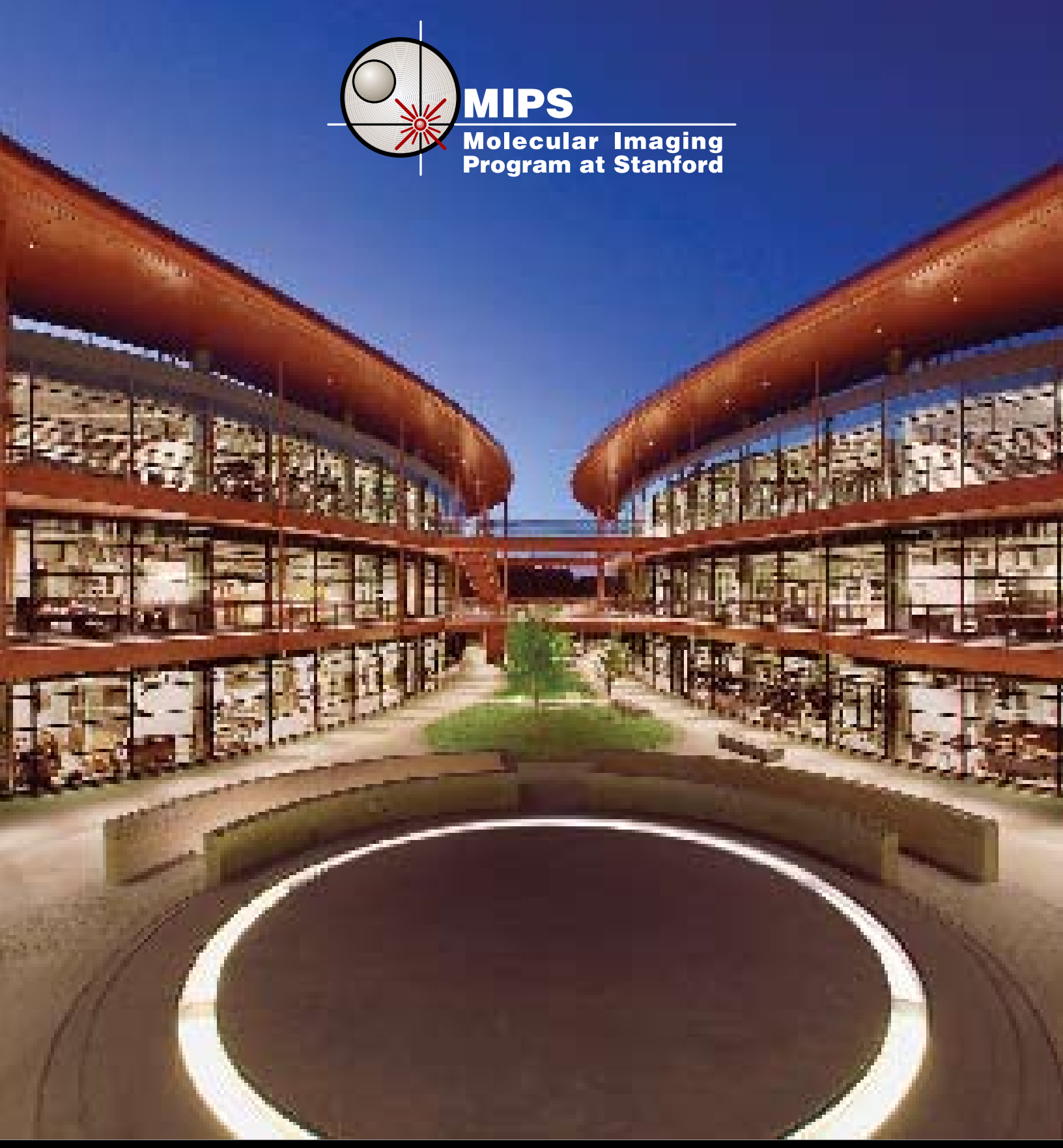


STANFORD
UNIVERSITY

MIPS
Molecular Imaging Program at Stanford

INTRODUCTION

The Molecular Imaging Program at Stanford (MIPS) was established as an inter-disciplinary program to bring together scientists and physicians who share a common interest in developing and using state-of-the-art imaging technology and developing molecular imaging assays for studying intact biological systems. A multimodality approach using imaging technologies such as positron emission tomography (PET), single photon emission computed tomography (SPECT), digital autoradiography, magnetic resonance imaging (MRI), magnetic resonance spectroscopy (MRS), optical bioluminescence, optical fluorescence, photoacoustics, Raman, and ultrasound are all technologies under active development and investigation. The goals of the program are to fundamentally change how biological research is performed with cells in their intact environment in living subjects and to develop new ways to diagnose diseases and monitor therapies in patients. Areas of active investigation include cancer research, microbiology/immunology, cardiovascular research, stem cell biology, quantitation and visualization, nanotechnology, early cancer detection, molecular probe development, developmental biology and pharmacology.

Sanjiv Sam Gambhir, MD, PhD
Director, Molecular Imaging Program at Stanford (MIPS)
Chief, Nuclear Medicine Division
Professor, Departments of Radiology and Bioengineering

Christopher Contag, PhD
Co-director, Molecular Imaging Program at Stanford (MIPS)
Director, Stanford Center for Innovation in In Vivo Imaging (SCI3)
Associate Professor, Pediatrics, Microbiology & Immunology, and Radiology

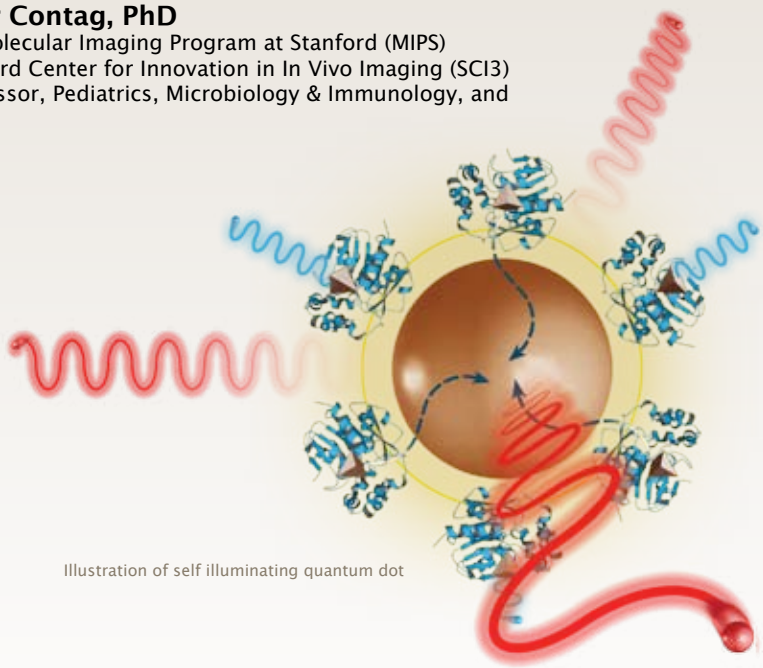


Illustration of self illuminating quantum dot

RESEARCH

The MIPS Program has several key research areas focusing on:

- identification of novel targets for molecular imaging
- synthesis and validation of radiolabeled, optical and other molecular probes for molecular imaging
- development of reporter gene strategies
- development of molecular imaging instrumentation for living subjects
- development of molecular imaging approaches/assays for interrogating cellular events in living subjects
- development of small animal models for molecular imaging
- development of software tools for visualization and analysis of molecular imaging data
- translation of molecular imaging strategies for clinical applicatons

FACULTY

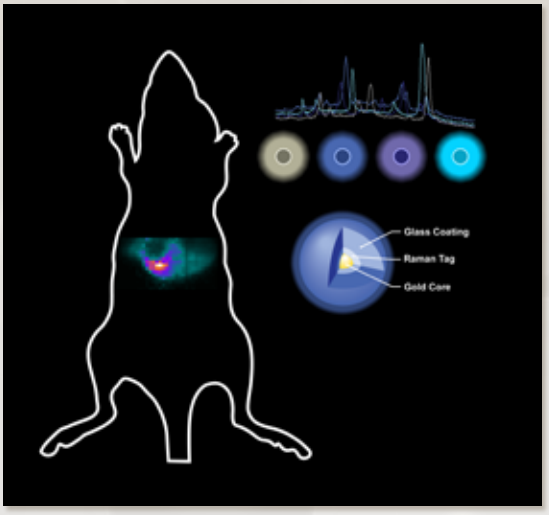
Sandip Biswal, MD – Molecular Imaging of Musculoskeletal Illnesses
Francis Blankenberg, MD – Nuclear Medicine Research
Xiaoyuan (Shawn) Chen, PhD – Molecular Imaging Probe Development
Zhen Cheng, PhD – Cancer Molecular Imaging Chemistry Laboratory
Christopher Contag, PhD – Molecular Biophotonics and Imaging Laboratory
Dean Felsher, MD, PhD – Cancer Biology Laboratory
Sanjiv Sam Gambhir, MD, PhD – Multimodality Molecular Imaging Laboratory
Edward Graves, PhD – Imaging Radiobiology Laboratory
Samira Guccione, PhD – Imaging and Therapeutic Platforms for Translational Medicine
Craig Levin, PhD – Molecular Imaging Instrumentation Laboratory
Michael McConnell, MD – Noninvasive Cardiac Imaging Laboratory
Michael Moseley, PhD – Moseley Laboratory
David Paik, PhD – Paik Laboratory
Sylvia Plevritis, PhD – Computational Cancer Research Laboratory
Jianghong Rao, PhD – Cellular and Molecular Imaging Laboratory
Brian Rutt, PhD – Rutt Laboratory
Mark Schnitzer, PhD – Schnitzer Laboratory
Shreyas Vasanawala, MD, PhD – Vasanawala Laboratory
Juergen Willmann, MD – Translational Molecular Imaging Laboratory
Joseph Wu, MD, PhD – Cardiovascular Gene and Cell Therapy
Lei Xing, MD – Xing Laboratory

