# **Who Will Benefit**

The UCSF Thoracic Oncology Program embodies UCSF's three-fold mission:

**Patient care** As a regional, national and international referral center for lung cancer, patients receive compassionate, state-of-the-art treatment from a multidisciplinary team of specialists.

**Research** Laboratory and translational research provides breakthroughs in our fundamental understanding of lung cancer, mesothelioma and other thoracic malignancies, while clinical research provides hope and new treatments for patients suffering from these diseases.

**Teaching** The Thoracic Surgery Residency Program provides trainees the opportunity to specialize and hone their skills in the rapidly evolving area of cardiothoracic surgery, producing some of the most distinguished leaders in the field.

If you are interested in participating in any of the research studies, please contact any of the physicians in the UCSF Thoracic Oncology Program.

If you would like to support the UCSF Thoracic Oncology Program, please contact Regan Botsford, Director of Development, at (415) 502-1573 or rbotsford@support.ucsf.edu.

Please visit us online: http://top.ucsf.edu/ http://toplab.ucsf.edu/

# The Thoracic Oncology Program at UCSF





To bring the latest therapies to patients who would otherwise not have access to them, the UCSF Thoracic Oncology Program established the Institute for Thoracic Surgery and Thoracic Oncology. This institute partners with Sequoia Hospital in Redwood City to enroll patients in clinical trials, and is about to expand to other hospitals in San Francisco and the South Bay.

#### Overview

Lung cancer is the leading cause of cancer death worldwide and the UCSF Thoracic Oncology Program is poised to conquer it. UCSF provides state-of-the-art care to patients with lung cancer, mesothelioma, esophageal cancer, sarcoma and cancer that has metastasized to the chest. Founded in 1995 by thoracic surgeon David M. Jablons, MD and thoracic oncologist Thierry Jahan, MD, UCSF's Thoracic Oncology Program has been at the forefront of groundbreaking laboratory research, innovative clinical trials, and compassionate, expert care for patients with lung cancer, mesothelioma, esophageal cancer and other thoracic malignancies.

Patients receive treatment from a dedicated multidisciplinary team of specialists. At UCSF, one of the world's leading biomedical research centers, patients also have access to clinical trials for promising new drugs. The Thoracic Oncology Program also collaborates with other world-class scientists and institutions to develop better treatments, and eventually a cure, for these deadly diseases.



#### Lisa Coussens, PhD

Professor, Anatomic Pathology and Cancer Research Institute

After working as a research associate at Genentech, Dr. Coussens received her PhD in Biological Chemistry from UCLA, and completed her postdoctoral fellowship in cancer biology at UCSF. She joined the faculty in 1999. Her many awards include the Hellman Family Award for Early Career Faculty, the V Foundation Scholar from the V Foundation for Cancer Research, and the Era of Hope Scholar Award from the Department of Defense Breast Cancer Research Program. Her lab focuses on the role of inflammatory cells and leukocyte proteases as critical regulators of skin, lung and breast cancer development.

#### Passi Jänne, MD, PhD

Assistant Professor, Department of Medicine, Harvard Medical School Dana-Farber Cancer Institute

Dr. Jänne received his MD and PhD from the University of Pennsylvania. He completed postgraduate training in internal medicine at Brigham and Women's Hospital and in medical oncology at the Dana-Farber Cancer Institute, where he currently works in the Lowe Center for Thoracic Oncology. His main research interests include the study of epidermal growth factor receptor mutations in non-small cell lung cancer and their impact on the efficacy of EGFR-targeted therapeutic agents.

#### II-Jin Kim, PhD

Assistant Research Geneticist

Dr. Kim received his DVM and PhD in Tumor Biology from Seoul National University in Korea. He completed a postdoctoral fellowship at the Korean Hereditary Tumor Registry at the Cancer Research Institute in Seoul, where he later served as a senior scientist. He was recruited to UCSF as a postdoctoral scholar in the UCSF Helen Diller Family Comprehensive Cancer Center in 2007, and was hired as an assistant research geneticist in Dr. Allan Balmain's laboratory at UCSF in 2008. Dr. Kim's current research focuses on a systems genetics analysis of matched tumor/normal tissue sample pairs for lung cancer, an approach which he plans to apply to adenocarcinomas and other types of lung cancers, including mesothelioma.

#### Frank McCormick, PhD, FRS

David A. Wood Distinguished Professor of Tumor Biology and Cancer Research E. Dixon Heise Distinguished Professor in Oncology Director, UCSF Helen Diller Family Comprehensive Cancer Center & Cancer Research Institute

Dr. McCormick's research is focused on signal transduction pathways in cancer cells, and ways of treating cancer based on these pathways. His laboratory's primary interest is the Ras pathway, although his group also studies metabolic differences between cancer cells and normal cells, and defects in cancer proteins related to mitotic checkpoints.

