularly targeted microbubbles can be challenging because of the low concentration of microbubbles that bind to the molecules expressed in cancer and the signal degradation caused by the presence of heterogeneous soft tissue between the ultrasound transducer and the tumor. Canary Center researchers have developed a solution for this problem by using a technique called short-lag spatial coherence beamforming. In their preclinical studies, they mimicked challenging clinical imaging conditions and showed that this new method can improve the signal-to-noise ratio of ultrasound molecular imaging by an average of 41%. This is an important step in improving the detection of very small cancers using ultrasound and microbubbles.

Hyun D, Abou-Elkacem L, Perez VA, Chowdhury SM, Willmann JK, Dahl JJ. Improved Sensitivity in Ultrasound Molecular Imaging With Coherence-Based Beamforming. *IEEE* 2018;37:241-50.

## Combining microbubbles and ultrasound to detect cancer



Ultrasound is a widely used imaging technique in patients with suspected breast or ovarian lesions. The introduction of microbubbles that can bind specifically to certain molecules expressed in cancer has made ultrasound a molecular imaging modality that may be able to improve cancer detection. Recently, Canary Center researchers have clinically translated these microbubbles in patients. In the first-in-human trial, women with breast or ovarian tumors were injected intravenously with microbubbles that target a receptor found on tumor neovasculature (KDR). These microbubbles accumulated in the blood vessels of malignant tumors but not benign tumors. This technology may be useful in differentiating malignant from benign lesions and possibly reducing unnecessary biopsies or surgeries in the future.

Canary Center researchers have used the same microbubbles successfully in patients with prostate cancer and have now engineered a novel targeted microbubble that binds to a molecule expressed on the cell-surface of pancreatic cancers (Thy1).

Willmann JK, Bonomo L, Carla Testa A, et al. Ultrasound Molecular Imaging With BR55 in Patients With Breast and Ovarian Lesions: First-in-Human Results. *Journal of Clinical Oncology* 2017;35:2133-40.  
Abou-Elkacem L, Wang H, Chowdhury SM, et al. Thy1-Targeted Microbubbles for Ultrasound Molecular Imaging of Pancreatic Ductal Adenocarcinoma. *Clinical Cancer Research* 2018;24:1574-85.

## Isolating extracellular vesicles to discover cancer biomarkers

Circulating tumor-derived extracellular vesicles have emerged as a promising source for identifying cancer biomarkers for early cancer detection. However, most isolation methods are tedious, nonstandardized, and require bulky instrumentation such as ultracentrifugation. Canary Center researchers have engineered a new extracellular vesicle isolation tool called ExoTIC (exosome total isolation chip), which is simple, easy-to-use, modular, and facilitates high-yield and high-purity extracellular vesicle isolation from biofluids. They have shown high extracellular vesicle isolation yields from various clinical samples, including plasma, urine, and lavage fluid, demonstrating the device's broad applicability. The ability of ExoTIC to efficiently isolate extracellular vesicles from small sample volumes also opens up avenues for point-of-care clinical testing from fingerprick quantities.

Liu F, Vermesh O, Mani V, et al. The Exosome Total Isolation Chip. *ACS Nano* 2017;11:10712-23.

## Mapping the glycoproteome to unravel dysregulations in cancer

Glycosylation is a post-translational protein modification that generates extreme proteomic diversity and contributes to a plethora of cellular functions. Dysregulation of the glycoproteome is often correlated with disease states including cancer. The ability to define the intact glycoproteome would help identify potential cancer biomarkers but remains very challenging due to the complexity of glycoproteoforms. To address these unique challenges, Canary Center researchers have teamed up with other biochemists to develop a mass-independent chemical glycoproteomics platform, termed isotope targeted glycoproteomics (IsoTaG). The use of this technology may increase our understanding of glycosylation alterations in cancer and potentially uncover a new class of cancer biomarkers.

Woo CM, Felix A, Byrd WE, et al. Development of IsoTaG, a Chemical Glycoproteomics Technique for Profiling Intact N- and O-Glycopeptides from Whole Cell Proteomes. *Journal of Proteome Research* 2017;16:1706-18.

## Levitating blood to decode rare circulating tumor cells

Magnetic levitation principles have been used previously to monitor and biologically characterize cells. Canary Center researchers have shown that different cell types with various sizes, ranging down to the sub-micron level, can be aligned at unique heights using these principles. They have developed a levitation device that can be used with a smartphone (i-LEV) to identify and quantify blood cells without using any labels in a point-of-care setting. They are further developing this technology and are validating a levitational sorting device (LeviSORT) that can sort cells from blood and other biofluids (urine, saliva, lavage fluid, etc.) with high-throughput and without biomarkers or labels. Isolating rare circulating tumor cells in this way can increase our understanding of cancer biology and may lead to the discovery of new biomarkers for early cancer detection.

Durmus, NG, Tekin HC, Guven S, Sridhar K, Arslan Yildiz A, Calibasi G, Ghiran I, Davis RW, Steinmetz LM, Demirci U. Magnetic Levitation of Single Cells. *Proc Natl Acad Sci USA* 2015; E3661-8.

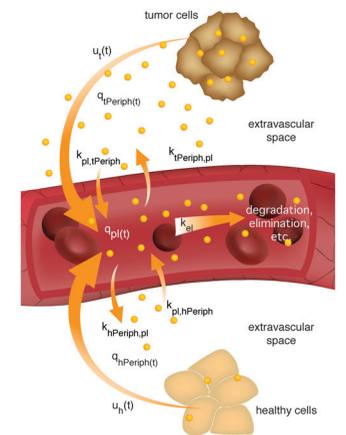
Baday M, Calamak S, Durmus NG, Davis RW, Steinmetz LM, Demirci U. Integrating Cell Phone Imaging with Magnetic Levitation (i-LEV) for Label-Free Blood Analysis at the Point-of-Living. *Small* 2016;12:1222-9.

## Creating one place to find all cancer biomarker information

There is a vast amount of conflicting information in the scientific literature about what proteins are good or bad biomarkers and which disease they might indicate. This makes it difficult to find and validate important biomarkers. To help solve this problem, Canary Center researchers have built an interactive database that allows users to find all existing information on a particular protein in one place, called Markerville. The ultimate goal of the project is to build a complete virtual model of cancer. Users of Markerville could learn everything known about a particular protein and also how it might be expected to serve as a biomarker in a given cancer. Researchers are continuing to develop and improve this platform. Markerville is publicly accessible at [www.markerville.org](http://www.markerville.org)

## Personalizing cancer blood biomarker screening strategies using mathematical modeling

An effective cancer biomarker screening strategy must distinguish aggressive from nonaggressive tumors at an early, intervenable time. However, for blood-based strategies to be useful, the quantity of biomarker shed into the blood and its relationship to tumor growth or progression must be validated. Canary Center researchers have shown that blood biomarkers highly shed from early-stage cancers in living subjects may serve as feasible reporters of tumor cell viability and disease aggressiveness. They developed a new mathematical modeling-based personalized cancer screening strategy to aid in early clinical decision making to determine when to intervene on a potentially aggressive cancer, when to proceed with active surveillance of a non-aggressive cancer, and how to optimally continue blood sampling in a patient whose disease state is unknown.

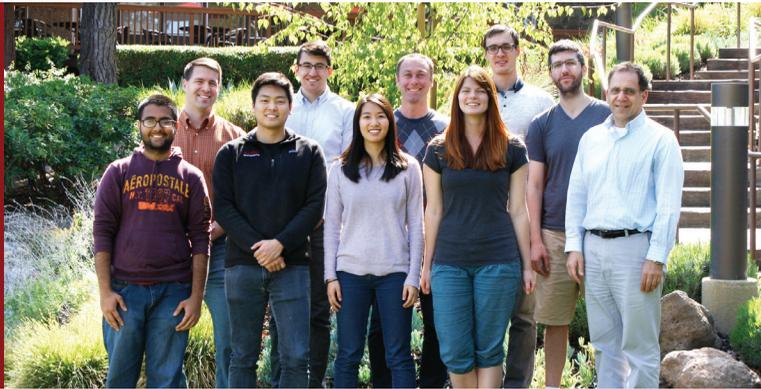


Hori, SS & Gambhir, SS Mathematical model identifies blood biomarker-based early cancer detection strategies and limitations. *Sci Transl Med* 2011;3: 109ra116.

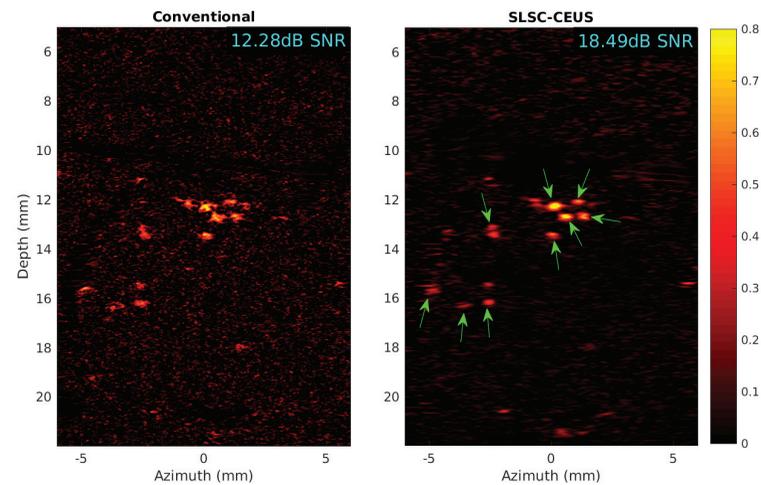
Hori SS, Lutz AM, Paulmurugan R, Gambhir SS. A Model-Based Personalized Cancer Screening Strategy for Detecting Early-Stage Tumors Using Blood-Borne Biomarkers. *Cancer Research* 2017;77:2570-84.

## ULTRASOUND RESEARCH GROUP

Jeremy Dahl, PhD



Our research group develops and implements ultrasonic beamforming and imaging methods. We have recently developed high sensitivity methods based on coherence beamforming for anatomical, flow, and molecular imaging. We have built these coherence-based imaging strategies into real-time imaging systems using a GPU-based software beamformer, and have utilized it to implement preclinical imaging studies with molecular ultrasound for the early detection of breast and pancreatic cancer. We are also developing volumetric molecular ultrasound imaging for breast cancer screening in collaboration with the Breast Imaging division in the department of Radiology.