INSTRUCTORS

Demir Akin, PhD – Deputy Director, Nanotechnology Center
Bonnie King, PhD – Deputy Director, Canary Center at Stanford for Early Cancer Detection

RESEARCH SCIENTISTS

Byeong-Cheol (Ben) Ahn, MD, PhD – Visiting Associate Professor
Michael Bachmann, ScD – Research Scientist
Carmel Chan, PhD – Research Scientist
Frederick Chin, PhD – Head, Cyclotron Radiochemistry
Aloma D'Souza, PhD – Research Scientist
David Dick, PhD – Head, Cyclotron Physics
Tim Doyle, PhD – Head, Small Animal Imaging Facility
Gayatri Gowrishankar, PhD – Research Scientist
Frezghi Habte, PhD – Research Scientist
Andrew Lamb – Cyclotron Production Technician
Amelie Lutz, MD – Research Scientist
Mohammad Namavari, PhD – Senior Research Scientist
Arutselvan Natarajan, PhD – Research Scientist
Laura Jean Pisani, PhD – MRI Physicist/Instrumentation Specialist
Paulmurugan Ramasamy, PhD – Research Scientist
Greig Scott – Research Scientist
Shahriar Yaghoubi, PhD – Research Scientist

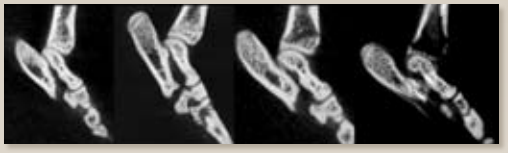


Raman molecular imaging in living mouse with Raman nanoparticles

Sandip Biswal, MD
Assistant Professor, Radiology

Molecular Imaging of Musculoskeletal Illnesses Laboratory

This laboratory is interested in the development of multimodality molecular imaging techniques to study a variety of musculoskeletal diseases including neuronal inflammation, cellular gene therapy for arthritis and fractures and musculoskeletal malignancies.



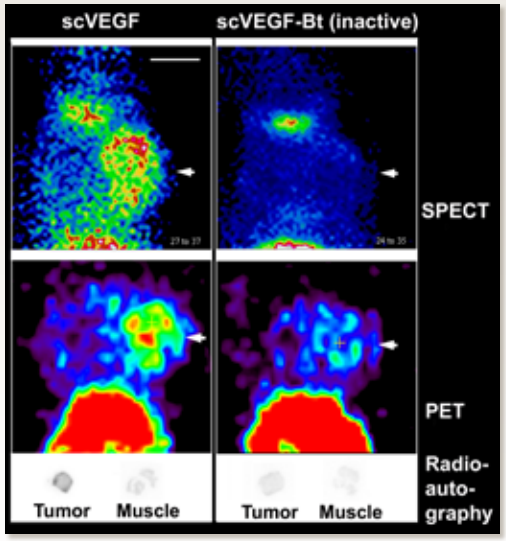
Serial reconstructed microCT images displaying bone mineral loss and osteolysis of the ankle and hindfoot were obtained in murine models of rheumatoid arthritis. Each ankle/foot images from left to right represent days 0, 6, 8 and 12 days post-arthritis induction.

Francis Blankenberg, MD
Associate Professor, Radiology, and Pediatrics

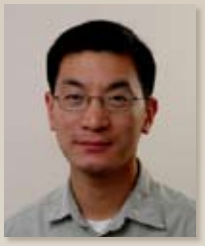
Nuclear Medicine Research Laboratory

This laboratory has two major areas of interest:

1. "Imaging of Cellular Stress and Apoptosis" using site-specifically labeled self-chelating annexin V derivatives for Tc99m (SPECT) or, in the near future, F18 (PET). The derivatives are used for imaging the effects of neuroprotective therapy in murine models of focal cerebral ischemia, renal cortical ischemia, rheumatoid arthritis, and acute or chronic pain
2. "Imaging of Tumor and Other Forms of Angiogenesis" using a newly developed single chain form of VEGF. Conjugated with several different chelators, scVEGF can be labeled for fluorescent, Tc99-SPECT, or Cu64-PET imaging of tumor angiogenesis or aneurysm formation in murine models.



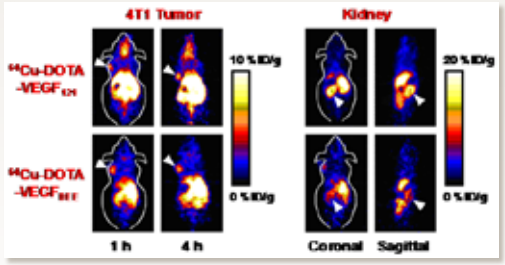
SPECT & PET imaging of tumor angiogenesis in mouse models



Xiaoyuan (Shawn) Chen, PhD
Associate Professor, Radiology

Molecular Imaging Probe Laboratory

Probe development is the key component for molecular imaging, which involves the efforts from molecular and cell biology to identify and validate novel molecular imaging targets, pharmacology to optimize the probes for best possible targeting efficacy and favorable in vivo kinetics, and image-capture techniques to non-invasively monitor the fate of molecular imaging probes in vivo. Aside from its basic diagnostic applications, molecular imaging also plays pivotal roles in treatment efficacy assessment, drug discovery, and understanding of molecular mechanisms in living systems. This laboratory is interested in developing and validating novel molecular imaging probes for visualization and quantification of molecular targets that are aberrantly expressed during tumor growth, angiogenesis and metastasis. The combination of anatomical (MRI and CT) and molecular imaging techniques (PET, SPECT, and optical imaging) will allow us to obtain molecular and functional information related to tumor growth and dissemination, and monitor specific molecular therapeutic efficacy. We are currently exploring



MicroPET images of 4T1 tumor-bearing mice injected with either 64Cu-DOTA-VEGF121 (binds to both VEGFR-1 and VEGFR-2) or 64Cu-DOTA-VEGFDEE (VEGFR-2 specific). 64Cu-DOTA-VEGFDEE, significantly reduced the dose-limiting renal toxicity without any reduction in tumor targeting efficacy.

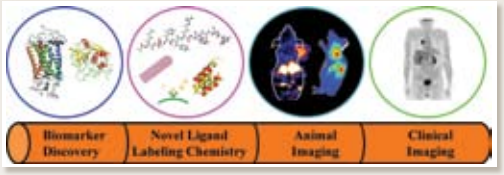
the molecular imaging and molecular therapy targeting integrin αvβ3, VEGF receptors (VEGFRs), and a wide variety of other disease markers.

Zhen Cheng, PhD

Assistant Professor, Radiology

Cancer Molecular Imaging Chemistry Laboratory

During the past several decades, remarkable progress has been achieved toward the understanding and treatment of cancer. Regardless of those successes, cancer still remains as the second leading cause of death. Therefore, new strategies which allow one to prevent, manage and eliminate cancer are highly desired. The overall objective of my laboratory is to develop novel molecular imaging probes and techniques for non-invasive detection of cancer and its metastasis at the earliest stage, so that cancer can be cured or transformed into a chronic, manageable disease. The techniques developed in my research will allow a close examination of the molecular, metabolic and physiological characteristics of cancers and their responses to therapy. In order to achieve this goal, my lab is aimed to identify novel cancer biomarkers with significant clinical relevance, develop new chemistry for probes preparation, and validate new strategies for probes high-throughput screening.



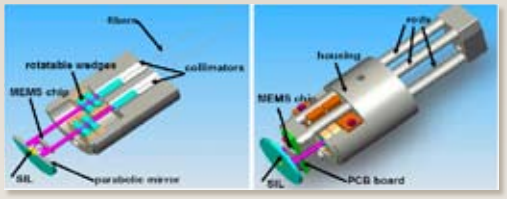
Development of molecular imaging probes and techniques: from biomarker discovery to clinical applications.

