LAM TREATMENT ALLIANCE
*Fast Tracking Treatment Research*

LAM CELL SUMMIT 2006

# LAM CELL SUMMIT 2006

LOCATION: Boston, MA - Harvard Medical School,
New Research Building,
77 Avenue Louis Pasteur, Room 1030F

DATE: June 30, 2006

TIME: 10am – 4pm

OVERVIEW: The LAM Cell is the focus of this meeting. We will address LAM Cell validation criteria, promising approaches to treatment research and the role of LAM tissue, and LAM tissue procurement and distribution.

PARTICIPANTS: - *(please see biosketches attached)*

- Dan Anderson, *PhD (MIT)*
- Jack Arbiser, *MD, PhD (Emory)*
- Joe Avruch, *MD, PhD, (MGH/HMS)*
- *Lew Cantley,*PhD (BIDMC/HMS)*
- Omid Farokhzad, *MD, PhD (BWH/HMS/MIT)*
- Amy Farber, *PhD, Executive Director LAM Treatment Alliance*
- Chris Fletcher, *MD (BWH/HMS)*
- *Judah Folkman, *MD (CHB/HMS)*
- Lisa Henske, *MD, PhD (FCCC)*
- Michael Jaklitsch, *MD (BWH/HMS)*
- Vera Krymskaya, *PhD (UPenn)*
- David Kwiatkowski, *MD, PhD (BWH/HMS)*
- *Robert Langer, *ScD (MIT)*
- *Sten Lindahl, *MD, PhD (Karolinska Institute)*
- Frank McCormack, *MD (University of Cincinnati)*
- Marsha Moses, *PhD (CHB/HMS)*
- Joel Moss, *MD, PhD (NIH-NHLBI)*
- Michael Nurok, *MD, Director, LAM Treatment Alliance*
- David Sabatini, *MD, PhD (MIT/Whitehead)*
- Cheryl Walker, *PhD (MD Anderson)*
- Vicky Whittemore, *PhD (TS Alliance)*

* Members of the LAM Treatment Alliance Scientific Advisory Board

CONVENERS:
Robert Langer, *MD, Chair - LAM Treatment Alliance Scientific Advisory Board*
Amy Farber, *PhD, Executive Director, LAM Treatment Alliance*
Michael Nurok, *MD, Director, LAM Treatment Alliance*

CONTACT: Please do not hesitate to call or email Amy Farber with questions:
amy_farber@hms.harvard.edu or (617) 470-8177

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## AGENDA

**10am** *(with light breakfast)*
PRELIMINARIES/INTRODUCTION:
Amy Farber, PhD, *Executive Director, LAM Treatment Alliance*
Dr. Robert Langer, *Scientific Chair, LAM Treatment Alliance*

INTRODUCTIONS: *(2 min. each)* Your experience and its relevance to defining the LAM cell and/or approaches to finding treatment (i.e. cell line, animal model, expression profiling, drug screening).

**11am**
DEFINING A LAM CELL: What do we know & what do we need to know?

A PRELIMINARY DEFINITION OF A LAM CELL AND OPEN QUESTIONS:
(DEFINITIVE characteristics, POSSIBLE characteristics, OPEN questions and JUSTIFICATIONS)

- Dr. Joel Moss *(10 min.)*
- Dr. Vera Krymskaya *(10 min.)*
- Dr. Jack Arbiser *(10 min.)*
- Dr. David Kwiatkowski *(10 min.)*
- Dr. Lisa Henske *(10 min.)*

DISCUSSION AND MOVEMENT TOWARDS CONSENSUS:

- Based on what we know about markers of LAM cells
  What constitutes a real, bona fide LAM cell?
- What surrogate cells might be acceptable, and for what purposes?

**1-1:30**pm *Lunch*

**1:35-2:45pm**
THE LAM CELL IN THE CONTEXT OF TREATMENT RESEARCH:
Approaches: What will we and others do with LAM cells?
What kind of tissue is needed for these studies?

GENETICS

ANIMAL MODEL

PROTEOLYTIC PROFILE

SIGNALING PATHWAYS

ANGIOGENESIS

OTHER

**2:50 - 4pm**

ACCESS TO LAM CELLS (Procurement and Distribution):
How do I get the LAM cells that I need?