# Key Collaborators

#### Allan Balmain, PhD, FRSE

Barbara Bass Bakar Distinguished Professor in Cancer Genetics

Dr. Balmain received his PhD in Organic Chemistry from the University of Glasgow, and completed postdoctoral fellowships at the University of Strasbourg in France and the German Cancer Research Centre in Heidelberg. He worked as a tenured staff member at the German Cancer Research Centre, a staff scientist, group leader and CRC special appointment at the Beatson Institute for Cancer Research in Glasgow, director of laboratory research and professor of medical oncology at the University of Glasgow, and vice president of research at Onyx Pharmaceuticals in Richmond, CA before joining the UCSF faculty in 1999. His research focuses on the elucidation of the genetics and biology of multistage carcinogenesis, with particular emphasis on mouse models of chemically induced skin tumor development.

#### V. Courtney Broaddus, MD

Professor of Medicine

Dr. Broaddus received her MD from the University of Pennsylvania, and completed her residency at the Hospital of the University of Pennsylvania. She completed her Pulmonary Disease fellowship at UCSF, and later joined the faculty. Since 1998, she has served as Chief of the Division of Pulmonary and Critical Care Medicine at San Francisco General Hospital (SFGH). She is also Associate Director of the Lung Biology Center at SFGH, where she directs a lab investigating apoptosis in mesothelioma and lung cancer lines, as models for highly resistant solid tumors. Her lab focuses on identifying mechanisms of resistance to apoptosis in these lines and identifying means of amplifying apoptosis.

#### George H. Caughey, MD

Professor of Medicine

Dr. Caughey received his MD from Stanford. After Medicine and Pulmonary subspecialty training at Pennsylvania Hospital and UCSF, he trained in lung research at UCSF's Cardiovascular Research Institute and at Genentech, joining UCSF's pulmonary faculty in 1986. He is the Julius and Lillian Nadel Endowed Chair and Chief of the Pulmonary and Critical Care Medicine Section at the San Francisco VA Medical Center. His lab research focuses on how extracellular proteases influence the pathology of lung diseases.





### Clinical Research

UCSF's Thoracic Oncology Program has a number of clinical trials which offer the latest treatments to patients with esophageal cancer, mesothelioma, non-small cell lung cancer and small cell lung cancer. Some examples of current clinical trials include:

Chemotherapy and Erlotinib: The epidermal growth factor receptor (EGFR) inhibitor erlotinib, in combination with chemotherapy, has led to improved survival in patients with pancreatic and lung cancer. EGFR is a target in esophageal cancer therapy since its overexpression is associated with more aggressive disease and poor survival. Early studies have shown some clinical activity of EGFR inhibitors in this disease alone or in combination with chemotherapy. This phase II clinical trial explores how safe and effective treatment with erlotinib and FOLFOX is in patients with advanced esophageal or gastro-esophageal cancer.

Dasatinib in Treating Patients With Previously Treated Malignant Mesothelioma: Currently, there is only one approved chemotherapy treatment for mesothelioma (cisplatin and pemetrexed) in the United States. Dasatinib has been shown to slow cancer growth in the laboratory and in animals by reducing the activity of one or more of the proteins that cause cancer cells to multiply and grow. Dasatinib is approved by the FDA for use in patients with chronic myeloid leukemia or acute lymphoblastic leukemia who have developed resistance or intolerance to imatinib (Gleevec), but is considered investigational for the treatment of mesothelioma. This phase II clinical trial is enrolling patients who have already had treatment with pemetrexed and in those whose cancer has recurred or progressed despite chemotherapy. Researchers are also studying patients' blood and tumor specimens to determine if there is a way to predict how effectively particular patients will respond to dasatinib.

Comparison of Standard-Dose versus High-Dose Conformal Radiotherapy with Concurrent and Consolidation Carboplatin/Paclitaxel +/- Cetuximab in Patients with Stage IIIA/IIIB Non-Small Cell Lung Cancer: Radiation therapy uses highenergy X-rays to kill tumor cells. Monoclonal antibodies such as cetuximab and chemotherapy drugs such as paclitaxel and carboplatin can block tumor growth. This randomized phase III trial is studying high-dose radiation therapy given together with cetuximab and chemotherapy to see how well it works compared with standard-dose radiation therapy and chemotherapy in treating patients with newly diagnosed stage III non-small cell lung cancer that cannot be removed by surgery.