Christopher Contag, PhD

Co-director, Molecular Imaging Program at Stanford (MIPS)
Director, Stanford Center for Innovation in In Vivo Imaging (SCI3)
Associate Professor, Pediatrics, Microbiology & Immunology, and Radiology

Molecular Biophotonics and Imaging Laboratory

The mission of our laboratory is to understand both the mechanisms of disease (cancer, infection and genetic diseases), and the complex genetic programs of mammalian development and stem cell biology. We monitor these processes noninvasively as they occur in living animals. The methods developed and used by our group can simultaneously reveal the nuances, and the overall picture of cellular and molecular processes in a living animal. Using these approaches we can rapidly assess the effects of antineoplastic therapies, antibiotics or antiviral drugs, revealing possible modes of action. These strategies result in significantly more information than can be obtained using a vivisectionist approach in that the animals are living and the data is obtained in real-time. One of our scientific goals is to develop tools that make the body essentially transparent for scientific discovery, and to use these tools to understand how pathogens cause disease and how the host organism responds to these pathogens, how the immune system monitors cell transformation in cancer, and the regulatory networks that control cell migration and development.



Miniaturized Microscopes for Early Detection of Cancer

Dean Felsher, MD, PhD

Associate Professor, Medicine (Oncology), and Pathology

Cancer Biology Laboratory

Our laboratory investigates how oncogenes initiate and sustain tumorigenesis. We have developed model systems whereby we can conditionally activate oncogenes in normal human and mouse cells in tissue culture or in specific tissues of transgenic mice. We utilize state of the art methods of imaging and imaging analysis to examine and model tumorigenesis.

In particular, using the tetracycline regulatory system, we have generated a conditional model system for MYC-induce hematopoietic tumors. Using the tet system, we have shown that cancers caused by the conditional over-expression of the MYC proto-oncogene regress with its inactivation. Thus, even though cancer is a multistep process, the inactivation of one oncogene

can be sufficient to induce tumor regression. Now, we are using these model systems to address three questions:

1. How do oncogenes initiate tumorigenesis?
2. How does oncogene inactivation cause tumor regression?
3. How do tumors escape dependence on oncogenes?

Sanjiv Sam Gambhir, MD, PhD
Director, Molecular Imaging Program at Stanford (MIPS)
Chief, Nuclear Medicine Division
Professor, Radiology, and Bioengineering

Multimodality Molecular Imaging Laboratory

This laboratory is developing imaging assays to monitor fundamental cellular/molecular events in living subjects including patients. Technologies such as micro positron emission tomography (microPET), bioluminescence optical imaging, fluorescence optical imaging, micro computerized axial tomography (microCAT), ultrasound, photoacoustics, Raman imaging are all being actively investigated in small animal models. Our goals are to marry fundamental advances in molecular/cell biology with those in biomedical imaging to advance the field of molecular imaging. We have a particular interest in cancer biology and gene therapy. Research in early cancer detection and pharmacological therapy assessment is also being performed. Assays to interrogate cells for mRNA levels, cell surface antigens, intracellular proteins and protein-protein interactions are under active development. We are also extending many of these approaches for human clinical applications using optical and PET-CT technologies.

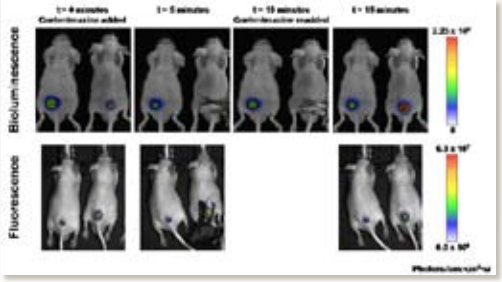
Gambhir lab image here...

Image description here...2 lines.

Edward Graves, PhD
Assistant Professor, Radiation Oncology

Imaging Radiobiology Laboratory

This laboratory is focused on the use of molecular imaging techniques in experimental radiobiology and clinical radiation oncology, and is involved in research spanning technique development, basic research, and clinical translation. We are currently engineering methods to image the lack of oxygen (hypoxia) in tumors as well as the downstream molecular effects of this phenotype. We are developing novel oxygen-insensitive and oxygen-calibrated reporter gene methods to accomplish this goal, and are also constructing and evaluating radiotracers for positron emission tomography (PET) that bind to hypoxia-regulated proteins. In addition, we are applying existing hypoxia-specific radiotracers such as [18F]-FAZA to study hypoxia in subcutaneous and orthotopic tumor models, and comparing these measurements of tumor oxygenation with indicators of hypoxia-regulated physiology obtained from our novel methods. Our laboratory is furthermore interested in preclinical models of radiation therapy that may be used to develop more effective radiation treatment strategies for human disease. We have recently modified a microCT scanner so that it may be used as a platform for image-guided conformal radiotherapy of small animal models of disease. This unit is currently being applied to study the significance of hypoxia imaging for tumor radiotherapy. Clinical translation of molecular image-based treatment strategies is being pursued through the development of a software package for three-dimensional display, analysis, and segmentation of image datasets. Through this myriad of approaches, we aim to effectively leverage the unique insights offered



Sensitivity of fluorescent and bioluminescent reporters to oxygen measured by tumor clamping.

Samira Guccione, PhD
Assistant Professor, Radiology

Imaging and Therapeutic Platforms for Translational Medicine Laboratory

The primary objective of our research effort is based on the development of new drug delivery methods including molecularly targeted imaging and therapeutic agents for cancer. We have two main research goals:

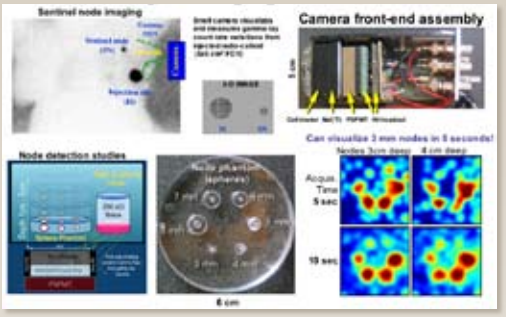
1. Development of molecularly targeted nanoparticles for in vivo imaging and drug delivery.
2. Use of external energy like focused ultrasound and lasers to enhance therapeutic outcomes.

To this end, we have applied nanotechnology platforms to image and treat vascular solid tumors (i.e. brain tumors). By synthesizing ligands that bind molecular targets on nanoparticle-based platforms, we make multimodality imaging agents for molecular imaging. These imaging agents allow in vivo biodistribution and pharmacokinetic characterization of each probe. Small animal models of disease are used to further test drug delivery capabilities of these targeted agents for therapeutic efficacy followed by toxicity evaluations. The second area of research uses focused ultrasound for local delivery of temperature sensitive liposomes containing drugs or genes. We have used heat shock protein promoter-driven gene expression to treat tumors in vivo by applying focused ultrasound locally to the tumors.

Craig Levin, PhD
Associate Professor, Radiology

Molecular Imaging Instrumentation Laboratory

This laboratory is interested in the development of novel instrumentation and software algorithms for in vivo imaging of molecular signals in humans and small laboratory animals. The goals of the instrumentation projects are to push the sensitivity and spatial, spectral, and/or temporal resolutions as far as physically possible. The algorithm goals are to understand the physical system comprising the subject tissues, radiation transport, and imaging system, and to provide the best available image quality and quantitative accuracy. The work involves computer modeling, position sensitive sensors, readout electronics, data acquisition, image formation, image processing, and data/image analysis algorithms, and incorporating these innovations into practical imaging devices. The ultimate goal is to introduce these new imaging tools into studies of molecular mechanisms and treatments of disease within living subjects.

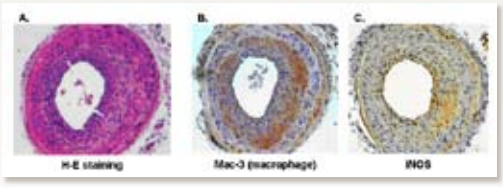


Miniature gamma ray camera for improved surgical staging of cancer

Michael McConnell, MD
Associate Professor, Medicine,
Molecular & Cellular Physiology, and Electrical Engineering

Noninvasive Cardiac Imaging Laboratory

This laboratory is interested in imaging cardiovascular disease, with a focus on coronary and vascular atherosclerosis and ischemic heart disease. Projects include cellular and structural characterization of atherosclerotic plaque by MRI, optical imaging (bioluminescence and fluorescence) of vascular inflammation, as well as noninvasive coronary angiography by MRI and MRI-guided cardiovascular interventions. Additional collaborative projects include real-time cardiac MRI and multi-modality imaging of cardiac stem cell transplantation.