### ACHIEVEMENTS

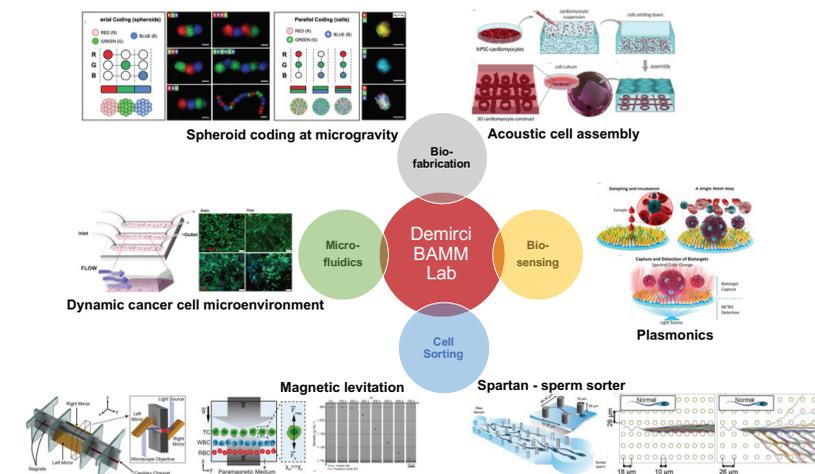
- Published a technique to enhance sensitivity for ultrasound molecular imaging for cancer early detection in IEEE Transactions on Medical Imaging, and presented the results at the 2016 World Molecular Imaging Congress and the 2016 IEEE International Ultrasonics Symposium.
- The National Science Foundation (NSF) awarded first-year graduate student Jasmine Shu a Graduate Research Fellowship for her work and pursuits in ultrasound and molecular imaging.
- The National Institutes of Health (NIH) awarded a R01 grant to the Translational Molecular Imaging and Dahl labs to develop a volumetric ultrasound molecular imaging system for breast cancer screening and translate the technology into the clinic.

## BIO-ACOUSTIC MEMS IN MEDICINE (BAMM) LAB

Utkan Demirci, PhD



One of the greatest achievements in medicine is the remarkable progress that has been made in understanding, diagnosing, monitoring, and treating disease conditions by creating innovative micro/nanoscale technologies. We have made seminal contributions and inventions for the development of microfluidic bio-imaging/sensing platforms for point-of-care diagnostics with broad medical applications. We have developed tools for detecting cells/cancer biomarkers and isolating exosomes from body fluids. We have created microfluidic tools to mimic the cancer microenvironment for investigating metastasis. We made breakthroughs in cell-sorting and single-cell imaging by magnetically levitating cells to isolate circulating tumor cells/clusters from blood with applications in precision medicine; developed a microfluidic technology for sperm selection resulting in 5,000+ newborns globally and integrated it with lens-free, super-resolution imaging. We created successful start-ups bringing these technologies into the clinic.

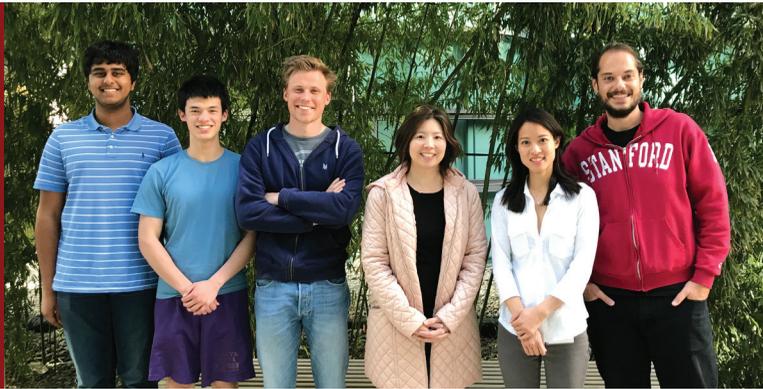


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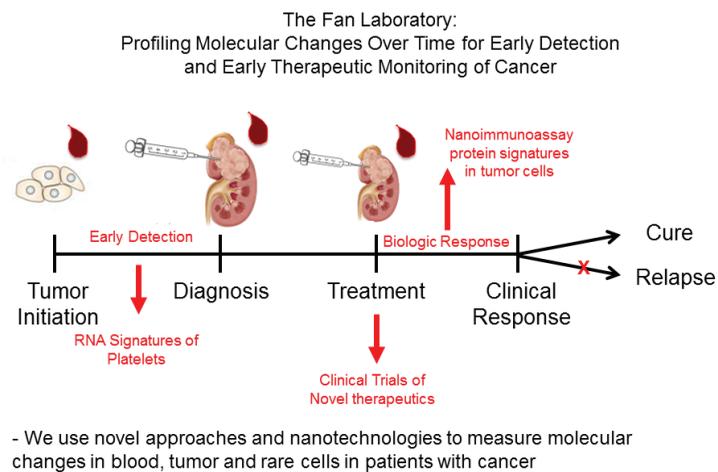
- Basic Scientist of the Year, Stanford University School of Medicine, Department of Radiology (2016).
- The Academy for Radiology & Biomedical Imaging Research Distinguished Investigator Award (2017).
- Elected to AIMBE College of Fellows (2017).
- Certificate of Appreciation, Institute for Experimental and Clinical Traumatology, Ludwig Boltzmann Institute, Vienna, Austria (2018).
- FDA Clearance for three technologies developed by our laboratory (2018).

FAN  
LAB

Alice Fan, MD



Dr. Fan is a physician scientist whose laboratory focuses on developing biomarkers for early detection and early measurement of therapeutic response in patients with urologic malignancies. She develops and applies novel technologies to determine the mechanism of activity of novel and standard agents directed against metabolic and oncogenic signaling pathways, define biomarkers for diagnosis and therapeutic response in patients with cancer, and investigate the immune response to targeted therapeutics. Dr. Fan's clinical focus is on patients with bladder, kidney and prostate cancer: she leads several clinical trials to test efficacy of novel agents, including a first-in-class glutaminase inhibitor in kidney cancer. Her research team in the lab and in the clinic is comprised of postdoctoral fellows, a research associate, clinical research coordinators and high school students.

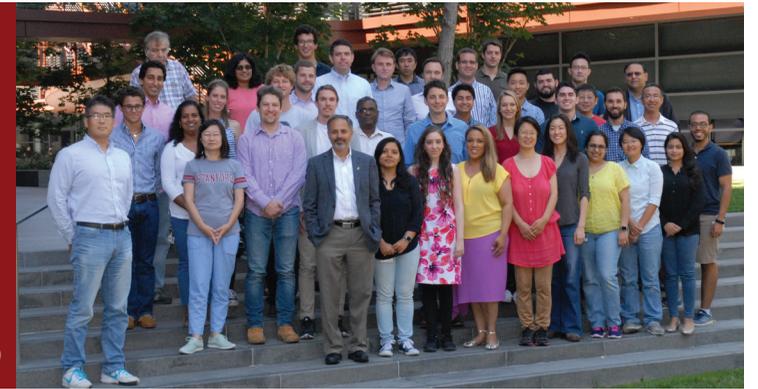


ACHIEVEMENTS

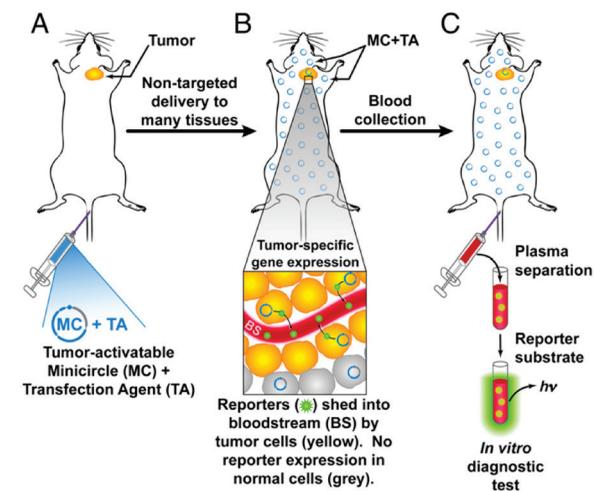
- K23 Mentored Patient-Oriented Research Career Development Award from the NIH/NCI.
- ASCO Career Development Award from the Conquer Cancer Foundation.
- Viola Chen, Fellow in Oncology, received a Pilot Grant from the Stanford Department of Medicine Translational Research and Applied Medicine Program.
- Research Scientist, Christian Hoerner received a Pilot Grant from the Stanford Department of Medicine Translational Research and Applied Medicine Program.

MULTIMODALITY  
MOLECULAR  
IMAGING  
LAB

Sanjiv Sam Gambhir, MD, PhD



The Multimodality Molecular Imaging Laboratory is developing in vitro and in vivo molecular imaging assays to monitor fundamental cellular/molecular events in living subjects, including patients. Technologies such as positron emission tomography (PET), optical (fluorescence, bioluminescence, Raman), ultrasound, and photoacoustic imaging are all under active investigation. Imaging agents for multiple modalities including small molecules, engineered proteins, and nanoparticles are under development and being clinically translated. Novel synthetic biomarker strategies to force cancer cells to produce a signal are also under active investigation. Our goals are to detect cancer early and to better manage cancer through the use of both in vitro diagnostics and in vivo molecular imaging. Strategies are being tested in small animal models and are also being clinically translated.



ACHIEVEMENTS

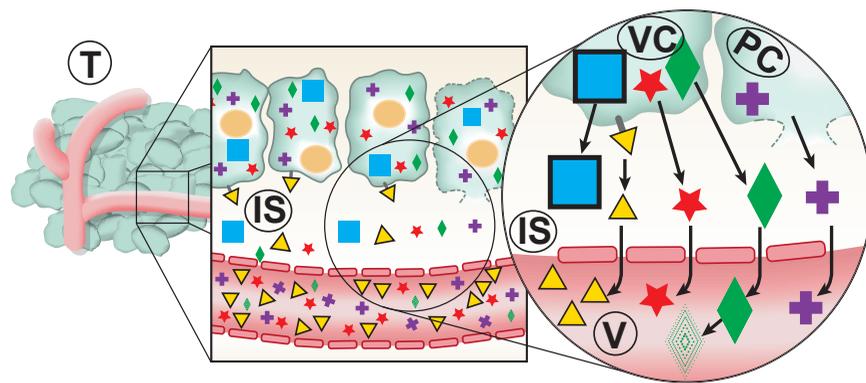
- First-in-man studies of a new  $\alpha\beta6$  PET tracer based on the knottin scaffold. This tracer should help identify several cancer types including pancreatic cancer for which there are no good imaging agents to date.
- Development of several new PET tracers for imaging the immune system including: checkpoint inhibitor imaging and the imaging of cell surface receptors (e.g., OX40) on activated T cells.
- Novel instruments including a combined ultrasound and photoacoustic transrectal device for the early detection of prostate cancer.
- Development of new Raman and photoacoustic molecular imaging strategies for improved cancer detection.
- Development of novel devices for in vivo selection of rare biomarkers using a magnetic wire technology.

**MULTI-SCALE  
DIAGNOSTIC  
LAB**

Parag Mallick, PhD



The Mallick lab focuses on translating multi-omic discovery into precision diagnostics. In particular, we use tightly integrated computational and experimental approaches to discover the processes underlying how cells behave (or misbehave) and accordingly how cancers develop and grow. We hope that by exploring these processes, and by formalizing our knowledge in predictive mathematical models, we will be able to better identify biomarkers that can be used to detect cancers earlier and describe how they are likely to behave (e.g., aggressive vs. indolent, drug sensitive vs. responsive). We are specifically working in three focus areas: Cancer Systems Biology, Multi-scale Biomarker Biology, and Technology Development.