WRAP-UP/ NEXT STEPS

# LAM CELL SUMMIT 2006 PARTICIPANTS

JUNE 30, 2006. HARVARD MEDICAL SCHOOL, BOSTON, MA



**Dr. Daniel Anderson** dgander@mit.edu

Daniel Anderson is a research associate in the department of chemical engineering at the Massachusetts Institute of Technology. He received his PhD in molecular genetics from the University of California at Davis. At MIT, he pioneered the use of high throughput methods in creating and screening biomaterials for drug delivery and tissue engineering. He has developed robotic technology allowing rapid nanoliter scale synthesis of 1000s of biomaterials, the testing of their effects on gene expression in stem cells and utility as drug delivery systems. The delivery systems he has developed provide new methods for nanoparticulate and microparticulate drug delivery, non-viral gene therapy, siRNA delivery, and vaccines. His work has resulted in the publication of over 30 papers and 25 patents.

**Dr. Jack Arbiser** jarbise@emory.edu

Dr. Arbiser joined the Dermatology Department at Emory after completing his PhD and medical school training, internship, and residency at Harvard, and then a three-year Howard Hughes Fellowship and junior faculty position in the laboratory of Dr. Judah Folkman.

Dr. Arbiser's research focuses on the regulation of angiogenesis and tumorigenesis by signal transduction pathways. The Arbiser laboratory has chosen three model systems to study these relationships. The first area is the common vascular birthmarks of children and their malignant counterparts, angiosarcomas. The second application of these studies are benign neoplasms which develop in the autosomal dominant syndrome tuberous sclerosis (TS). The third application of these studies is in the pathogenesis of malignant melanoma.

Dr. Arbiser's lab is also using expertise in signal transduction to study angiogenesis in the human disorder tuberous sclerosis. Tuberous sclerosis is a common autosomal dominant disorder characterized by the development of benign and malignant tumors of the skin, kidney, and brain. The Arbiser laboratory has developed relevant cell lines from these tumors which can be tested for sensitivity to drugs that may ameliorate tuberous sclerosis (Amer J Pathol 2002;161:781-6, Amer J Pathol 2001;159:483-91). In addition, cell lines have been developed from murine tumors of mice heterozygous for tuberin, a major tuberous sclerosis gene, which will allow both in vitro and in vivo testing for drugs which may prevent and treat the neoplastic complications of tuberous sclerosis. Finally, transgenic mice have been developed in Dr. Arbiser's lab, which overexpress a mutant tuberin in all tissues, yet results in a tissue specific phenotype in skin and brain. These

mice may help explain the tissue specific nature of hamratomas and neoplasms in tuberous sclerosis, and may separate the hamartoma phenotype from the neoplastic phenotype.

Finally, the Arbiser laboratory is interested in determining the factors which cause transformation in melanoma, especially the transition from radial growth (noninvasive) melanoma to vertical growth (invasive) melanoma. The lab has already demonstrated that MAP kinase activation is required for the development of early radial growth melanoma (Clin Cancer Research, 2002;12:3728-33, J Biol Chem 2003; 278 (11): 9790-9795), and is currently demonstrating the role of phosphoinositol-3 kinase, reactive oxygen, and NFkB activation in the formation of melanoma.

### Dr. Joe Avruch

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Dr. Avruch received his MD from Washington University School of Medicine in 1965, followed by an internal medicine residency at Barnes Hospital, St. Louis and a research fellowship in biological chemistry and medicine at MGH. Dr. Avruch is a Professor of Medicine at the Harvard Medical School in the Department of Molecular Biology, and has been Chief of the Diabetes Unit in the department of Medicine at the MGH since 1979. He is director of the NIH sponsored Boston Area *Diabetes and Endocrinology Research Center.*

Dr. Avruch directs a vigorous ongoing program of laboratory-based research, and is internationally recognized for a series of discoveries that have enabled an understanding of how insulin, related growth factors, as well as insulin antagonists control cell function. Dr. Avruch's research is aimed at identifying the molecular structure, function and regulation of the elements that mediate signal transduction initiated by the insulin receptor, related receptor tyrosine kinases and counter-acting, anti-insulin signalling pathways. The initial impetus for this effort arose from the considerable evidence indicating that impairment of insulin signal transduction, manifest in vivo as a resistance to the hypoglycemic actions of insulin, was the precursor lesion for a large majority of individuals with Type 2 diabetes. As elucidation of the signaling pathways responsive to insulin progressed, it became evident that many of the effectors identified also participated in the implementation of mitogenic and cell differentiation programs. Thus the mechanisms uncovered in this effort proved to have important implications not only for metabolic regulation and its disorders i.e., diabetes and obesity, but also for states characterized by disordered cell growth regulation. Ongoing research projects in his lab include work on the elucidation of the Insulin and Nutrient regulation of the mTOR kinase and the identification of New elements in the Ras signaling.