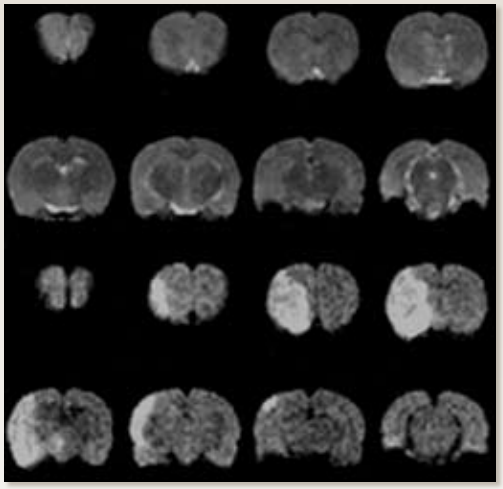


Carotid artery post-ligation showing neointima hyperplasia (A) as well as abundant macrophage infiltration (B), with corresponding iNOS expression (C) in iNOS-luc+ FVB mice treated with high-fat diet and diabetes induction.

Michael Moseley, PhD
Professor, Radiology

Research and Diagnosis of Disease States Using Magnetic Resonance Laboratory

This laboratory's interests involve research and diagnosis of disease states using new techniques of magnetic resonance (MR) in research and clinical research. Water diffusion-sensitive MR imaging of the brain and other tissues offers a unique tissue contrast mechanism. Mapping brain water diffusion has revolutionized our knowledge of the onset and evolution of cerebral stroke, making the MR scanner a potential "operating room" of choice for early and effective treatment of stroke and vascular disease. Because these diffusion and blood flow maps can be rapidly acquired, rapid identification of tissues that are in need of thrombolytic therapy or cytotoxic protection in the first critical hours following stroke or during surgery can be made. This non-invasive mapping of water motion and diffusion represents a new field of imaging and has created a breakthrough in assessment and treatment in a variety of disease states.

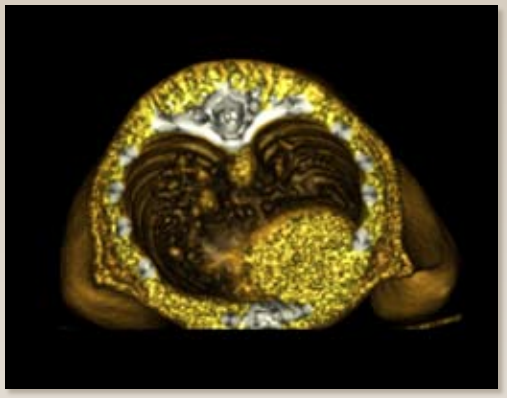


Rat diffusion-weighted MRI in acute stroke, 50 micron resolution. ***Top rows***: T2-weighted MRI is insensitive to early effects of stroke in brain. ***Bottom rows***: Diffusion imaging with MR shows clear effects of acute stroke, due to slowed water diffusion (causing an image brightness) in dying brain.

David Paik, PhD
Assistant Professor, Radiology

Paik Laboratory

This laboratory's research interests lie at the intersection of radiology, molecular biology and informatics. We focus on developing and validating computational methodologies for extracting useful information content from anatomic, functional and molecular images, drawing upon image processing, computer vision, computer graphics, computational geometry, machine learning, biostatistics, modeling and simulation. The lab also works on integrating image-based information with non-imaging biomedical information such as genomics and proteomics.

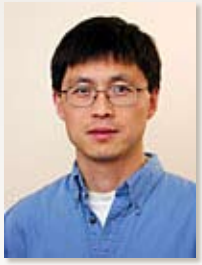


Work done in collaboration with Dean Felsher on modeling tumor growth and regression kinetics in mouse models. Cutaway volume rendering of a microCT of mouse showing multiple lung tumors that were individually tracked over time.

Sylvia Plevritis, PhD
Associate Professor, Radiology

Plevritis Laboratory

This laboratory develops novel computational tools for analyzing high throughput genomics and proteomics data in order to understand the molecular mechanisms of cancer initiation, progression and treatment. This laboratory also develops computer simulation models to quantify the effectiveness and cost-effectiveness of mammography and breast MRI in screening for breast cancer and CT in screening for lung cancer.

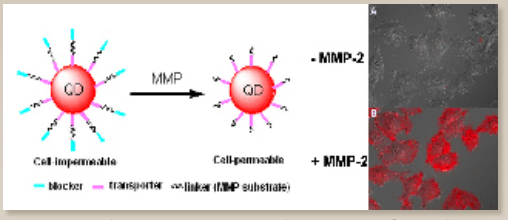


Jianghong Rao, PhD
Assistant Professor, Radiology

Cellular and Molecular Imaging Laboratory

This laboratory is focusing on the development of non-invasive imaging methods to image tumor-specific molecular markers such as mRNAs of oncogenes and over-expressed proteinases for better understanding of tumor biology. Towards this goal, we take an interdisciplinary approach of combining synthetic and physical or-

ganic chemistry, molecular biology with imaging techniques such as fluorescence microscopy, whole body fluorescence/bioluminescence imaging. A recent emphasis in the lab is to apply nanotechnology to develop novel nanosensors for bioimaging and tumor detection.



Proteases such as MMP-2 can gate the entrance of peptide functionalized quantum dots into cells through the hydrolytic cleavage to remove the blocking peptides on the conjugates.

Brian Rutt, PhD
Professor, Radiology

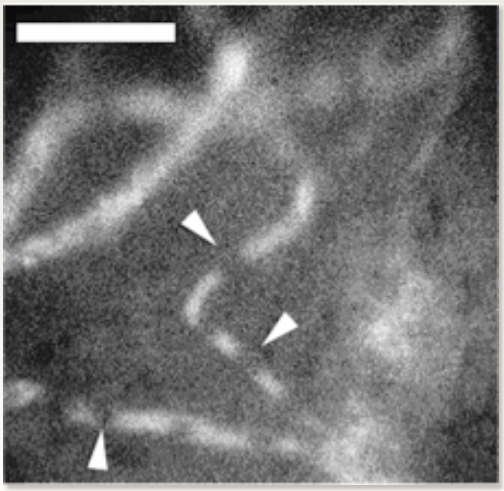
Rutt Laboratory

This laboratory is interested in developing and using in-vivo ultra-high field (e.g. 7 Tesla) Magnetic Resonance techniques to study human diseases. The increased sensitivity and enhanced contrast mechanisms at these high field strengths should provide insight to unsolved problems, especially in neuroscience and cancer.

Mark Schnitzer, PhD
Assistant Professor, Biology

Schnitzer Laboratory

This laboratory has two major research efforts that are mutually complementary:



An image of capillaries and red blood cells within the osseous spiral lamina vasculature, acquired by fluorescent microendoscopy in an anesthetized guinea pig. Scale bar = 50 micron.

1. In vivo two-photon fluorescence imaging studies of cerebellar-dependent learning and memory and
2. Fiber optic fluorescence microendoscopy.

The laboratory has invented two forms of fiber optic imaging, one- and two-photon fluorescence microendoscopy, which enable minimally invasive imaging of blood cells and neurons in deep brain tissues. The laboratory is further developing microendoscopy technology, studying how experience or environment alters neuronal properties, and exploring clinical applications. By combining imaging, electrophysiological, behavioral, and computational approaches, the lab seeks to understand cerebellar dynamics underlying learning, memory, and forgetting.

Shreyas Vasanawala, MD, PhD
Assistant Professor, Radiology

Vasanawala Laboratory

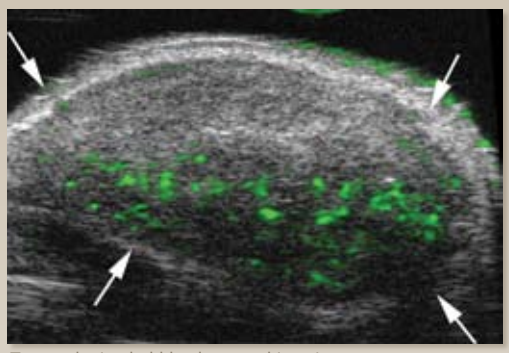
This laboratory focuses on developing molecular imaging techniques to investigate liver disease. We are interested in early imaging markers of diffuse liver disease as well as early detection, characterization, and therapeutic response of liver tumors, with an emphasis on magnetic resonance techniques. Our approaches include developing hyperpolarized magnetic resonance methods to probe metabolism in animal models and multinuclear magnetic resonance imaging.

Jüergen Willmann, MD
Assistant Professor, Radiology

Translational Molecular Imaging Laboratory in Abdominal Radiology

This laboratory focuses on the development and clinical translation of novel molecular and functional imaging biomarkers with special focus on imaging abdominal and pelvic cancer including pancreatic, liver, renal, ovarian, and prostate cancer. We further advance clinically available radiological imaging modalities such as ultrasound, magnetic resonance imaging (MRI), and positron emission tomography (PET) as promising imaging tools for early detection and treatment monitoring of abdominal and pelvic cancer. Our mission is to integrate novel molecular and functional imaging strategies into clinical

protocols for improved patient care in the near future.