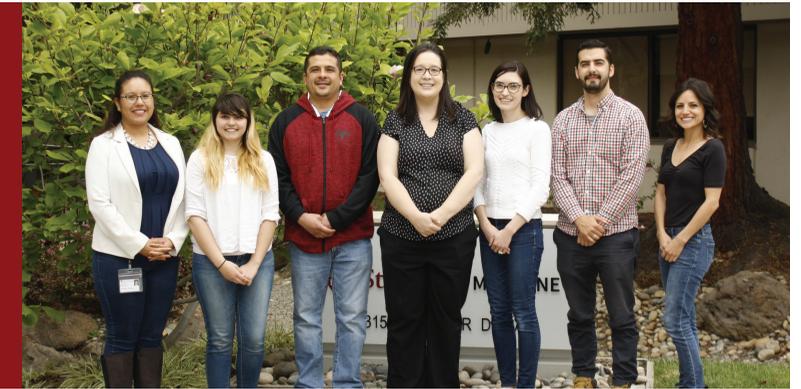


**ACHIEVEMENTS**

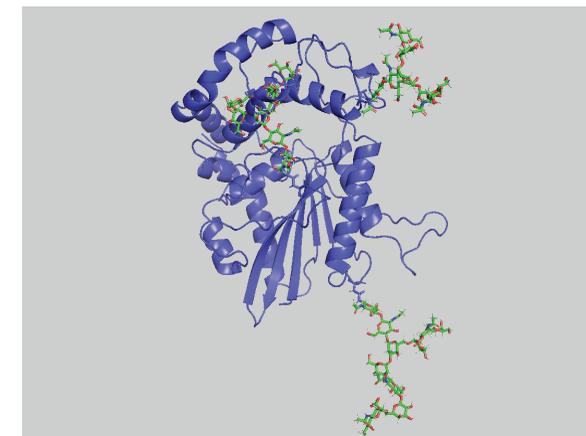
- Development of the DISK/Spellbook ecosystem - a set of open-source tools to accelerate the extraction of knowledge from complex multi-omics data.
- Machine reading tools for extracting biomarkers from scientific articles.
- Use of multi-dimensional pathology data to demonstrate the role of the tumor microenvironment in driving tumor heterogeneity and drug resistance.

**CANCER  
MOLECULAR  
DIAGNOSTICS  
LAB**

Sharon Pitteri, PhD



The Pitteri Laboratory is dedicated to early detection of aggressive cancer through the development of new in vitro diagnostic strategies. We are investigating molecules in blood, tissue, and other bodily fluids that can be used as disease biomarkers. To develop molecular signatures for disease diagnosis, we are particularly interested in exploiting aberrant glycosylation—a well-established but poorly understood feature—in tumorigenesis. Our recent work has focused primarily on breast and prostate cancers, where we have focused on distinguishing benign from malignant lesions and distinguishing indolent from aggressive disease, respectively. We have active collaborations with clinicians and other scientists to apply our technologies to study clinical samples, cell lines, and mouse models.

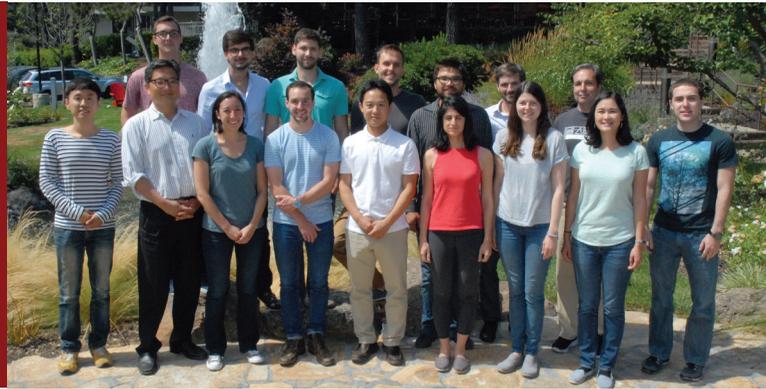


**ACHIEVEMENTS**

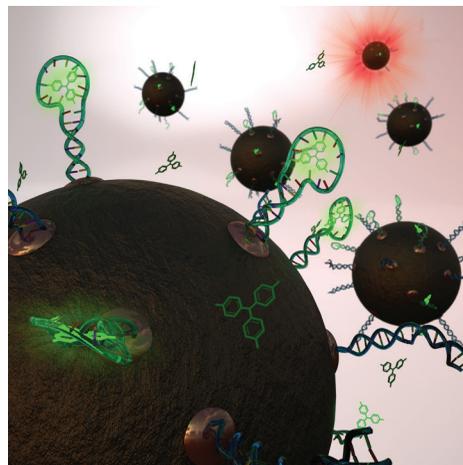
- Collection of interstitial fluid in the Breast Imaging Clinic to measure proteins in the tumor microenvironment that are capable of distinguishing benign from malignant lesions.
- Development of methods to systematically identify, localize, characterize, and quantify glycosylated proteins in biological samples.
- Understanding of differential protein glycosylation in prostate tumor samples from men with aggressive vs. indolent cancer, and in blood samples from men with benign vs. malignant disease.

**SOH  
LAB**

H. Tom Soh, PhD



In order to achieve early and accurate detection of diseases, antibodies have been extensively used to specifically bind to disease biomarkers. Unfortunately, there are many types of important disease biomarkers, such as metabolites and carbohydrates, which antibodies do not recognize. This has been a major problem for advancing molecular diagnostics in the clinic. To address this problem, our lab develops synthetic antibodies (called “aptamers”). To generate these aptamers, we use the principles of evolution (mutation, selection, and amplification) in the laboratory to create novel molecules that do not exist in nature. We then use these aptamers to develop advanced biosensors that can achieve extremely sensitive detection of biomarkers in clinical samples. For example, our laboratory pioneered the development of “real-time biosensors” that can continuously measure target molecules directly in living animals. We hope to expand these measurement techniques and bring them into the clinic to accurately detect diseases at their earliest stages.

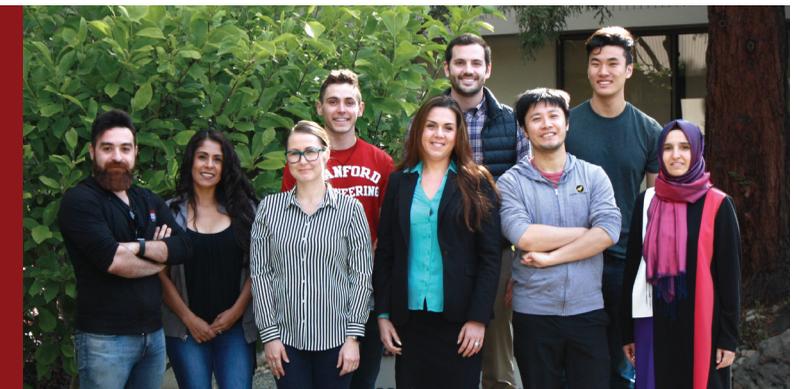


**ACHIEVEMENTS**

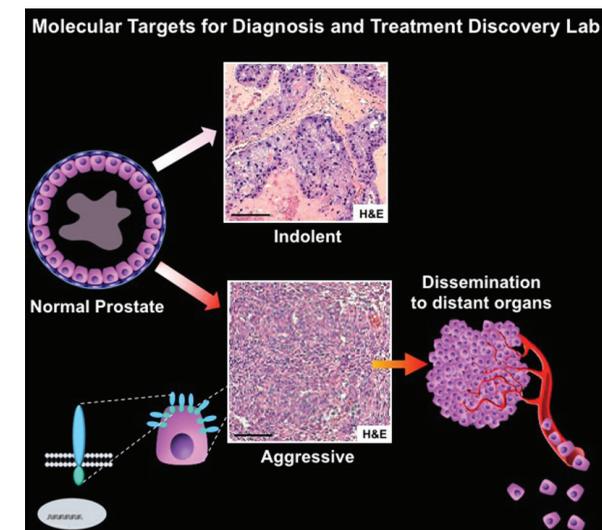
- Developed high-throughput technology to discover aptamers with non-natural chemical functionalities with excellent specificity.
- Developed the first real-time biosensors to continuously measure specific biomolecules in the body, in real time.
- Demonstrated the first real-time closed-loop control of drug level in live animals.

**MOLECULAR  
TARGETS FOR  
DIAGNOSIS AND  
TREATMENT  
DISCOVERY  
LAB**

Tanya Stoyanova, PhD



Dr. Stoyanova’s research focuses on understanding fundamental molecular mechanisms underlying cancer development. Currently, her group studies signaling cascades initiated by cell surface receptors, which are involved in the early event of prostate cancer initiation and regulation of the transition from indolent to aggressive disease. The Stoyanova lab is also interested in developing new clinically relevant animal models to study genetic events and molecular mechanisms underlying cancer development. The goal of Dr. Stoyanova’s laboratory is to improve the stratification of indolent from aggressive prostate cancer and aid the development of better therapeutic strategies for advanced disease. Additionally, the lab is interested in understanding molecular mechanisms that govern the self-renewal activity of adult stem cells and cancer stem cells.



**ACHIEVEMENTS**

- Stoyanova Lab received DOD Idea Development Award.
- Dr. Meghan Rice awarded Early Investigator Research Award.
- Austin You Su received 2018 Stanford Undergraduate Advising & Research Major Grant to support full-time immersive summer research.
- Mark Buckup, 2017 Canary Summer Intern received Verily Young Scientist Award.

**TRANSLATIONAL  
MOLECULAR  
IMAGING  
LAB**

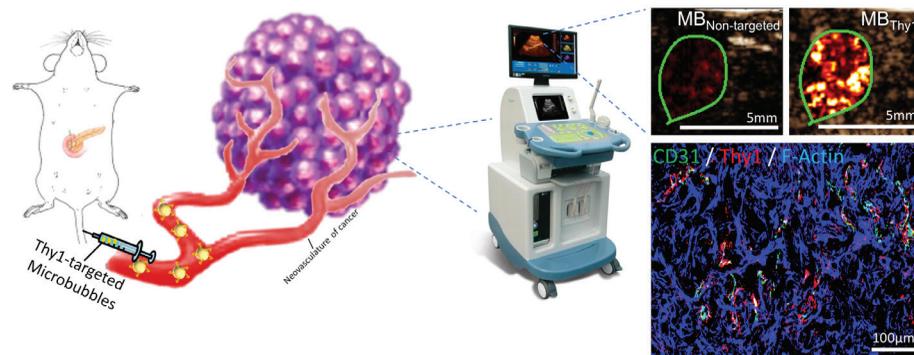


Juergen Willmann, MD

\*Dr. Juergen Willmann passed away January 8, 2018. His lab remains active and continues his work.

The Translational Molecular Imaging lab develops and tests ultrasound contrast agents using ultrasound molecular imaging for identifying and monitoring diseases with a goal to translate this approach to the clinic for improved patient management. Ultrasound molecular imaging uses intravascular contrast microbubbles that are functionalized to bind to vascular targets differentially expressed in diseased conditions compared to normal vasculature. Using these microbubbles, our lab has shown that foci as small as <1 mm can be detected in pancreatic and breast cancer demonstrating its potential for early cancer detection. This approach can also be used to visualize and monitor regions of diseased bowel undergoing active inflammation. We have also successfully explored their use as a drug delivery vehicle for cancer therapy. Finally, our lab has performed the first-in-human clinical trial using these novel contrast agents in women with ovarian and breast cancer.