### Dr. Lew Cantley

lewis_cantley@hms.harvard.edu

Dr. Cantley obtained a Ph.D. in Biophysical Chemistry from Cornell University in 1975. He did postdoctoral research at Harvard from 1975 until 1978 and

joined the Department of Biochemistry and Molecular Biology at Harvard as an Assistant Professor in 1978. In 1985 he was appointed Professor of Physiology at Tufts University School of Medicine. In 1992 he returned to Harvard as Professor in the Department of Cell Biology at Harvard Medical School and Chief of the Division

of Signal Transduction at Beth Israel Hospital. He is a founding member of the new Department of Systems Biology at Harvard Medical School and retains his position as Chief of the Division of Signal Transduction at Beth Israel Deaconess Medical Center. Dr. Cantley conducts research on the molecular basis for cancer and metabolic diseases using biochemical, cell biological and animal-based studies. Dr. Cantley was elected to the American Academy of Arts and Sciences in 1999 and to the National Academy of Sciences in 2001. Among his other awards are the ASBMB Avanti Award for Lipid Research (1998), the Heinrich Weiland Preis for Lipid Research (2000) the Caledonian Prize from the Royal Society of Edinburgh (2002) and the Pezcoller Award for Cancer Research (2005).

### Dr. Omid Farokhzad ofarokhzad@partners.org

Dr. Farokhzad is Assistant Professor at Harvard Medical School and a practicing physician in the Department of Anesthesiology at Brigham and Women's Hospital (BWH). He is a graduate of Boston University School of Medicine and completed his post-graduate clinical training at BWH, and his research training within the Harvard-MIT Division of Health Sciences and Technology in the Laboratory of Dr. Robert Langer at MIT. Dr. Farokhzad is the recipient of a NIH - National Institute of Biomedical Imaging and Bioengineering Career Award (2005-2009). Dr. Farokhzad´s research interests are in development of smart delivery vehicles and nanomaterials for cancer therapy. He has developed technologies for targeted drug delivery to cancer cells including nanoparticle-aptamer bioconjugates which target prostate cancer cells and BioMEMS devices for modeling the interaction of these conjugates with their target cells for high throuput optimization of these conjugates in vitro.

### Dr. Christopher D. M. Fletcher cfletcher@partners.org

Dr. Fletcher graduated from St. Thomas's Hospital Medical School in London and obtained postgraduate qualifications from the Royal College of Pathologists (MRCPath - 1988) and the University of London (M.D. - 1991) in the United Kingdom. Dr. Fletcher's main areas of interest include the clinicopathologic and molecular genetic analyses of soft tissue tumors. Dr. Fletcher has published extensively on the pathology of soft tissue tumors and is probably best known for his work challenging the diagnostic entities of pleomorphic malignant fibrous histiocytoma and hemangiopericytoma. He has also described for the first time a variety of lesions, including, among others, angiomyofibroblastoma, retiform hemangioendothelioma, spindle cell liposarcoma, myoepithelial lesions of soft tissue and low-grade myofibroblastic sarcoma. He has worked extensively on

cytogenetic/morphologic correlations in soft tissue tumors. He is Chairman of the WHO Working Group on the classification of soft tissue tumours and is editor of the new WHO classification which was published in 2002. He has more than 400 publications, including more than 290 original papers on soft tissue neoplasms and several books, among which are the two-volume Diagnostic Histopathology of Tumors, now in its 2nd edition, and the 3rd series AFIP Fascicle on Soft Tissue Tumors. He is on the editorial board of 17 journals and is President of the Association of Directors of Anatomic and Surgical Pathology. Before moving to the United States in 1995. Dr. Fletcher was the Director of the Soft Tissue Tumour Unit at St. Thomas's Hospital in London and Professor of Surgical Pathology in the University of London; he is currently Professor of Pathology at Harvard Medical School, Director of Surgical Pathology at Brigham and Women's Hospital, Boston, Massachusetts and Chief of Onco-Pathology at the Dana-Farber Cancer Institute in Boston.