Targeted microbubble ultrasound imaging

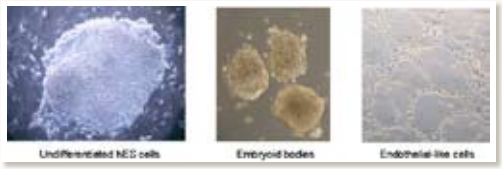
Joseph Wu, MD, PhD

Assistant Professor, Medicine, Radiology

Cardiovascular Molecular Imaging Laboratory

This laboratory is composed of a multi-disciplinary team that combines expertise in stem cell biology, molecular biology, cardiovascular physiology, and molecular imaging.

To better understand stem cell biology in vivo, we use novel molecular markers that enable us to follow the fate of transplanted stem cells noninvasively. These include monitoring survival, proliferation, and differentiation as related to embryonic stem cells and bone marrow stem cells. The highly sensitive imaging devices we use include bioluminescence, fluorescence, positron emission tomography, and magnetic resonance scanners. We are actively engaged in studying the differentiation of human embryonic stem cells into endothelial and cardiac cells, which will have important applications for regenerative medicine applications in the future. Our laboratory also works on gene expression profiling of stem cell markers as well as optimizing cardiac gene therapy protocols. The eventual goal is to establish molecular imaging as a platform for translational research in cellular and gene therapies for ischemic heart disease in the 21st century.



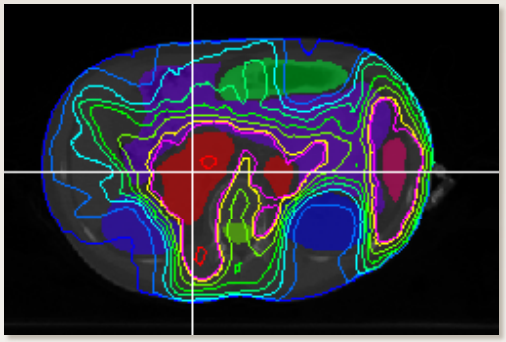
Differentiation of human embryonic stem cells into endothelial cells.

Lei Xing, MD

Associate Professor, Radiation Oncology

Xing Laboratory

This laboratory is focused on image instrumentation, image reconstruction, image processing, radiation therapy treatment planning, and image guided intervention. We are developing novel solutions to advance various clinical imaging modalities (such as CT, cone beam CT (CBCT), MRI, and PET), and investigating strategies for image guided therapeutics and treatment response assessment. We are working on 4D CT/CBCT/PET image reconstruction methods, scatter and dose reduction techniques in CBCT, integration of CBCT image devices with linear accelerators, image registration (particularly, deformable image registration) and image segmentation. We are embarking a systematic research on image guided radiation therapy (IGRT), which include patient simulation, dose optimization and treatment planning, real-time monitoring of tumor motion during dose delivery, and adaptive replanning. We are also working on biological image guided radiation therapy (BIGRT) to establish biologically--as opposed to anatomically--conformal radiation therapy. In BIGRT, the radiation dose is customized according to the biological image findings.



An intensity modulated radiation therapy (IMRT) treatment plan for a Hodgkin's disease patient.

Small Animal Imaging Facility

Stanford Center for Innovation in In Vivo Imaging (SCI^3)

http://mips.stanford.edu/public/sci3.adp

The mission of the Stanford Center for Innovation in In Vivo Imaging (SCI^3) is the application and advancement of technologies for in-vivo biological assessment and imaging in animal models. The instrumentation will support the development of reagents and approaches that will reveal in vivo changes at the molecular and cellular level such that a greater understanding can be gained in animal models.

In this manner the power of repeated measures can be applied to these models enriching the data sets and improving the statistics. This core will provide a test bed for evaluating human imaging reagents and strategies.

The flexibility and rapid analyses of the animal models will greatly accelerate the development of these molecular imaging strategies as well as novel therapeutic strategies for a variety of diseases. The Clark Center houses the SCI^3 core resources and instrumentation.

The Small Animal Imaging Core Facility is partially supported by funds from the Stanford Digestive Disease Core, the Stanford Comprehensive Cancer Center and the Stanford ICMIC, and is operated by the Departments of Pediatrics (Neonatology) and Radiology.

Lucas Expansion Building

The Lucas Expansion houses a 7.0T whole-body MR system and administrative offices for additional faculty, staff, and students. The expansion is also a focal point for molecular imaging activity, housing the cyclotron and radiochemistry facilities for radiopharmaceutical production as well as a number of the people involved in the effort.

The Richard M. Lucas Center for Magnetic Resonance Spectroscopy and Imaging

http://rsl.stanford.edu/lucas/

The Lucas Center opened in July 1992 as one of the few centers in the world with major centralized resources devoted to research in magnetic resonance imaging (MRI), spectroscopy (MRS) and X-Ray/CT imaging. The Center has pioneered MRI/MRS/X-Ray/CT technology while developing new techniques that benefit patients with stroke, cancer, heart disease, and brain disorders. The Center is a National Center for Research Resources funded by the National Institutes of Health (NIH). It provides office and laboratory facilities for twelve full-time faculty and their complement of research associates, postdoctoral fellows, graduate students, and support staff. The Center supports collaborative and original research using volunteers and patients as well as intact animal models.

Radiochemistry Facility

http://mips.stanford.edu/public/lucas.adp

The Radiochemistry Facility is on the first floor of the Lucas Expansion building. The heart of the Radiochemistry Facility is a GE PETtrace cyclotron, which is used for the production of radioisotopes for clinical and research use. Surrounding the cyclotron are an FDG production lab and research hot labs. The hot labs, fully equipped with hot cells and shielded fume hoods, are used for the production of research radiopharmaceuticals as well as provide space for radiochemistry research to develop new radiopharmaceuticals. These radiopharmaceuticals are used to support both clinical and research PET studies at the Stanford University Medical Center and the Stanford Center for Innovation in In Vivo Imaging (SCI3).

Dr. David Dick with the GE PETtrace cyclotron

7.0T small animal MRI system

Establishment of the Lucas Center was made possible through the generous support of the Richard M. Lucas Foundation for Cancer Research, and other donors such as the Baxter Foundation, the Levinthal Foundation, and the Phil N. Allen Trust. Richard M. Lucas (Apr 17, 1926 – Oct 6, 1981) was an entrepreneur, outdoorsman and philanthropist. The foundation, created in his memory by his family, Mary, John and Don Lucas, dedicated the Richard M. Lucas Center with the vision that the Center would become the site for unprecedented interdisciplinary research illuminating an understanding of human physiology and lighting the way to revolutionary advances in the diagnosis and treatment of human disease.

In Vivo Cellular and Molecular Imaging Center (ICMIC) – NCI P50

Sanjiv Sam Gambhir, MD, PhD, Principle Investigator

http://mips.stanford.edu/public/grants/icmic/

The vision of ICMIC@Stanford is to bring together researchers from various disciplines to form synergistic teams that will make significant advances in the use of multimodality molecular imaging strategies for better linking pre-clinical models of cancer with the clinical management of cancer. Members of these teams will include trainees that will gain access to a highly multidisciplinary experience, and who will become well-equipped to establish independent, multidisciplinary research programs. Projects will mainly include those that have a high potential for linking pre-clinical imaging models with clinical imaging for improved cancer patient management.

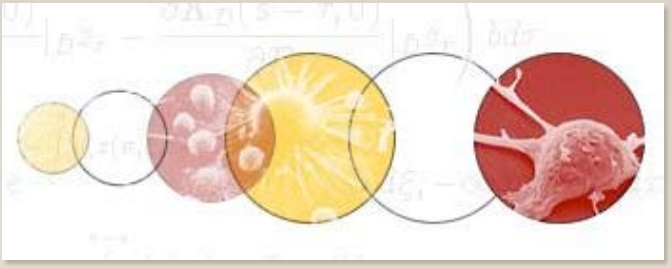
Legend for ICMIC fig here

Integrative Cancer Biology Program (ICBP) – NCI P20

Sylvia Plevritis, PhD, Principle Investigator

http://icbp.stanford.edu/

Genomic and proteomic probes of cancerous and normal tissue require new computational methods for data analysis. The goal is to develop the computational tools that will aid in the discovery of molecular perturbations implicated in cancer initiation and progression. We aim to elucidate the genetic, signaling and metabolic pathways of malignant processes through the integration of experimentation and computational methods. By revealing the molecular pathways of cancer, our work promises to advance the basic knowledge of the disease and enable the development of molecularly targeted therapies that will ultimately reduce cancer mortality.