Sunitinib, Cisplatin, and Etoposide in Treating Patients With Extensive-Stage Small Cell Lung Cancer: Sunitinib may stop the growth of tumor cells by blocking some of the enzymes needed for cell growth and by blocking blood flow to the tumor. Drugs used in chemotherapy, such as cisplatin and etoposide, work in different ways to stop the growth of tumor cells, either by killing the cells or by stopping them from dividing. Giving sunitinib together with cisplatin and etoposide may kill more tumor cells. This phase I/II trial is studying the side effects and best dose of sunitinib when given together with cisplatin and etoposide and to see how well they work in treating patients with extensive-stage small cell lung cancer.

# Laboratory Research

Cancer treatment is rapidly proceeding towards the era of personalized medicine where treatment is based on the distinctive molecular characteristics of a patient's tumor. This knowledge will allow patients to receive novel combinations of therapies that will maximize clinical benefit, more accurately predict disease outcome, and allow patients at the highest risk of relapse to receive the most aggressive treatment.

The Thoracic Oncology Lab is pursuing a variety of strategies to treat and cure lung cancer, mesothelioma, esophageal cancer and other cancers. These include the investigation of molecular pathways such as Wingless-int (Wnt) and Hedgehog (Hh), the role of inflammation in lung carcinogenesis, isolation of lung cancer stems cells, and the Lung Cancer Systems Genetics Project. Our lab has developed novel targeted therapeutics using recombinant DNA technology and monoclonal antibodies against these cancers. We are aggressively pursuing more effective treatments that will slow the growth of these diseases, and eventually point to a cure.

Some of our current research initiatives include:

Cancer Stem Cells: Recent evidence supports the existence of cancer stem cells, which are distinct populations of cells found within tumors that have the capacity for self-renewal and differentiation, similar to adult stem cells. We are working to develop drugs that are toxic to these cancer stem cells, helping to stop cancer at its "root."

Gene Expression: Researchers are studying the output of gene products within a cancer cell, particularly the level of messenger RNA (mRNA) produced. mRNA is a molecule that carries the blueprint for production of cellular proteins. The amount of mRNA present suggests what genes are active in the cell, serving as a "genetic signature" correlated with clinical outcomes. Recent research suggests that there may be two genetically distinct types of lung cancer — a milder and a more aggressive form. Developing ways to determine which type of cancer a particular patient has could help determine which course of treatment would be most beneficial.

Inflammation in Lung Carcinogenesis: In collaboration with scientists in Anatomic Pathology, the Thoracic Oncology Laboratory is investigating the role of inflammation in the development of lung cancer. They are researching the lineages of abnormal leukocytes, or white blood cells. They are also studying which leukocyte abnormalities might stimulate irregularities in the Wnt and Sonic hedgehog signaling pathways — cellular communication processes that regulate growth and, when unchecked, can lead to unregulated, cancerous growth — and how exactly this might occur.



**Liang You, MD, PhD**Associate Adjunct Professor of Surgery

Dr. You received his MD from Jinzhou Medical College in Jinzhou, China, and his PhD in Pathology from the Medical College of Ohio. After several years at the National Cancer Institute, Dr. You was recruited in 1997 to UCSF's Thoracic Oncology Laboratory. Dr. You has helped identify several novel biomarkers and therapeutic targets in lung cancer and mesothelioma. He is currently investigating recombinant human WIF-1 protein as a cancer therapy and seeking out new therapeutic targets and novel interventions.

# Thoracic Oncology Laboratory: Postdoctoral Fellows

# Adam Beltrán, MD

Postdoctoral Fellow

Dr. Beltrán received his medical degree from the University of Dundee Medical School in Scotland, where he also received a degree in Pathology/Cellular and Molecular Basis of Disease. He completed his general surgery internship at Tayside University Hospitals, his general medicine internship at Glasgow Royal Infirmary, and his general surgery residency at Leeds University Hospital. He was recruited as a postdoctoral fellow in 2006 to the Thoracic Oncology Laboratory, where his research is focused on dissecting the mechanisms of interaction between the Wnt and Hedgehog signaling pathways, as well as the role of complex inflammatory mechanisms, in the development of esophageal cancer.

# Surgical Residents

#### Johannes Kratz, MD

Postdoctoral Fellow

Dr. Kratz received his MD from Harvard University, and is a surgical resident at Massachusetts General Hospital. He comes to the Thoracic Oncology Laboratory under the auspices of the Wyeth Scholarship of the American College of Surgeons for the Study of Inflammation. While at UCSF, he is focusing on the role of inflammation in thoracic carcinomas and on developing gene expression assays as prognostic indicators in lung cancer.