*In vivo* Ultrasound Molecular Imaging of Pancreatic ductal adenocarcinoma



**ACHIEVEMENTS**

- Published first-in-human clinical trial results on KDR-targeted ultrasound molecular imaging.
- Three new clinical trials on ultrasound molecular imaging of pancreatic, breast, and ovarian cancer.
- Performed first-in-human clinical trial: 3D liver perfusion imaging with ultrasound in patients and preclinical 3D perfusion imaging studies to predict treatment response.
- First-in-human study on ultrasound spectroscopy in patients with hepatocellular carcinoma (HCC); also developed an imaging-guided drug delivery approach for therapy of HCC.

The Canary Center Operations Team is comprised of the Shared Resource Facilities Staff, the Lab and Facilities Coordinator, and the Administrative Associates. The team leader is Dr. Mark Stolowitz, Deputy Director of Operations. The team facilitates ongoing operations of the shared resource facilities, including scheduling and maintenance of shared laboratory equipment and scientific instruments. Further, the team facilitates the onboarding of arriving trainees, provides training for new instrument users, and maintains health and safety related standards. Finally, the team facilitates the Canary Center’s scientific programs by providing support as required.



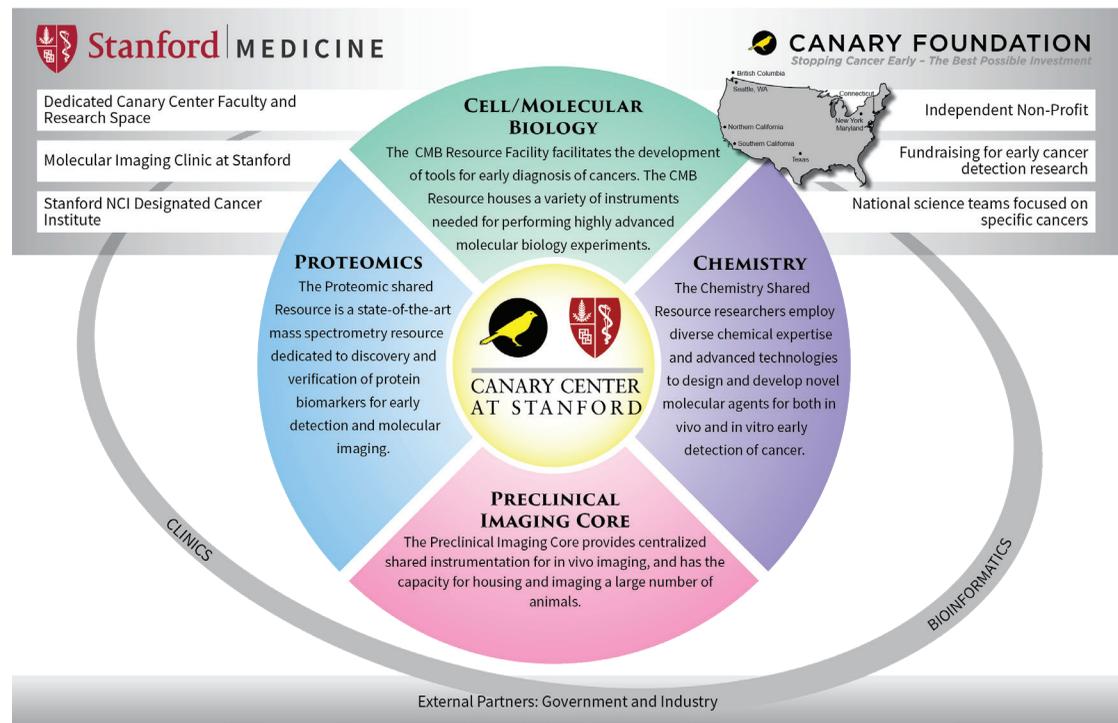
Operations Team back row, L to R: Jessica Zuniga, Ken Lau, Stephanie van de Ven, Mark Stolowitz, Eva Bajorek, Fuad Nijim. Front Row L to R: Tyler James, Grayling Thompson, Sindhuja Ramakrishnan, Toni Benevento



Sindhuja Ramakrishnan  
CMB Resource Facility



Ken Lau  
Proteomics Resource Facility



## CELL/MOLECULAR BIOLOGY RESOURCE

The Cell and Molecular Biology Shared Resource Facility (CMB Resource) at the Canary Center facilitates the development of tools for early diagnosis of cancers. The CMB Resource is well equipped for developing molecular imaging probes. Specifically, this resource develops and characterizes antibody and ligand-based probes for targeted molecular imaging thus aiding faculty, scientists and students at the Center who focus on developing highly sensitive multifunctional optical, PET and MRI probes for imaging cancers by targeting cancer-specific cellular targets.

The CMB Resource houses a variety of instruments needed for performing highly advanced molecular biology experiments. The instruments used by the resource include, for example: a highly sensitive fluorescent microscope with a time-lapsed imaging functionality, a real-time PCR machine, a microplate reader with fluorescence and bioluminescence capabilities, a fluorescent cell sorter, an IVIS-Lumina – highly sensitive cooled charge coupled device camera for imaging bioluminescence and fluorescence of different wavelengths, and an automated peptide synthesizer. The CMB Resource is also equipped with a tissue culture facility that includes BSL-2+ capabilities.

The goal of the CMB Resource mimics that of the Center in that it aims to promote the development and advancement of methods for cancer early detection. The Cell and Molecular Biology Shared Resource Facility works closely with Center Members of the other Shared Resources to forward the Center's research efforts.

## CHEMISTRY RESOURCE

The Chemistry Shared Resource Facility (Chemistry Resource) at the Canary Center provides analytical and synthetic chemistry support to the Center's scientists. The Chemistry Resource provides equipment and instrumentation to facilitate the synthesis, analysis and characterization of both small and large biologically significant molecules. Chemists working in the Chemistry Resource employ diverse chemical expertise and advanced technologies to design and develop novel molecular agents for both in vivo and in vitro early detection of cancer. The molecular agents that are being developed encompass imaging agents such as optical, photoacoustic and multimodality probes, as well as agents intended for non-imaging strategies such as blood biomarker sensors. Close interaction between the Chemistry Resource and other Shared Resources at the Center not only facilitates validation and optimization of the developed probes, but also promotes an interdisciplinary approach to early cancer detection. This is crucial for in-depth understanding of the disease, as well as for successful clinical translation of the most promising molecular agents.

## PROTEOMICS RESOURCE

The Proteomics Shared Resource Facility (Proteomics Resource) associated with the Canary Center is a shared resource that supports Canary Center Members, Associate Members, and Canary Foundation Science Teams. The facility supports the mission of the Center to foster research leading to the development of blood tests and molecular imaging approaches to detect and localize early cancers. The facility houses mass spectrometry (MS), liquid chromatography (LC), and sample preparation systems employed primarily for biomarker discovery and verification studies. Stanford researchers with interests in cancer early detection seeking access to the resources available in the facility should do so in collaboration with Canary Center Members. At present, the Proteomics Resource supports four mass spectrometers including: (1) Thermo LTQ Orbitrap Elite; (2) Thermo LTQ Orbitrap Velos; (3) Agilent 6490 triple quadrupole; and (4) AB SCIEX 5800 TOF/TOF (MALDI) systems. Other instruments available in the shared resource include an Agilent AssayMAP Bravo liquid-handing robotic system, FortéBio Octet 384 system for biomolecular interaction analysis, as well as several systems for peptide and protein fractionation and sample preparation.



Thermo Orbitrap Elite Mass Spectrometer with UltiMate RSLCnano LC

**PRECLINICAL IMAGING CORE**



**Frezghi Habte, PhD**  
Director,  
Preclinical Imaging  
Core at Porter



**Heike Daldrup-Link, MD**  
Director, Stanford Center  
for Innovation in In-vivo  
Imaging



**Part of the Stanford Center for Innovation in In-vivo Imaging (SCI3)**

As an expansion to the Stanford Center for Innovation in In-vivo Imaging (SCI3), the Preclinical Imaging Core at Porter Drive was established to support the Canary Center at Stanford for Cancer Early Detection. Its mission is to provide access to state-of-the-art and first-of-its-kind preclinical imaging instruments to facilitate the translation of research from in vitro tests to small animal investigations and clinical practice. This enables evaluation and advancement of novel imaging technologies and biological concepts in living murine models. Researchers are trained in the use of each of the imaging modalities available, and several facilities are located on the Stanford campus (at The James H. Clark Center, Lorry I. Lokey Stem Cell Research Building, Comparative Medicine Pavilion, and Shriram Center for Bioengineering & Chemical Engineering) to enable ease of access for scientists and their research animals.

The Preclinical Imaging Core provides access to a spectrum of imaging modalities, including instruments routinely found in hospitals but optimized for small animal work (such as ultrasound, MRI, CT, and PET), instruments developed specifically for small animal work (such as optical imaging), as well as new equipment that has just been developed (such as photoacoustic imaging). All instruments are designed to image living subjects and allow for repeated imaging, which reduces the number of animals that researchers need to use. The flexibility and rapid analyses of such animal models greatly accelerate the development of molecular imaging strategies. The facility also houses a dedicated surgical procedure room, a histology slide scanner that converts glass slides into digital slides using both brightfield and fluorescence, and several advanced image analysis workstations.

The Preclinical Imaging Core operates as a Stanford School of Medicine Service Center and is supported by the Canary Center at Stanford, the Stanford Cancer Institute, as well as user fees. It is operated by the Departments of Radiology and Pediatrics. Dr. Frezghi Habte is the director of the Preclinical Imaging Core at Porter Drive and Dr. Heike Daldrup-Link oversees the entire Stanford Center for Innovation in In-vivo Imaging (SCI3).



**Intercept Lung Cancer Through Immune, Imaging & Molecular Evaluation (InTIME)**

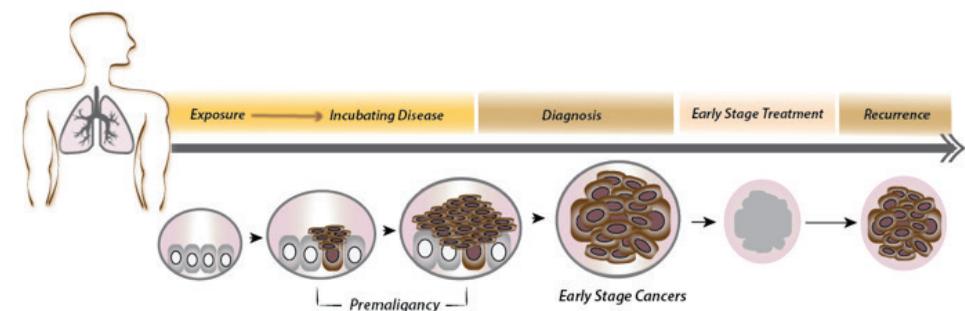
SU2C Dream Team - Principal Investigators: Sanjiv Sam Gambhir, MD, PhD (Stanford University); Avrum Spira, MD (Boston University); Steven Dubinett, MD (University of California Los Angeles); Julie Brahmer, MD (Johns Hopkins University); Matthew Meyerson, MD, PhD (Harvard University), Charles Swanton, MD, PhD (University College London)

Lung cancer is the leading cause of cancer death in the United States and worldwide, in large part due to our inability to intercept the disease prior to it progressing to an advanced stage. To address this problem, we have assembled a multidisciplinary Dream Team that brings together the diverse and unique expertise needed to transform lung cancer interception and prevention. Our collaborative team unites scientists and clinicians from many fields of lung cancer research, from prevention through early detection and treatment. Together, we will use state-of-the-art technologies, many developed within our team, to understand genetics, immunology, radiological imaging, and treatment response, of patients who show evidence of abnormal lung tissue that puts them at high risk to develop lung cancer.