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Center for Cancer Nanotechnology Excellence Focused on Therapy Response (CCNE) – NCI U54

Sanjiv Sam Gambhir, MD, PhD, Principle Investigator

http://mips.stanford.edu/public/grants/ccne/

Like the National Cancer Institute (NCI), we believe that nanoscience applied to cancer research is critical to the future of eliminating cancer, and we are convinced that nanotechnology will make a significant impact on cancer diagnosis and management in potentially revolutionary ways. Ex vivo diagnostics used in conjunction with in vivo diagnostics can markedly impact future cancer patient management by providing a synergy that neither strategy alone can offer.

Our goal is to develop and validate nanotechnology so that we will eventually be able to predict which patients will likely respond to a specific anti-cancer therapy and to monitor their response to therapy. Through an integrated, cohesive five-year plan, we are pursuing the use of ex vivo protein nanosensors and in vivo nanoparticles (quantum dots) for molecular imaging. As shown in the left panel below, our future vision is that eventually patients will have their tumors biopsied and blood samples drawn for protein profiling by ex vivo nanosensors to predict their response to a given therapy. In addition, they will also be imaged by a ring scanner, as shown below, with molecular imaging probes of different types to predict their response. Post-treatment and potentially during treatment, patient response will be evaluated by blood analysis, usually without another biopsy, and molecular imaging to ensure the accurate differentiation of responders from non-responders. To achieve this clinical potential, nanotechnology will first be developed as well as tested in small animal models and will eventually be translated to the clinic.

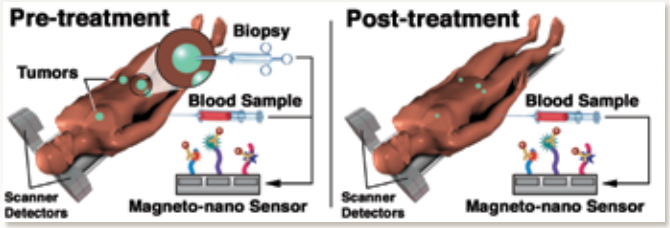


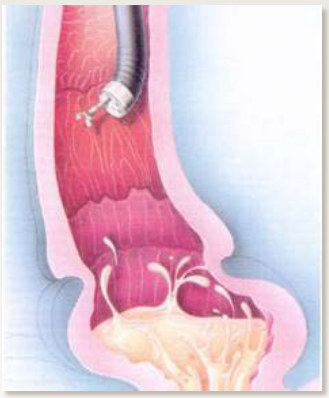
Illustration of the use of nanotechnology to monitor patient anti-cancer therapy and response.

Network for Translational Research in Optical Imaging (NTROI) – NIH U54
Christopher Contag, PhD, Principle Investigator

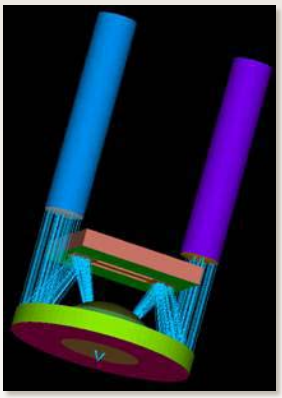
A Miniature Dual-Axes Confocal Microscope for the Early Detection of Cancer in the Esophagus

http://ntroi.stanford.edu/

In this project, an interdisciplinary team of investigators at Stanford University, and partner institutions, is involved in a translational research program that combines imaging-technology development with biomarker discovery for the early detection of cancer in the esophagus. New imaging technologies have often been a key to the early detection and treatment of cancer. Examples include MRI and mammography, which save lives through early detection. In this project, a unique endoscopic imaging tool that performs a noninvasive "optical biopsy" of esophagus tissues is being developed for detecting pre-cancerous conditions in the esophagus. The power of this tool, the miniature dual-axes confocal microscope, is that it images tissue structure with enough clarity and resolution to identify pre-cancerous tissues. This technology is also compatible with the use of optically-labeled biomarkers being developed in our group to specifically tag and identify pre-cancerous tissues. The combination of developing an advanced imaging technology, which greatly improves upon current in vivo imaging techniques, as well as the development of biomarkers specifically formulated for use with this imaging technology to locate pre-cancerous tissues, is an extremely powerful strategy. Studies show that 90% of the cancers in hollow organs originate in the epithelial layers. The technologies being developed here, of "optical biopsy" and biomarker-assisted detection in the esophagus, are widely applicable to the early detection of cancer in all hollow organs such as the lung, colon, stomach, cervix, uterus, etc., and will have great utility for monitoring at-risk patients and assessing outcome.



Confocal Microendoscopy in the Esophagus



Dual-Axes Confocal Technology

Stanford Molecular Imaging Scholars (SMIS) Program – NIH T32

Sanjiv Sam Gambhir, MD, PhD, Principle Investigator

http://mips.stanford.edu/smis/

SMIS
Stanford Molecular Imaging Scholars Program

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, 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 componening hematology/oncology rounds.

SMIS fellows will be recruited into a three-year program to audit coursework and complete research with at least two complementary mentors. Clinical exposure will take place in the second year. The program requires fellows to

1. complete a minor focus in specialized coursework including one mandatory molecular imaging course and two elective courses selected from the following: molecular basis of cancer, animal virus/host interactions, gene therapy, cellular and molecular pharmacology, and tumor immunology,
2. complete a major focus through a mentored research project, and
3. complete a significant grant preparation to help gain experience and confidence in the grant application process.

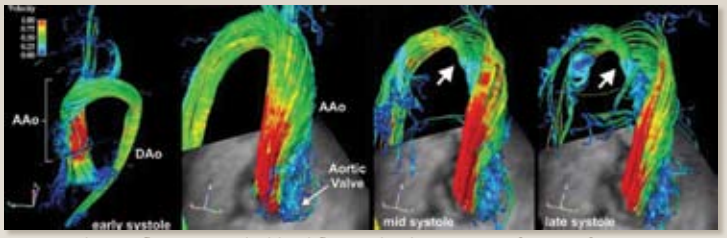
Involvement of fellows in all aspects of research conferences is required and essential. This includes attending various research conferences such as Molecular Imaging Program at Stanford (MIPS) Monthly Seminar Series, MIPS/Nuclear Medicine Grand Rounds, and Molecular Pharmacology Seminar Series. Fellows are also required to attend or present at the weekly MIPS Journal Club. Additional conferences are available and fellows are encouraged to attend based on their interests and schedules. All fellows and mentors will be expected to attend quarterly dinner meetings where fellows will be given an opportunity to present on their research, both orally and by poster.

Multi-Disciplinary Training Program in Cardiovascular Imaging @ Stanford (CVIS) – NIH T32

Michael McConnell, MD, Principle Investigator

http://cvmedicine.stanford.edu/education/cvis/

The Multi-Disciplinary Training Program in Cardiovascular Imaging @ Stanford (CVIS) is funded by the National Institute of Biomedical Imaging and Bioengineering of the National Institutes of Health to bring together post-doctoral fellows and faculty from three complementary areas – clinical, engineering, and molecular imaging – to train the next generation of CV imaging investigators for successful careers. With the impact of cardiovascular disease on US and world health and the rapid advances in imaging technologies and cardiovascular biology, it is critical that fellows be provided a broad, multi-disciplinary, and collaborative training program to foster their ability to translate CV imaging research into clinical application.



3D streamlines reflecting systolic blood flow in the thoracic aorta for a Marfan patient after T.

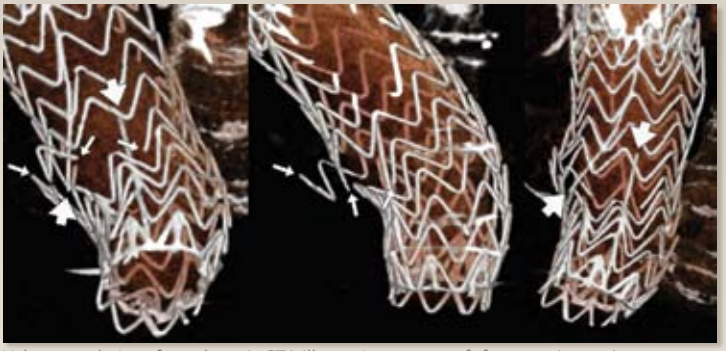
The CVIS will train 4 post-doctoral fellows from MD and PhD backgrounds together over a two-year period, combining CV imaging research with a structured educational program. There are 16 faculty mentors from the Schools of Medicine and Engineering, including Cardiovascular Medicine, Radiology, Molecular Imaging, Electrical Engineering, and Bioengineering.

CVIS fellows will pursue research over the two-year period with the goals of oral presentations, publications, and initial grant submission to propel career advancement. Fellows will have a primary research mentor as well as a secondary mentor from a complementary area (e.g., a clinical secondary mentor to complement a bioengineering primary mentor). There will also be broad exposure for all fellows to clinical imaging modalities and facilities with the Stanford University Medical Center. Fellows with clinical training are welcome to maintain some clinical activities, however as an NIH research training program this will be limited to 10% effort.