UCSF's Thoracic Oncology
Program has established or
co-chaired many conferences,
including the International Lung
Pan Pacific Cancer Conference,
the UCSF/UC Davis Thoracic
Oncology Conference, the UCSF
Clinical Cancer Update, Summit
2007, and the International
Association for the Study of Lung
Cancer's 13th World Conference
on Lung Cancer in 2009.

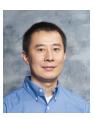
# Radiation Oncology



**Sue S. Yom, MD, PhD**Assistant Professor of Clinical Radiation Oncology

Dr. Yom received her MD from the University of Pennsylvania and a PhD in English. She did her residency in radiation oncology at the University of Texas–MD Anderson Cancer Center. She joined the UCSF faculty in 2007. Her specialty is the treatment of thoracic and head and neck cancers and the development of new radiotherapy techniques.

Thoracic Oncology Laboratory: Principal Investigators



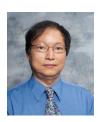
**Biao He, PhD**Associate Adjunct Professor of Surgery

Dr. He received his PhD in Molecular Genetics from the University of Virginia. He served as a postdoctoral researcher and assistant research molecular biologist at the UCSF Helen Diller Family Comprehensive Cancer Center before being recruited to the UCSF faculty in 2004 for his knowledge of Wnt signaling and RNA interference (RNAi). His current research is focused on the molecular mechanisms of non-small cell lung cancer and mesothelioma. He is also developing targeted therapies against these diseases.



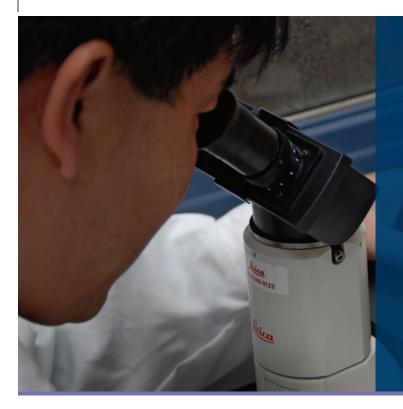
Minh To, PhD Assistant Adjunct Professor of Surgery

Dr. To received his PhD in Molecular/Medical Genetics from the University of Toronto, and completed a postdoctoral fellowship at UCSF, working primarily on mouse models of human cancers. In 2008, he was recruited to the UCSF Department of Surgery as an Assistant Adjunct Professor of Surgery. His current research utilizes mouse models to study the mechanism of lung cancer susceptibility and biology, and to identify novel targets for therapeutic intervention. Dr. To is also heavily involved in a collaborative study with Drs. Allan Balmain and David Jablons that uses a "systems genetics" approach for large scale molecular analysis of human lung cancers in relation to clinical outcomes.



**Zhidong Xu, PhD**Associate Adjunct Professor of Surgery

Dr. Xu received his PhD from the University of Texas Medical Branch in Galveston in Molecular Mutagenesis. He is a molecular biologist and senior scientist in the Thoracic Oncology Laboratory. In 1998, Dr. Xu was recruited by David M. Jablons, MD to the Thoracic Oncology Laboratory. In 2001, he became an Assistant Professor in the Department of Surgery. Dr. Xu's research is focused on the molecular biology of non-small cell lung cancer and mesothelioma, including development of novel targeted therapeutics based on recombinant DNA technology.



The Thoracic Surgical
Oncology Program
is the embodiment
of the UCSF's
three-fold mission
of teaching, research
and — most important —
patient care.

Kras Pathway: Mutations in the Ras family of genes occur frequently in human cancers, and mutations in specific Ras genes are associated with particular types of cancer. For example, mutations in the Kras gene are associated with lung, pancreatic and colon cancers. Researchers are studying why Kras is associated with these types of cancer, and are learning more about which specific alternations contribute to carcinogenesis — findings that could have major implications for the design of targeted therapies.

Lung Cancer System Genetics: UCSF has one of the world's largest lung cancer tissue banks, with samples of both normal and tumor tissue from 1,100 lung cancer patients. These samples have been flash frozen and are in pristine condition, unlike many tissue banks where samples degrade because they are stored in paraffin. Interrogation of these samples includes analysis of mutations in inherited DNA, mutations that may result from environmental factors such as smoking or air pollution, extra copies or deletions of particular genes, and the exact genetic products produced by a cancer cell. By conducting this comprehensive investigation, researchers are identifying biomarkers that identify the specific type of lung cancer a patient has, and which treatments are most effective to treat it.