First, we will create a molecular atlas of pre-cancer of the lung. These studies will identify which types of pre-cancerous lung tissue require aggressive treatment and which treatments will block the development of these abnormal lesions to invasive lung cancer.

Second, we will develop two diagnostic tools that can be directly applied in the clinic for simple, yet accurate, detection of early lung cancer: 1) the use of nasal swabs, blood and radiological imaging (including a novel PET imaging approach using 18F FSPG) to confirm whether lung abnormalities found on chest imaging are lung cancer or benign lung disease; 2) blood tests that can identify patients at the earliest stages of lung cancer recurrence, thus enabling timely and effective intervention.

Our third goal is to develop tests to identify which individuals are most likely to benefit from a number of treatment strategies to intercept lung cancer, including emerging immunotherapies. Ultimately, we aspire to make it possible for every person at risk for lung cancer to have a personalized interception approach.

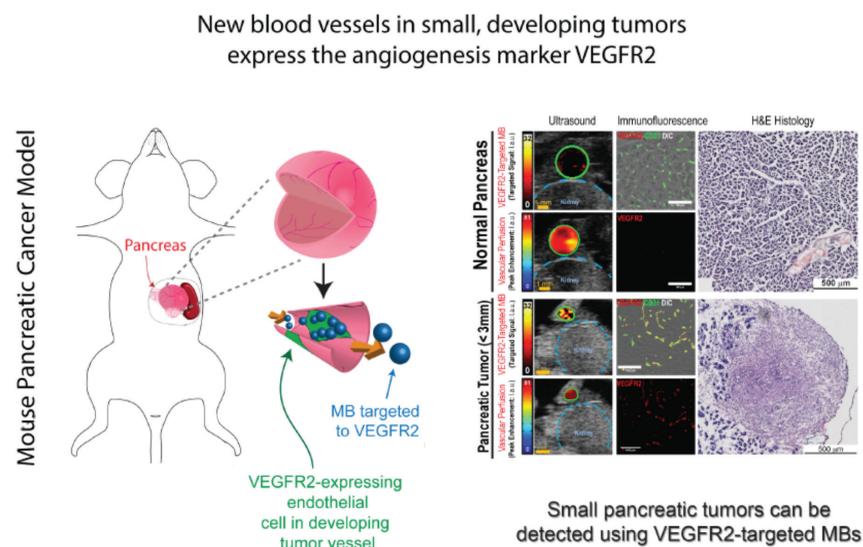


## Molecular Imaging Methods for the Detection of Pancreatic Ductal Adenocarcinoma

NCI U01 - Principal Investigators: Andrei Iagaru, MD; Walter Park, MD

As part of the Pancreatic Cancer Detection Consortium, we aim to drive biomarker development and validation by establishing standardized biorepositories of high-risk individuals, and by evaluating two innovative molecular imaging strategies to detect pancreatic ductal adenocarcinoma (PDAC) much earlier than is currently possible. We have previously studied two different molecular imaging approaches for early cancer detection. The first approach involves contrast-enhanced ultrasound (CEUS) using micron-sized microbubbles. We have shown that CEUS targeted to a vascular endothelial growth factor receptor type 2 (VEGFR2; also called kinase insert domain receptor, KDR) can detect sub-centimeter PDAC lesions in a transgenic mouse model. The second approach focuses on a novel positron emission tomography (PET) tracer that selectively binds to integrin  $\alpha\beta6$ , a cell surface receptor that is overexpressed in PDAC. In both approaches, a clinical grade agent with an FDA IND exists to allow first-in-human clinical studies for earlier detection of PDAC.

Our scientific team has broad complementary expertise in pancreatology, abdominal radiology, nuclear medicine, statistics, and pancreatic pathology. Our goals are to 1) collaboratively develop a standardized annotated biorepository with longitudinal follow-up of patients at high risk for PDAC; 2) perform first-in-human clinical trials to determine the feasibility, efficacy, and safety of KDR-targeted molecular CEUS in patients with resectable PDAC; 3) perform a first-in-human clinical trial to determine the feasibility, efficacy, and safety of  $\alpha\beta6$ -targeted PET-CT in patients with PDAC; and 4) begin prospective pilot clinical trials using KDR-targeted molecular CEUS in patients at high risk for PDAC. In all trials, we will collect biospecimens to support future integration of these imaging approaches with novel circulating biomarkers. The success of these first-in-human trials and systematic banking of biospecimens will support further collaborative studies for the earlier detection of PDAC.



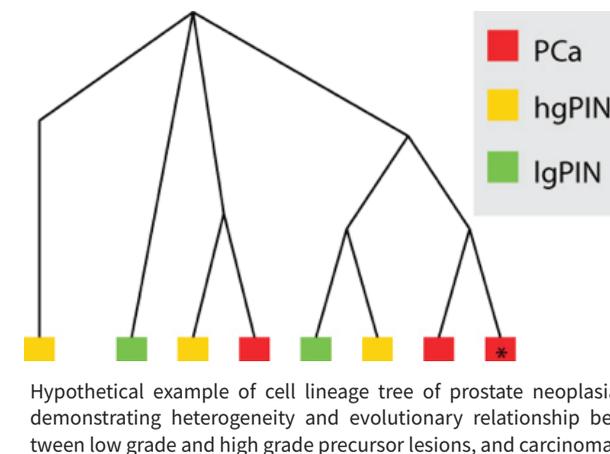
## Stanford Molecular and Cellular Characterization Laboratory

NCI U01 - Principal Investigator: James Brooks, MD

Nearly all prostate cancers are detected by screening with serum Prostate Specific Antigen (PSA). Unfortunately, aggressive screening over the last 25 years has led to detection of many small, early stage prostate lesions not destined to progress or kill men. However, physicians lack tools to distinguish early lesions that are aggressive from those that are indolent. To address this problem, we have brought together a multidisciplinary team composed of experts in urology, pathology, cancer genomics, proteomics, bioinformatics and biology. Together, we will characterize early prostate cancers and their precursor lesions for genomic and proteomic changes and use these data to construct evolutionary trees. From this we will identify clinically useful changes that could be used to distinguish indolent (“dead-end”) lesions from those that are potentially aggressive.

We will focus on 1) investigating the early genomic evolution of good and bad outcome prostate cancer in histologically defined prostate cancers and precursor lesions in fixed tissues; and 2) defining the genomic heterogeneity of good and bad outcome prostate cancer and the downstream consequences in transcript, protein and glycoprotein expression in frozen tissues. An integrated approach using fixed and frozen tissues will allow us to delineate the early genomic lesions in prostate cancer, define which are selected to evolve into more aggressive and which end up as non-aggressive (“dead-end”) lesions, and characterize the downstream effects of these selected changes in cellular transcription, protein expression, and protein glycosylation.

A systematic study of the events in prostate cancer during its development and evolution will help address the issues of overtreatment by providing prognostic features and biomarkers that help select men for definitive treatment or observation.





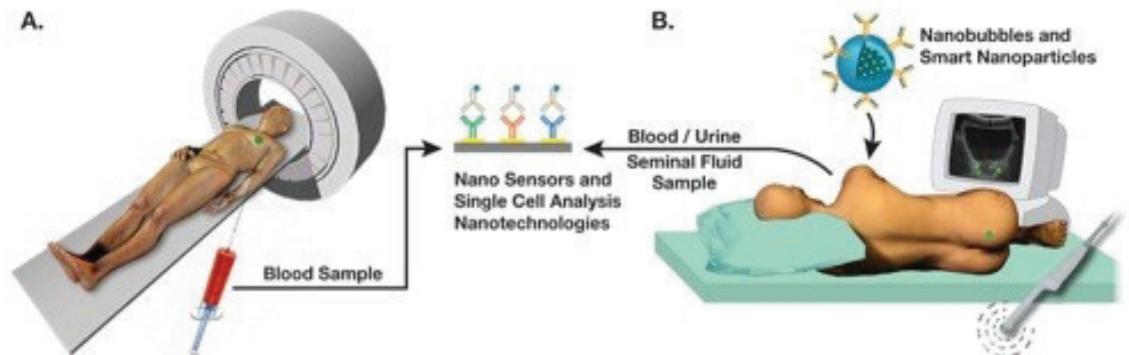
**Center for Cancer Nanotechnology Excellence for Translational Diagnostics**

NCI U54 - Principal Investigators: Sanjiv Sam Gambhir, MD, PhD; Shan X. Wang, PhD

The Center for Cancer Nanotechnology Excellence for Translational Diagnostics (CCNE-TD) is a consortium composed of a highly interdisciplinary team of scientists whose expertise areas are synergistic and have a long collaboration history (the first CCNE cycle was funded in 2006). The CCNE-TD has two focus areas: 1) predicting and monitoring cancer therapy response in lung cancer and 2) merging nano-based in vitro diagnostics with nano-based imaging for earlier cancer detection and prognostication of prostate cancer.

CCNE-TD investigators will utilize nanotechnology to measure changes in cancer patterns via 1) magneto-nanosensors that can measure changes in serum and other bodily fluids, and 2) imaging using cancer-triggered-self-assembling and disassembling nanoparticles. Our nanotechnologies will be used to interrogate single cells for DNA, RNA, proteins, and micro- or nanovesicles to discover and validate potential biomarkers. We will also develop novel nano-based imaging technologies (e.g., nanobubble enhanced ultrasound imaging) to image cell-associated proteins in small animal models and clinically translate these technologies for human prostate cancer imaging.

CCNE-TD has two technological arms: 1) in vitro genomic/proteomic/cellomic nanosensors, and 2) in vivo molecular imaging using gold-based, nanobubble-based, and self-assembling and disassembling nanoparticles. The latter arm is directly focused on molecular imaging of specific cellular protein targets. It is the goal of the CCNE-TD to help identify these targets for specific cancers (lung and prostate) and to utilize these targets as ways to home in on cancer cells. Our new class of nanoparticles that can self-assemble intracellularly in conjunction with our advanced magnetic resonance imaging (MRI) expertise, is expected to directly impact the development of medical imaging modalities for clinical translation. With our highly interactive program focused on developing and validating nanotechnology for earlier cancer detection, prognostication, and therapy response monitoring, we will imagine, invent, and innovate for the benefit of cancer patients.