The CVIS educational program emphasizes collaborative interaction in 4 major areas

1. Multi-Modality CV Imaging,
2. Multi-Disciplinary Innovation,
3. Translational CV Imaging, and
4. Research Career Development.

These include courses in Biodesign, Molecular Imaging, and Team Challenge – where fellows will work together to identify and propose solutions for high-impact CV imaging challenges. In addition, there is a weekly Clinical CV Imaging Conference and a monthly Translational CV Imaging Research Seminar. These will be complemented by workshops on study design, biostatistics, biomedical ethics, and grant/manuscript writing. Finally, fellows will have access to a wide range of courses and seminars to enhance their primary fields of research throughout Stanford University and the Schools of Medicine and Engineering. CVIS fellows, Program Directors, and faculty mentors will meet quarterly to exchange research ideas and provide feedback. Fellows will also participate in the semi-annual Stanford Cardiovascular Institute retreat.



Volume renderings from thoracic CTA illustrating stent-graft fractures (arrows).

COURSES

Multimodality Molecular Imaging in Living Subjects (BioEngineering 222/Radiology 222)

http://mips.stanford.edu/public/classes/

An exploration of imaging technology and its use in modern biology, including:

1. Basic physics of SPECT, MRI, PET, CT, Optical (bioluminescence and fluorescence) imaging;
2. Design and synthesis of fluorescent and radioactively labeled probes for biological imaging;
3. Cardiovascular, Neurological, and Tumor Angiogenesis imaging with MRI;
4. In vivo multi-modality imaging of gene expression with bioluminescence, fluorescence, and PET;
5. Human application of molecular imaging in diagnosis and therapy.

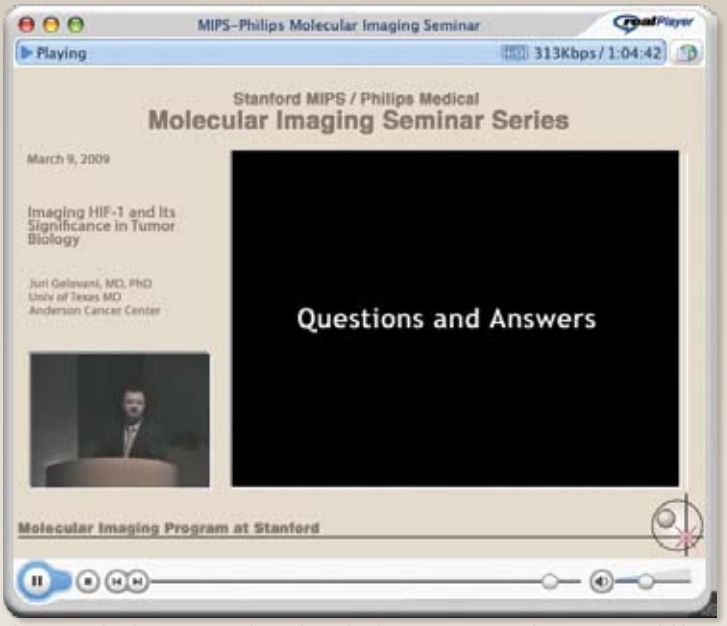
This course is intended for graduate students in the medical school (Cancer Biology, Biophysics, Molecular Pharmacology, Molecular & Cellular Physiology, Radiation Oncology, Radiology), and from Bioengineering and Engineering.

MIPS Molecular Imaging Seminar Series

Mondays, 4:30PM – Various Presenters
Clark Center Auditorium (or Munzer Auditorium, Beckman Bldg)
http://mips.stanford.edu/public/mi_seminar.adp

MIPS Nanobiotechnology Seminar Series

3rd Tuesday of every month, 4:30PM – Various Presenters
Clark Center Auditorium (or Munzer Auditorium, Beckman Bldg)
http://mips.stanford.edu/public/nanobiotech_seminar.adp



The MIPS Molecular Imaging and Nanobiotechnology Seminar Series lectures are available as a video web cast or audio podcast. Please visit the MIPS web site for details.

Nuclear Medicine Monday Lectures

Clinical Research Meeting, Case of the Month, or
Clinical Journal Club
Mondays, 7:30AM – Various Presenters
Nuclear Medicine Library, Room H0341
http://nuclearmedicine.stanford.edu/education/conferences.html

Grand Rounds

Tuesdays, 8:00AM – Various Presenters
Location: Clark Center, Room S360.
http://nuclearmedicine.stanford.edu/education/conferences.html

Nuclear Medicine Wednesday Lectures

Case Conference or Clinical Journal Club
Wednesdays, 7:30AM – Various Presenters
Nuclear Medicine Library, Room H0341
http://nuclearmedicine.stanford.edu/education/conferences.html

MIPS Journal Club

Every other Thursday, 12:00PM – Various Presenters
Edwards Seminar Room R358
http://mips.stanford.edu/public/journal_club.adp

Canary Center @ Stanford for Early Detection

http://canarycenter.stanford.edu/

The Cancer Center @ Stanford for Early Detection

The Canary Center at Stanford, a world-class facility dedicated to cancer early detection programs, is under development at a newly-leased Stanford facility located on California Avenue in Palo Alto. The mission of the center is to foster research leading to the development of blood tests and molecular imaging approaches to detect and localize early cancers. The Center will be the first in the world to integrate research on both in vivo and in vitro diagnostics to deliver these tests, housing state-of- the-art instrumentation for:

1. proteomic research to develop early blood/body fluid markers and,
2. molecular imaging studies to develop tests to verify the presence and location(s) of tumors.

The Center is being developed through an alliance between the Canary Foundation (http://www.canaryfoundation.org), founded by Don Listwin, the Department of Radiology, and the School of Medicine. It will be led by Dr. Sanjiv Sam Gambhir, Professor of Radiology & Bioengineering and Director of the Molecular Imaging Program at Stanford, and include new faculty hires in both ex vivo and in vivo diagnostics. The center will have direct links to the Cancer Center at Stanford with a view towards translating the early detection research into clinical practice.

Molecular Imaging Clinic

A new Molecular Imaging/Nuclear Medicine clinic will begin construction in mid 2009 and should be completed in 2010. This facility will house state-of-the-art clinical imaging equipment including PET-CT, and SPECT-CT. It will help to consolidate most of the clinical molecular imaging activities within the hospital and medical school.

3D rendering of new Molecular Imaging Clinic

RECENT AWARDS

June, 2008

- Adam de la Zerda Received Stanford University's Bio-X Graduate Student Fellowship
- Dr. Gambhir Awarded the Tesla Medal from the United Kingdom Royal College of Radiologists in England for his Work in Multimodality Molecular Imaging of Living Subjects
- Guillem Pratx Received Society of Nuclear Medicine Travel Award
- Qizhen Cao Received 2-year Postdoctoral Fellowship from the Tobacco-Related Disease Research Program (TRDRP) to Work on Lung Cancer Imaging and Therapy
- Peter Olcott Received Society of Nuclear Medicine Predoctoral Molecular Imaging Scholar Program Award
- Zongjin Li Awarded the Mitzi and William Blahd, MD Pilot Research Grant from the Education and Research Foundation for the Society of Nuclear Medicine

July, 2008

- Peter Olcott Received SNM Predoctoral Molecular Imaging Scholar Program Award
- Dr. Gambhir Served as a Guest Editor of the Journal of Nuclear Medicine on a Special Issue for Cancer Imaging
- MIPS Research Entitled, "Molecular Imaging in Drug Development" Featured on Nature Reviews Drug Discovery Cover

August, 2008

- An Article Published in PLOS Medicine Entitled "Cancer Screening: A Mathematical Model Relating Secreted Blood Biomarker Levels to Tumor Sizes" Received Coverage in the News Media
- A Paper on Photoacoustic Molecular Imaging has been Published in Nature Nanotechnology Received Significant Media Coverage in Radio Broadcasts
- A Paper on the Immunogenicity of Human Embryonic Cells Received Considerable Media Coverage

September, 2008

- Research from the Multimodality Molecular Imaging Lab is Featured on the Cover of Nano Letters
- Adam de la Zerda and Min-kyung So Both Received Young Investigator Awards in the World Molecular Imaging Congress 2008 in Nice, France
- Dr. Wu Received NIH Director's New Innovator Award
- Adam de la Zerda Received Bio-X Travel Award to Attend the World Molecular Imaging Congress 2008

October, 2008

- Dr. Gambhir Elected as Member of the Institute of Medicine of the National Academies
- Dr. Wu Awarded Edward Mallinckrodt, Jr. Foundation Junior Faculty Grant