Wnt Signaling Pathway: Wingless-int (Wnt) proteins regulate many growth processes, such as embryonic development. When overexpressed, they may contribute to rampant cell proliferation and failure of defective cells to commit suicide. Aberrant activation of Wnt signaling is strongly implicated in cancers such as non-small cell lung cancer, including bronchioalveolar carcinoma, mesothelioma, esophageal, colorectal and nasal-pharyngeal carcinomas; and pre-malignant conditions such as Barrett's esophagus, in which esophageal cells alter in response to chronic gastrointestinal reflux disease. Researchers are investigating various proteins and molecules that affect the Wnt signaling pathway and could serve as diagnostic markers for cancer. Further discoveries could help pinpoint attractive targets for therapies that could halt unregulated cell growth and induce defective cells to destroy themselves.

Key Faculty

Thoracic Surgery



**David M. Jablons, MD**Professor and Chief, Section of General Thoracic Surgery
Program Leader, Thoracic Oncology Program
Ada Distinguished Professor of Thoracic Oncology

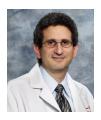
Dr. Jablons received his MD from Albany Medical College of Union University and completed his internship at Oak Knoll Naval Hospital in Oakland, CA and his surgical residency at Tufts University. He also completed fellowships in surgical oncology at the National Cancer Institute/National Institutes of Health, cardiothoracic surgery at New York Hospital-Cornell University Medical Center, lung transplantation at Brigham and Women's Hospital, and thoracic surgery at New York Hospital/Memorial Sloan Kettering Cancer Center before coming to UCSF in 1995. He is currently the leader of the Thoracic Oncology Program and director of the Thoracic Oncology Laboratory. He was also conference co-chair of the World Lung Cancer Conference in 2009.



Jasleen Kukreja, MD, MPH Assistant Professor of Surgery

Dr. Kukreja received her MD from UCLA and her MPH from Harvard University. She completed residencies at UCLA, Brigham and Women's Hospital in Boston, and UCSF and has done several fellowships at Brigham and Women's Hospital. She completed her cardiothoracic training at UCSF. As a Cancer and Leukemia Group B (CALGB) clinical research fellow, Dr. Kukreja received extensive training in the design of clinical trials. Dr. Kukreja treats patients with tumors of the chest including lung cancer, esophageal cancer, mediastinal tumors, mesothelioma, lung volume reduction surgery for emphysema, and lung transplantation.

Building on 15 years of collaborative work with leading scientists in China, the Institute also launched the China Clinical Trials Consortium (CCTC). This consortium will offer potentially life-saving therapeutics to thousands of patients in China, where an epidemic of lung cancer and mesothelioma is predicted in the next two decades as a result of widespread smoking, increasing industrial pollution, unregulated asbestos control and apparent genetic susceptibilities. Results from these clinical trials will help accelerate the pace of clinical research.



**Michael J. Mann, MD** Assistant Professor of Surgery

Dr. Mann received his MD from Stanford, where he also completed a residency in general surgery and a postdoctoral fellowship in cardiovascular disease. After a surgery residency at Brigham and Women's Hospital in Boston, he came to UCSF for a residency in cardiothoracic surgery. He joined the UCSF Thoracic Oncology Program in 2003. He is assistant director of the Thoracic Surgery Training Program and has invented several novel drugs and drug delivery technologies.



Pierre R. Theodore, MD
Assistant Professor of Surgery
Van Auken Endowed Chair in Thoracic Surgery

Dr. Theodore received his MD from the University of Virginia and then completed residencies in general and cardiothoracic surgery at Johns Hopkins Hospital. His fellowships also include transplant biology at Harvard University and cardiothoracic surgery at La Pitie-Saltpetriere Hospital in Paris. He focuses on minimally invasive thoracic surgery and is an experienced lung transplant surgeon.

Medical Oncology



Thierry Marie Jahan, MD
Associate Professor of Medicine
Bonnie J. and Anthony Addario Endowed Chair in Thoracic Oncology

Dr. Jahan received his MD from George Washington University and then completed a residency and fellowship in internal medicine at Cedars Sinai Medical Center/UCLA. After a fellowship in hematology and oncology at UCSF, he joined the faculty here. With Dr. Jablons, he founded the Thoracic Oncology Program.

Pulmonology



**Lorriana E. Leard, MD**Assistant Professor of Medicine

Dr. Leard received her MD from the University of California, San Diego, and then completed a residency in internal medicine at the University of Texas Southwestern. She was a fellow in both pulmonary/critical care medicine and in lung transplantation before joining the faculty in 2006. Her expertise allows her to diagnose and stage lung cancers using less invasive, yet highly precise methods. She is working to develop a lung cancer screening protocol at UCSF.