**Canary Center at Stanford and Cancer Research UK Cambridge Centre collaborate to fund innovative research to help diagnose cancer earlier**



The Canary Center at Stanford has recently established a transatlantic partnership with the CRUK Cambridge Centre Early Detection Programme to tackle some of the most challenging questions in early cancer detection: how to identify those at the highest risk of cancer, finding new ways to spot and cure the very first signs of cancer, and how to develop cost effective, non-invasive and reliable methods for early cancer detection. To bring outstanding academic and clinical researchers from the US and UK together, the two centers are jointly funding four research projects exploring innovative ways to detect prostate, lung, esophageal, and renal cancers at an early stage:



**A multi-modal approach to discover novel blood-based biomarkers for early detection of poor prognosis prostate cancer**

Tanya Stoyanova, an assistant professor of radiology at the Canary Center, is partnering with Vincent Gnanapragasam, an urologist at Cambridge University Hospitals, to identify different types of tumors in men with prostate cancer.



**Levitating a sponge for the early detection of esophageal adenocarcinoma**

Utkan Demirci, a professor of radiology at the Canary Center, is working with Rebecca Fitzgerald, Cambridge's early detection program co-lead, to detect early signs of esophageal cancer.



**Early cancer detection through transcriptomic analysis of host immune cells**

Tom Soh, a professor of radiology at the Canary Center, is exploring new ways to detect early-stage lung cancer through his partnership with Robert Rintoul, a thoracic consultant at Cambridge University Hospitals.

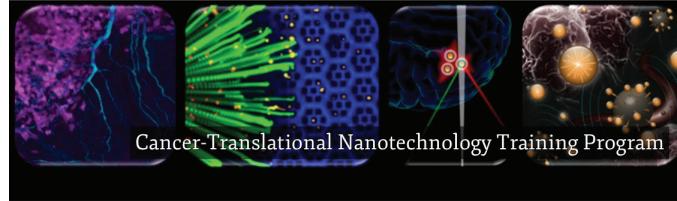


**Early detection of renal cell carcinoma using DNA methylation markers in urine**

Oliver Gevaert, an assistant professor of medicine and of biomedical data science at Stanford, and John Leppert, an associate professor of urology at Stanford, are teaming up with Charlie Massie, a group leader in Cambridge's early detection program.



## Cancer-TNT Program Cancer-Translational Nanotechnology Training Program



NCI T32

PIs: Jianghong Rao, PhD, Dean Felsher, MD, PhD  
Program Manager: Billie Robles

<http://med.stanford.edu/ctnt.html>

The Cancer-Translational Nanotechnology Training (Cancer-TNT) Program is led by Drs. Jianghong Rao and Dean Felsher and is funded by the National Cancer Institute. The vision of this three-year postdoctoral fellowship program is to train a new generation of scientists with the skills and educational backgrounds from the areas of engineering, chemistry, materials science, cancer biology and medicine. This program will provide the opportunity for talented scientists to learn the intricacies of merging nanotechnology with the biological and medical sciences, specifically for use in cancer, in addition to becoming leaders in the rapidly growing field of cancer nanotechnology.

## SCIT Program Stanford Cancer Imaging Training Program



NCI T32

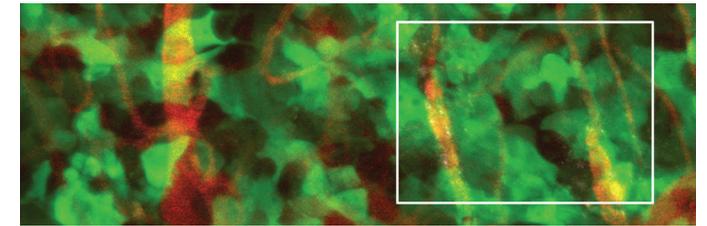
PIs: Sandy Napel, PhD, Bruce Daniel, MD  
Program Manager: Sofia Gonzales, MS

<http://scitprogram.stanford.edu>

The Stanford Cancer Imaging Training (SCIT) Program, funded by the National Cancer Institute, aims to train the next generation of researchers in the development and clinical application of advanced techniques for cancer imaging. Our coursework, rich mentored training opportunities, and outstanding resources, provide an active, vibrant program that attracts students nationwide. Graduates from our program are highly sought after, filling faculty and industry research positions internationally.

The SCIT program is surrounded by and draws from numerous departments, programs, and resources with core relevant competencies to imaging science. Trainees will have access to our exceptional imaging facilities, including the Richard M. Lucas Center for Imaging in the Department of Radiology, as well as additional research space in more than 10 other buildings throughout the School of Medicine. The SCIT Program also facilitates unique research collaborations with the Bio-X Program, the Center for Biomedical Imaging at Stanford (CBIS), the Molecular Imaging Program at Stanford (MIPS), the Radiological Sciences Laboratory (RSL), and the Integrative Biomedical Imaging Informatics at Stanford (IBIIS) Program.

## SMIS Program Stanford Molecular Imaging Scholars Program



NCI T32

PI: Craig S. Levin, PhD  
Program Manager: Sofia Gonzales, MS

<http://smisprogram.stanford.edu>

The Stanford Molecular Imaging Scholars (SMIS) program is a diverse training program bringing together more than thirteen departments, predominantly from the Stanford Schools of Medicine and Engineering, in order to train the next generation of interdisciplinary leaders in molecular imaging. Oncologic molecular imaging is a rapidly growing area within molecular imaging which combines the disciplines of chemistry, cell/molecular biology, molecular pharmacology, physics, bioengineering, imaging sciences, and clinical medicine to advance cancer research, diagnosis and management.

The goals of SMIS are to train postdoctoral fellows through a diverse group of over 40 basic science and clinical faculty mentors representing 8 program areas, incorporating formal courses in molecular imaging, molecular pharmacology, cancer biology, cancer immunology, virology, and gene therapy, with a clinical component including hematology/oncology rounds.

## CSBS Program Cancer Systems Biology Scholars Program



NCI R25

PIs: Sylvia Plevritis, PhD, Garry Nolan, PhD  
Program Manager: Theresa McCann

<http://med.stanford.edu/csbs.html>

The Stanford Cancer Systems Biology Scholars (CSBS) Program is a multidisciplinary training program for cancer and biocomputational researchers who want to embark on a systems biology approach to discover clinically-relevant cellular and molecular networks underlying cancer risk, initiation, progression and treatment response. Drs. Sylvia Plevritis, PhD, and Garry Nolan, PhD lead the CSBS program, comprised of 36 faculty mentors from 19 departments with independent cancer-focused funding.

With funding from the National Cancer Institute, we are able to offer the CSBS postdoctoral fellowships to well-qualified applicants from various backgrounds: (1) cancer biologists who want to be cross-trained in computational sciences and (2) computational scientists who want to be cross-trained in cancer biology. CSBS is a two-year postdoctoral training program focused on innovative, multidisciplinary cancer research education that seamlessly integrates experimental and computational biology in order to systematically unravel the complexity of cancer.



## Canary CREST Program

### Canary Cancer Research Education Summer Training Program

NCI R25  
<http://canarycenter.stanford.edu/canarycrest.html>

To train the next generation of interdisciplinary scientists, we offer a unique summer research training opportunity for undergraduate students, namely, the Canary Cancer Research Education Summer Training (CREST) Program. Funded by the National Cancer Institute, the program offers a 10-week research experience in one of our state-of-the-art labs. Each participant is matched with a faculty mentor who helps them craft a research project. Senior scientists and postdoctoral fellows assist the faculty in supervising and mentoring the students. Participants work in a dynamic lab environment on challenging projects that involve a broad range of research techniques. Additionally, students learn about the field of cancer early detection (from in vitro diagnostics to in vivo molecular imaging) through specially-designed short classroom sessions, as well as participate in professional development and career seminars. The program culminates with a symposium, where students present individual posters on their research projects in front of their peers, faculty and lab mentors, and other Stanford scientists.



**Program Director**  
 H. Tom Soh, PhD  
 Professor



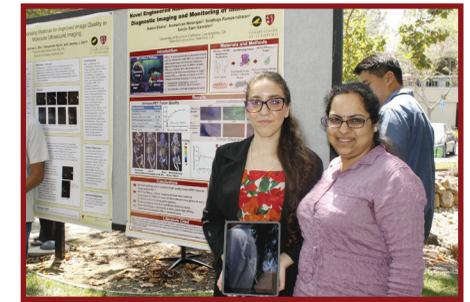
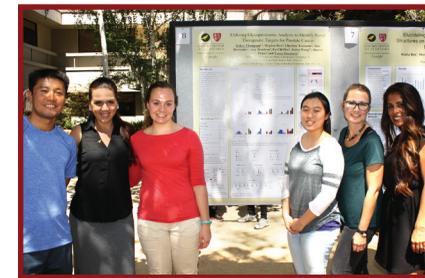
**Program Director**  
 Utkan Demirci, PhD  
 Professor



**Program Administration**  
 Stephanie van de Ven, MD, PhD



**Program Coordinator**  
 Jessica Zuniga



## CANARY CENTER RELATED COURSES

### BioEngineering 222 / Radiology 222

#### Instrumentation and Applications for Multimodality Molecular Imaging of Living Subjects

Focuses on instruments, algorithms and other technologies for imaging of cellular and molecular processes in living subjects. Introduces preclinical and clinical molecular imaging modalities, including strategies for molecular imaging using PET, SPECT, MRI, Ultrasound, Optics, and Photoacoustics. Covers basics of instrumentation physics, the origin and properties of the signal generation, and image data quantification.

### BioEngineering 224 / Radiology 224

#### Probes and Applications for Multimodality Molecular Imaging of Living Subjects

Focuses on molecular contrast agents (a.k.a. “probes”) that interrogate and target specific cellular and molecular disease mechanisms. Covers the ideal characteristics of molecular probes and how to optimize their design for use as effective imaging reagents that enable readout of specific steps in biological pathways and reveal the nature of disease through noninvasive imaging assays.

### BioEngineering 225 / Radiology 225

#### Ultrasound Imaging and Therapeutic Applications

Covers the basic concepts of ultrasound imaging including acoustic properties of biological tissues, transducer hardware, beam formation, and clinical imaging. Also includes the therapeutic applications of ultrasound including thermal and mechanical effects, visualization of the temperature and radiation force with MRI, tissue assessment with MRI and ultrasound, and ultrasound-enhanced drug delivery. Course website: <http://bioe225.stanford.edu>

### BioEngineering 229

#### Advanced Research Topics in Multimodality Molecular Imaging of Living Subjects

Covers advanced topics and controversies in molecular imaging in the understanding of biology and disease. Lectures will include discussion on instrumentation, probes and bioassays. Topics will address unmet needs for visualization and quantification of molecular pathways in biology as well as for diagnosis and disease management. Areas of unmet clinical needs include those in oncology, neurology, cardiovascular medicine and musculoskeletal diseases.

### BioEngineering 301C

#### Diagnostic Devices Lab

This course exposes students to the engineering principles and clinical application of medical devices through lectures and hands-on labs, performed in teams of two. Teams take measurements with these devices and fit their data to theory presented in the lecture. Devices covered include X-ray, CT, MRI, EEG, ECG, Ultrasound and BMI (Brain-machine interface).