November, 2008

- Paper on Quantum Dot Imaging Featured in ScienceWatch
- Guillem Pratx Received Top Student Presentation 2008 IEEE MIC
- Dr. Willmann Received the Radiology 2008 Editor's Recognition Award with Distinction
- 2008 Medical Imaging Conference Trainee Grants Recipients
- Yi Gu recieved the Bio-X Program Travel Award to Attend 2008 IEEE MIC
- Hen-Tzu Lin Awarded Helena Anna Henzl Gabor Young Women in Science Fund Travel Grant
- Research Featured on Cover of the Journal of Nuclear Medicine
- Paper on Therapeutic T-Cells Received Media Coverage

December, 2008

- Shin Kamaya Received 2008 RSNA Trainee Scholar Award
- Dr. Willmann Received the 2008 RSNA Research Award
- Natesh Parashurama Received Dean's Fellowship
- MIPS Research on Early Cancer Detection Featured in WIRED Magazine

January, 2009

- Dr. Willmann Received 2009 Research Award of the Society of Gastrointestinal Radiologists
- Research Featured in ScienceDaily
- Adam de la Zerda Received SPIE 2009 Best Poster Presentation Award

March, 2009

- MIPS Research on Faster Pediatric MRI, Based on Compressed Sensing Received Lauterbur Award
- MIPS Research on Microfluidic Automation of Phage Display Featured in Chemical Technology
- Dr. Wu Received 2009 Douglas P. Zipes Distinguished Young Scientist Award

April, 2009

- Keren Ziv Received Human Frontier Science Program Fellowship
- MIPS Research on Raman Molecular Imaging and Photoacoustic Molecular Imaging Featured in Science
- Kazim Narsinh and Andrew Lee Received Howard Hughes Medical Institute Research Fellowship
- MIPS Research Received the Journal of Nuclear Medicine's 2008 Best Basic Science Paper
- Dr. Vasanawala Received the Caffey Award From Society for Pediatric Radiology
- Amelie Lutz Received the Marsha Rivkin Center for Ovarian Cancer Research Scholar Award
- Dr. Cheng Received Young Investigator Award by the Melanoma Research Alliance

May, 2009

- Zheng Miao Received First Prize in Basic Science from Society of Nuclear Medicine

RECENT PUBLICATIONS

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Van der Bogt KE, Swijnenburg RJ, Cao F, Wu JC. Molecular imaging of human embryonic stem cells: keeping an eye on differentiation, tumorigenicity and immunogenicity. Cell Cycle 2006;5(23):2748-52.

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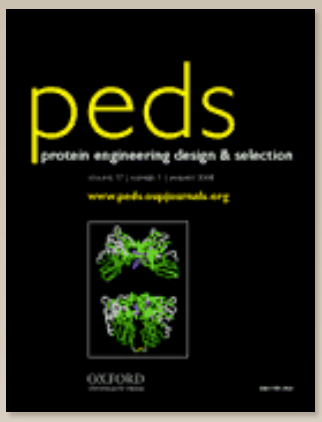
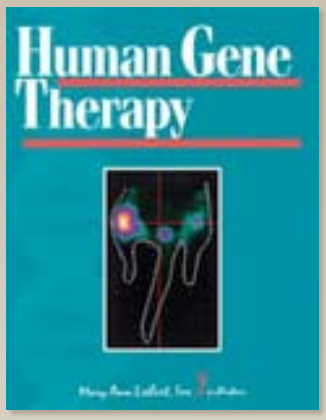
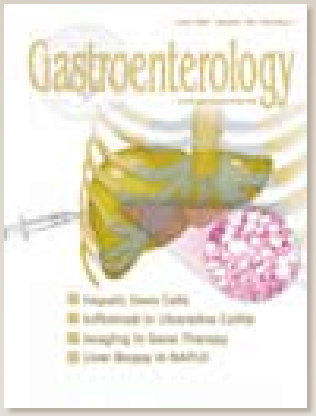
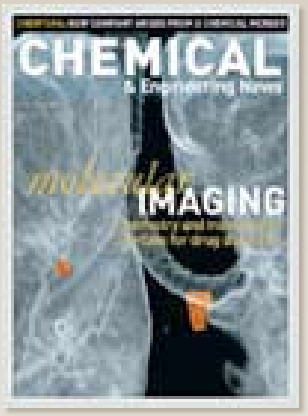
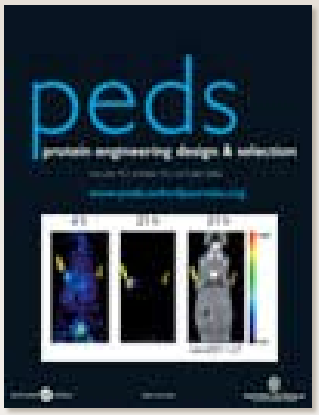
RECENT JOURNAL COVERS

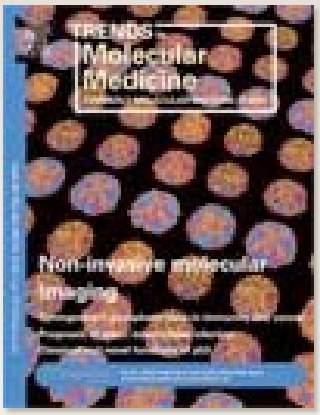


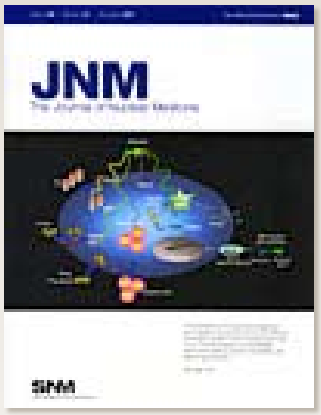


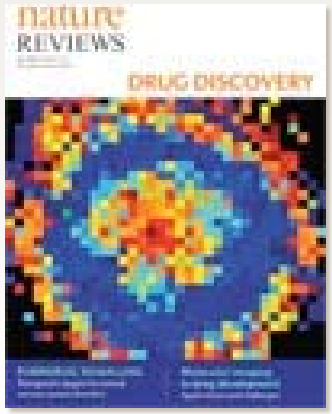












MIPS
Molecular Imaging
Program at Stanford

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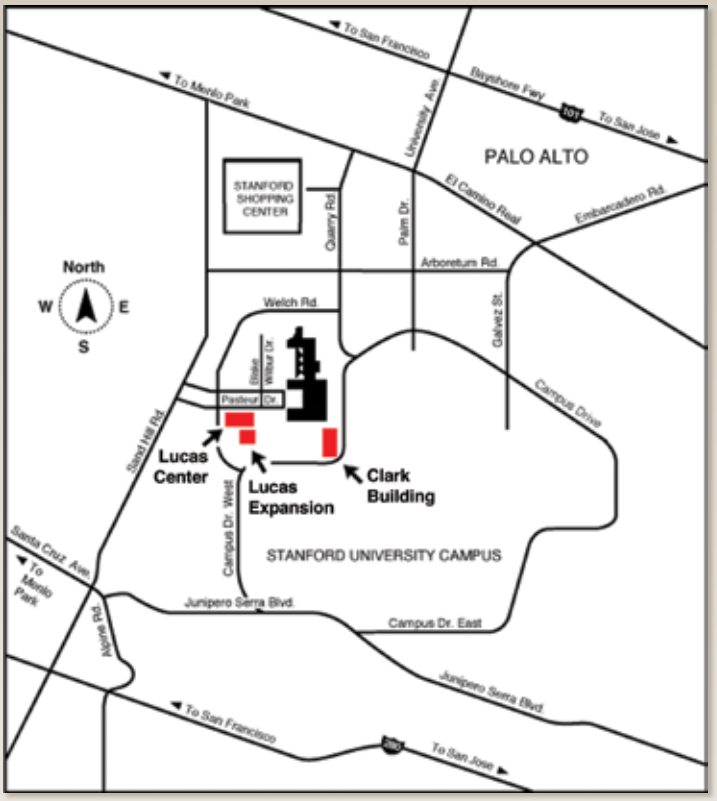
Richard M. Lucas Center


Lucas Expansion


James H. Clark Center



MIPS brochure produced by: Sanjiv Sam Gambhir, MD, PhD, Jim Strommer and Sofia Gonzales

Directions to the Molecular Imaging Program at Stanford

From Bayshore US Highway 101 North or South

Exit on University Ave. South/West. Proceed for several miles on University Ave. University Ave. becomes Palm Dr. after you pass El Camino Real. Take Palm Dr. past Arboretum Rd. Then turn right on Campus Drive and follow this road directly to the Clark Building. Parking is free after 4:00 pm right next to the Clark building (west side).

From 280 North or South

Exit Sand Hill Rd. East. Follow this road for several miles. Take a right on Arboretum Rd. Then take a right on Quarry Rd. Then turn right on Campus Drive and follow this road directly to the Clark Building. Turn right into the parking lot before the stop sign at Welch Road and Campus Drive. Parking is free after 4:00 pm right next to the Clark building (west side).

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