### Electrical Engineering 235

#### Analytical Methods in Biotechnology

This course provides fundamental principles underlying important analytical techniques used in modern biotechnology. The course comprises of lectures and hands-on laboratory experiments. Students will learn the core principles for designing, implementing and analyzing central experimental methods including polymerase chain reaction (PCR), electrophoresis, immunoassays, and high-throughput sequencing. The overall goal of the course is to enable engineering students with little or no background in molecular biology to transition into research in the field of biomedicine.

### Medicine 221

#### Translational Research and Applied Medicine (TRAM)

Open to graduate students and medical students, this course enables students to learn basic principles in the design, performance and analysis of translational medical research studies. The course includes both didactic seminars from experts in translational medicine as well as the opportunity to design and present a translational research project. Students enrolling for 3 units are paired with a TRAM translational research project and work as a team with TRAM trainees and faculty on a weekly basis, as arranged by the instructor, and present a final project update at the end of the quarter.

### Radiology 230

#### Ultrasound Instrumentation for Imaging and Therapy

This course teaches the physics, materials, modeling and processing steps involved in the design and fabrication of medical ultrasound transducers for diagnostic imaging and therapeutic applications. Students will learn how to consider various tradeoffs in the design and selection of clinical probes for particular uses, and a lab activity will reinforce the fundamentals of transducers and demonstrate how to assess probe performance in the real world.

### Radiology 235

#### Advanced Ultrasound Imaging

The focus of this course is on advanced ultrasound imaging techniques for medical imaging applications. Topics include beamforming, adaptive beamforming, Fourier beamforming, synthetic aperture techniques, speckle, speckle reduction, k-space, harmonic imaging, coherence imaging, phase aberration, radiation force imaging, elastography, quantitative ultrasound, Doppler and flow imaging, ultrasound modeling and advanced ultrasound theory.

### Radiology 280

#### Early Clinical Experience in Radiology

Provides an observational experience as determined by the instructor and student.

### Radiology 370

#### Medical Scholars Research

Provides an opportunity for student and faculty interaction, as well as academic credit and financial support, to medical students who undertake original research. Enrollment is limited to students with approved projects.

## LECTURES

### Radionuclide Imaging Basic Science Lectures

Fridays, 12:00 pm–1:00 pm

Nuclear Medicine Library, H2211

### Nuclear Medicine & Molecular Imaging Clinical

#### Lecture Series

Mondays, 12:00 pm–1:00 pm

Nuclear Medicine Library, H2211

### Nuclear Medicine & Molecular Imaging Clinical Case Conference

Wednesdays, 11:00 am–12:00 pm

Nuclear Medicine Reading Room

## SEMINAR SERIES

### Cancer Early Detection Seminar Series

Seminars highlighting new research in Cancer Early Detection.

Quarterly (Thursdays)

Munzer Auditorium Beckman Center

<http://canarycenter.stanford.edu/seminars/early-detection.html>



### CME Radiology Grand Rounds

Global Learning Objectives:

1. Critically analyze research, guidelines and appropriate use criteria to develop best-practice diagnosis and treatment strategies.
2. Evaluate latest innovations in imaging to assess safety and effectiveness.

Every other Friday

<http://med.stanford.edu/radiology/education/grandrounds.html>

### Precision Health and Integrated Diagnostics (PHIND) Seminar Series

Monthly

Clark Auditorium

<http://med.stanford.edu/phind/events.html>

### Stanford Cancer Imaging Training (SCIT) Program Seminar Series

Quarterly colloquium presentations by trainees. Lucas Expansion, Glazer Learning Center

<http://med.stanford.edu/scitprogram/seminar.html>

## JOURNAL CLUBS

### MIPS Journal Club

Every other Thursday  
Clark Center

[http://med.stanford.edu/mips/events/journal\\_club](http://med.stanford.edu/mips/events/journal_club)

### IMAGINING the Future

Seminars by world-renowned scientists aimed at catalyzing interdisciplinary discussions in all areas of medicine and disease.

Quarterly (Wednesdays)

Berg Hall, Li Ka Shing Center

<http://med.stanford.edu/mips/imagining-the-future.html>

### Integrative Biomedical Imaging Informatics at Stanford (IBIIS) Seminar Series

Third Wednesday of every month

<http://ibiis.stanford.edu/events/seminars.html>

### Medical Imaging Seminars

Occasional Wednesdays

Li Ka Shing Center

<http://cbis.stanford.edu/events/MIseminar.html>

## INDUSTRY

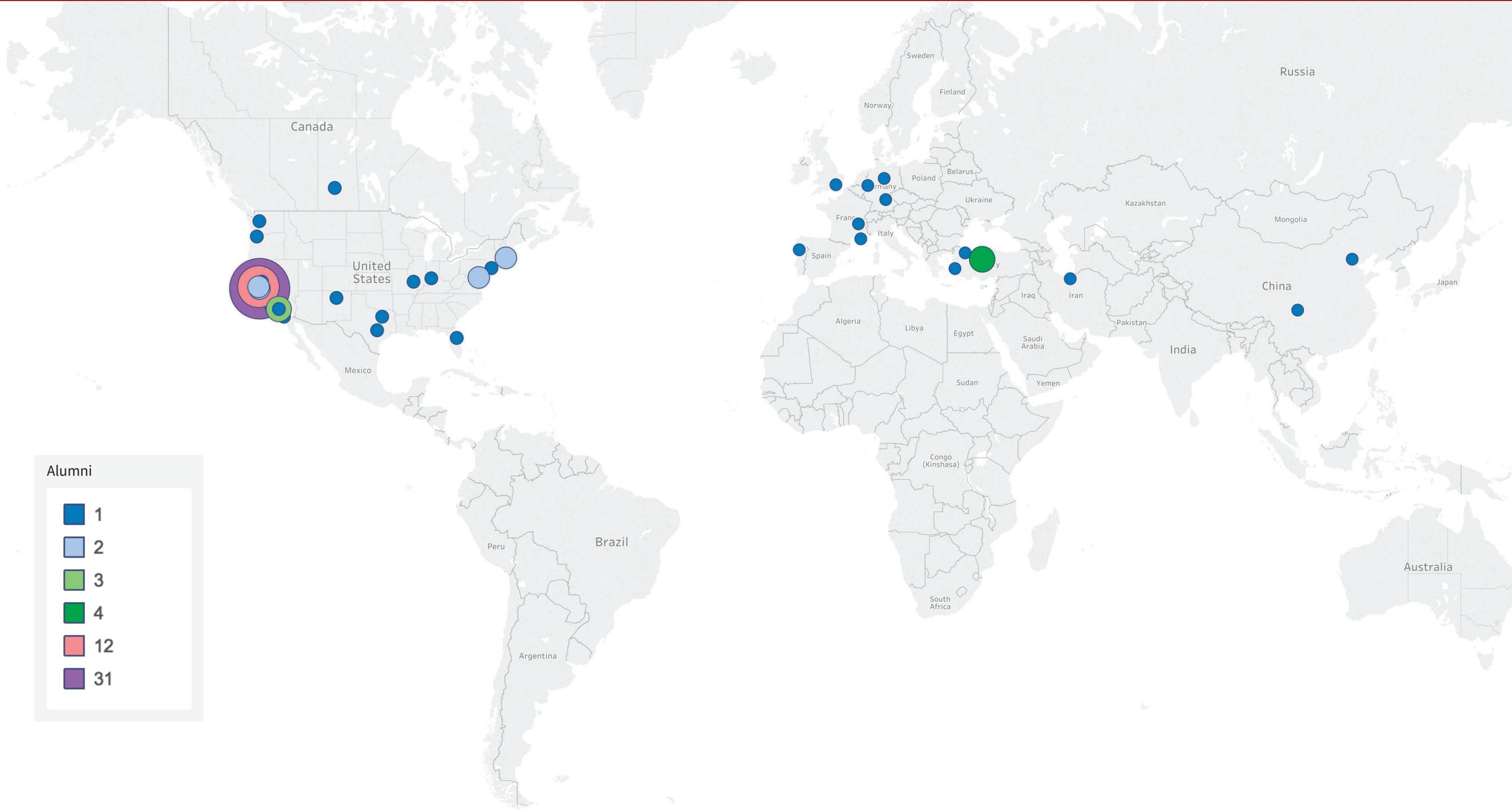
- Akron Biotechnology, LLC
- Bayer
- D-Wave Systems
- GE Global Research
- GE Healthcare
- Google
- Life Molecular Imaging
- MabVax Therapeutics
- Merck
- Novocure Inc.
- Oncomed
- Philips Healthcare
- Royal Philips
- Siemens Healthineers
- Taiwan Semiconductor Manufacturing Company
- Thermo Fisher Scientific
- Verily
- Vortex Biosciences

## INSTITUTIONS

- Cambridge University, UK
- Cold Spring Harbor Laboratory
- KOC University, Turkey
- Bogazici University, Turkey
- Duke University
- Information Sciences Institute (ISI), USC
- Institute for Experimental and Clinical Traumatology, Ludwig Boltzmann Institute, Vienna, Austria
- Johns Hopkins University
- Knight Cancer Institute, OHSU
- Lawrence J. Ellison Institute of Transformative Medicine, USC
- Ludwig Institute for Cancer Research, UCSD
- Mayo Clinic
- MD Anderson Cancer Center
- Memorial Sloan Kettering Cancer Center
- Ohio State University College of Engineering
- University of British Columbia
- University of California, Los Angeles
- University of California, Santa Barbara
- University of California, San Francisco
- University of Erlangen Nuremberg, Germany
- University of Louisville J.B. Speed School of Engineering
- University of Nebraska Medical Center
- Van Andel Institute

## GIFT GIVING FOUNDATIONS

- Ben and Catherine Ivy Foundation
- Canary Foundation
- Cancer Research UK
- Chan Zuckerberg Biohub
- Duke University, Coulter Foundation
- Lustgarten Foundation
- National Science Foundation
- Prostate Cancer Foundation
- Peter Michael Foundation
- Stand Up To Cancer
- The Teal Foundation



Affiliated  
Departments  
(Stanford) **12**

Canary Center  
Trainees **79**

Canary Center  
Faculty **8**

Affiliated Canary  
Center Faculty **34**

Canary Center  
Alumni **105**



## Canary Center/ CRUK Cambridge Centre Collaboration

The Canary Center at Stanford has recently established a transatlantic partnership with the CRUK Cambridge Centre Early Detection Programme to tackle some of the most challenging questions in early cancer detection: how to identify those at the highest risk of cancer, finding new ways to spot and cure the very first signs of cancer, and how to develop cost effective, non-invasive and reliable methods for early cancer detection.



## The Early Detection of Cancer Conference International Collaboration

The annual Conference brings together experts in early detection from multiple disciplines to share groundbreaking research and progress in the field. The Conference is part of a long-term commitment to invest in early detection research, to understand the biology behind early stage cancers, find new detection and screening methods and enhance uptake and accuracy of screening. This annual conference is presented by OHSU Knight Cancer Institute, Canary Center at Stanford, and Cancer Research UK.



## MIPS/Canary Trainees Council (MCTC)

The MIPS/Canary Trainees Council launched in February 2018. The Council will be a great resource to trainees and faculty alike.

The aims of the MCTC are:

- To enrich both the training and social experiences of MIPS and Canary trainees.
- To give trainees a platform to voice their needs (e.g., scientific, professional, career, wellness, etc.).
- To act as a link between trainees and faculty to facilitate the above needs.
- To create a strong peer network amongst trainees.
- To strengthen the community for all members.

## SMASH = SMASH Rising



To create greater diversity in science, the Canary Center at Stanford has started a new collaboration with SMASH, the signature STEM education initiative of the Kapor Center, based in Oakland.

The SMASH Rising Program at the Canary Center is a 7-week research internship program for students from underrepresented communities entering their first or second year of college. Students work on a scientific research project under mentorship of a professor and various researchers at the Canary Center. They also participate in professional development activities to gain essential workplace skills and build their network.

With this initiative, we aim to empower brilliant underrepresented students by exposing them to cutting-edge cancer research and technology development, training them in hypothesis testing and experimental design, building their problem-solving and critical thinking skills, and giving them access to resources and social capital that allow them to pave a successful career path in the sciences.



## Precision Health and Integrated Diagnostics (PHIND)

The PHIND Center is the first center in the world to focus on precision health and integrated diagnostics. We bring together faculty from all across campus to initiate new collaborations and strengthen existing ones. Additionally, we attract the top scientists and physician-scientists in the world who are focused on building the future of precision health. Our faculty work in areas such as disease risk analytics, biomarkers of health, early molecular changes of cells/tissues transitioning from normal to disease, health economics of diagnostics, and development of new noninvasive ways to detect small molecular changes anywhere within the body using remote sensing. Finally, a key goal is to not only develop and test the strategies in our own community and hospitals, but to launch a new generation of companies that will help to bring the discoveries and inventions at Stanford out for use all over the world to help society at large.



## Project Baseline

### Project Baseline

We used to think the world was flat, until teams of pioneers discovered new lands and pushed the boundaries of knowledge. We are at a similar turning point with health and disease: we now have the advanced tools and technologies to explore health in greater depth and detail than previously imaginable.

Project Baseline is a collaboration between Verily, Stanford Medicine, Duke University School of Medicine, and Google to collect comprehensive health data and use it as a map and compass, pointing the way to disease prevention.



## The New Stanford Hospital

Stanford Hospital & Clinics has rebuilt its 1950s-era hospital facilities to accommodate new medical technology, increase capacity needs and meet seismic-safety requirements. The new facilities feature individual patient rooms, an enlarged Level-1 trauma center and Emergency Department and new surgical, diagnostic and treatment rooms. The rebuild of Stanford Hospital is the next step in the hospital's successful 50-year history. The new facilities are leading the way for continued success in providing advanced patient care and treatment to the surrounding communities.



## The New Lucile Packard Children's Hospital

Lucile Packard Children's Hospital is expanding its walls in order to meet growing community needs for specialized pediatric and obstetric care. In order to serve this growing patient base, an expanded facility adjacent to the current Packard Children's Hospital was built and opened in November 2017.

As part of Packard Children's mission to provide family-centered care, the completed Packard Children's Hospital Expansion features additional single-patient rooms and more space for families to be with their child during treatment and recovery. The expansion provides patients and doctors with the most modern clinical advancements and technology while also addressing the specialized needs of pediatric and obstetric patients and their families.

## 2016

### June 2016

- Dr. Catherine Going awarded the American Society for Mass Spectrometry Postdoctoral Award.
- Cheylene Tanimoto and Christine Yeh receive the Stanford Undergraduate Advising and Research Conference Grants.

### July 2016

- Christine Yeh receives Firestone Medal & Stanford Alumni Association Award.

### August 2016

- Dr. Parag Mallick's research featured in the Stanford Report.

### September 2016

- Dr. Tanya Stoyanova receives McCormick-Gabilan Faculty Award.
- Dr. Sharon Pitteri receives U01 award from NIH Common Fund.

### November 2016

- Dr. Meghan Rice receives Helena Anna Henzl-Gabor Young Women in Science Award.

### December 2016

- Canary Seed Grant winners include: Drs. Utkan Demirci, Sharon Pitteri, Tanya Stoyanova, Tom Soh & Associate Members.

## 2017

### February 2017

- Dr. H. Tom Soh named Chan Zuckerberg Biohub Senior Investigator.
- Dr. Sarah Totten receives American Association for Cancer Research (AACR) Minority Scholar in Cancer Research Award as well as a travel award from the U.S. Human Proteome Organization (HUPO).

### April 2017

- Dr. Parag Mallick featured in Stanford Medicine News on how epigenetics is changing our understanding of cancer biology.
- Dr. Juergen Willmann and Dr. Sanjiv Sam Gambhir featured in Stanford Medicine News for their first-in-human ultrasound molecular imaging studies in patients with breast and ovarian lesions.
- Canary Center welcomes New Associate Faculty Member Dr. Olivier Gevaert.



### June 2017

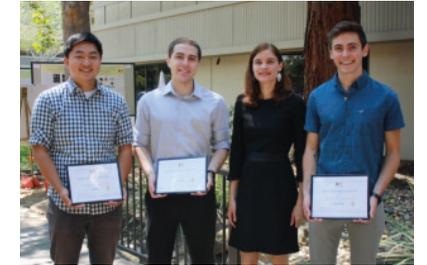
- Dr. Utkan Demirci and Dr. Juergen Willmann receive the 2017 Academy for Radiology & Biomedical Imaging Research Distinguished Investigator Award.
- Dr. Meghan Rice receives Best Poster Award at the Canary Foundation Early Detection Symposium.

### July 2017

- Stanford launches Project Baseline Study by enrolling first participant.
- Canary Center receives the NCI R25 training grant for the Canary CREST Program.

### August 2017

- Dr. Sarah Totten receives Katharine McCormick Advanced Postdoctoral Fellowship.
- Canary Center welcomes New Associate Faculty Dr. Sanjay Malhotra.
- Canary Center summer internship students Mark Zhu, Alex Codik and Mark Buckup win the Verily Young Scientist award.



### September 2017

- The Canary Center Team raises over \$35,000 at the 2017 Canary Challenge.
- Dr. Sanjiv Sam Gambhir appointed President of the IS3R.

### November 2017

- Canary Center welcomes New Associate Faculty member Dr. Joyce Wu.

### December 2017

- Dr. Parag Mallick featured in Stanford News article highlighting Science meets Art at Stanford.
- Dr. H. Tom Soh named National Academy of Inventors Fellow.

## 2018

### January 2018

- Dr. Utkan Demirci featured in Advanced Science News.
- Canary Center at Stanford and Cancer Research UK Cambridge Centre collaborate to fund innovative research to help diagnose cancer earlier.
- Dr. Utkan Demirci featured in Advanced Science paper and Stanford News.

### May 2018

- Dr. Sanjiv Sam Gambhir and his colleagues find a way to track the effectiveness of a cancer immunotherapy in the body.
- Drs. Jeremy Dahl, Sanjiv Sam Gambhir and Ramasamy Paulmurugan named 2018 Academy for Radiology & Biomedical Imaging Research Distinguished Investigators.
- Dr. Sharon Hori, receives Department of Defense, Breast Cancer Research Program, Breakthrough Award.
- Dr. Tanya Stoyanova receives Department of Defense, Prostate Cancer Research Program, Idea Development Award.
- Dr. Meghan Rice, Postdoctoral Fellow in Stoyanova Lab awarded Department of Defense, Prostate Cancer Research Program, Early Investigator Research Award.
- Stanford Undergraduates Alisha Birk and Austin You Su receive Undergraduate Advising and Research Major Grant.
- Canary Center welcomes New Associate Faculty member Dr. Jiangbin Ye.

### June 2018

- Dr. Sanjiv Sam Gambhir receives 2018 Benedict Cassen Prize.
- Canary Center welcomes New Associate Faculty member Siddhartha Jaiswal.

### July 2018

- Stanford Researchers develop Magnetic Wire that Increases Detection of Circulating Tumor Cells.

### August 2018

- Maggie Wang, Makenna Laffey and Renuka Ramanathan win the Canary CREST Young Scientist award.

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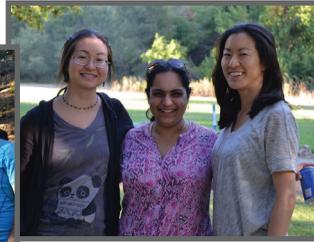
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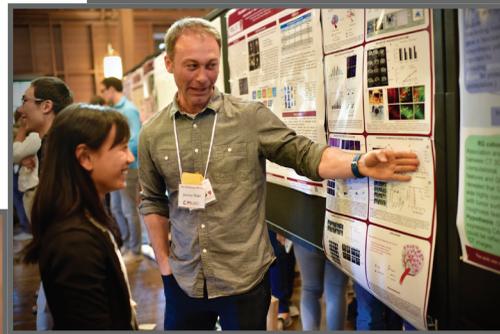
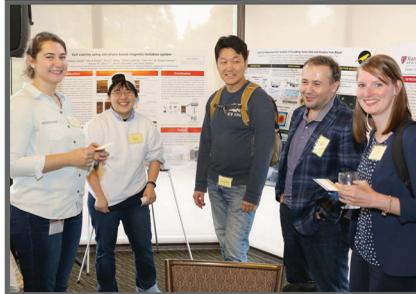
2017 Canary Challenge



2015 Summer Picnic



2016 Canary Summit



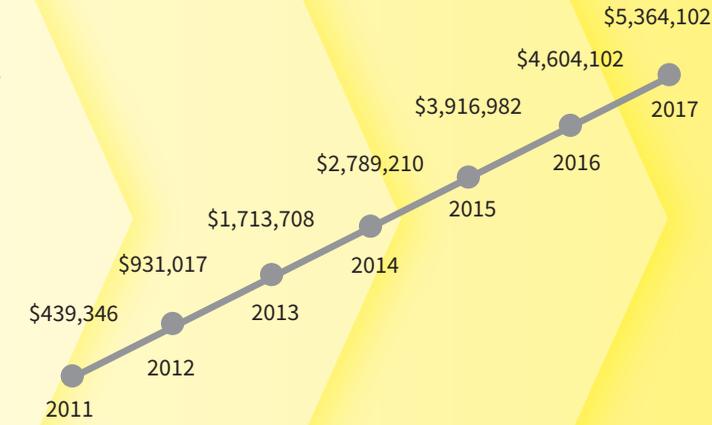
2017 Radiology Research Retreat



# CANARY >> CHALLENGE

The Canary Challenge is an annual cycling event and 5K walk/run that increases awareness and raises funds for the Canary Center at Stanford for Cancer Early Detection. Each year in September, an amazing community of cyclists, volunteers, and sponsors come together to take part in one of Northern California's premier fundraising events. Together, they have raised millions of dollars to support research programs that are improving cancer detection and survivorship. In 2017 alone, more than 800 participants raised over \$750,000. Established in 2011, the Canary Challenge is organized by the Canary Foundation, the world's first non-profit organization dedicated solely to the funding, discovery, and development of tests for cancer early detection. Learn more about the Canary Challenge at [www.canarychallenge.org](http://www.canarychallenge.org)

## FUNDS RAISED (cumulative total over years)



[www.canarychallenge.org](http://www.canarychallenge.org)