### Dr. Judah Folkman

Judah.Folkman@childrens.harvard.edu

Dr. Folkman is the founder of the field of angiogenesis research. He has made seminal discoveries on the mechanism of angiogenesis, which have opened a field of investigation now pursued worldwide. Dr. Folkman's hypothesis (1971) that solid tumors are angiogenesis-dependent initiated studies of angiogenesis in tumor biology and in disciplines as diverse as developmental biology, ophthalmology and dermatology. His laboratory reported the first purified angiogenesis molecule, the first angiogenesis inhibitor and proposed the concept of angiogenic disease. All of these discoveries have been translated into numerous clinical trials. Angiogenesis inhibitors are now approved by the FDA in the U.S., and in 28 other countries. Largely because of Dr. Folkman's research, the possibility of antiangiogenic therapy is now on a firm scientific foundation, not only in the treatment of cancer, but of many non-neoplastic diseases as well.

Dr. Folkman's exceptional achievements have been recognized by many national and international awards. In 1990, he was elected to the National Academy of Sciences. He is also a member of the American Academy of Arts and Sciences, the American Philosophical Society and the Institute of Medicine. In addition to his distinguished accomplishments in research, Dr. Folkman has served as a surgeon and teacher. He began his career as an Instructor in Surgery for Harvard's Surgical Service at Boston City Hospital, was promoted to Professor of Surgery at Harvard Medical School, and became the Julia Dyckman Andrus Professor of Pediatric Surgery in 1968. From 1967 he served as Surgeon-in-Chief at Children's Hospital Boston for 14 years. Dr. Folkman is also a Professor of Cell Biology at Harvard Medical School and is currently the Director of the Vascular Biology Program in the Department of Surgery at Children's Hospital. He holds honorary degrees from fifteen universities and is the author of 394 original peer-reviewed papers and 106 book chapters and monographs.

## Dr. Elizabeth Henske ep_henske@fccc.edu

Dr. Henske is a Member with Tenure of the Fox Chase Cancer Center in Philadelphia. She earned her undergraduate summa cum laude from Yale University, where she majored in Molecular Biophysics and Biochemistry, and her MD degree from Harvard Medical School. She completed her Internship and Residency in Internal Medicine and Fellowship in Hematology/Oncology at the Massachusetts General Hospital in Boston, followed by Post-doctoral training in the laboratory of David Kwiatkowski at the Brigham and Women's Hospital. Dr. Henske's research is currently focused on the cellular mechanisms through which mutations in the TSC genes lead to tumor formation in TSC and LAM.

## Michael Jaklitsch mjaklitsch@partners.org

Dr Michael Jaklitsch is an Associate Professor of Surgery at Harvard Medical School and an active General Thoracic Surgeon at Brigham and Women's Hospital. He is the Surgical Director of the Lung Transplant Program at Brigham, and the Director of Clinical Research for the Division of Thoracic Surgery.

Dr Jaklitsch is a native of Maryland, graduated Cum Laude from Tulane University in New Orleans, and graduated from the University of Maryland School of Medicine in 1986. He completed 3 junior years of general surgery residency at the University of Alabama Birmingham before spending 2 years as a Research Fellow under the direction of Dr Ellis Unger in the Cardiology Branch of the National Heart Lung and Blood Institute in Bethesda from 1989 to 1991. He then completed his chief residency in general surgery at UAB in 1993. He attended the Clinical Effectiveness program of the Harvard School of Public Health as part of a Thoracic Oncology Fellowship at the Dana Farber Cancer Institute from 1993-1994. He then completed a 3-year cardiothoracic residency at the University of Minnesota from 1994-97. He joined the faculty of the Division of Thoracic Surgery at Brigham and Women's Hospital in 1997.

Dr Jaklitsch's basic science efforts have been aimed at elucidating cell-matrix interactions and intracellular signal pathways in non-small cell lung cancer cell lines. In addition, he has recently worked on an in-vitro perfusion technique to preserve and assess the quality of lungs explanted from a donor prior to lung transplantation. This research could be applied to preserving and studying lung mechanics of lungs with LAM that have been explanted at the time of lung transplantation. Additionally, Dr Jaklitsch's commitment to the lung transplant program at Brigham and Women's Hospital places him in a role to be clinically involved in the surgical treatment of LAM patients.

## Dr. Vera Krymskaya krymskay@mail.med.upenn.edu

Dr. Krymskaya received her PhD from the Department of Biophysics at the Moscow State University after completing pre-doctoral training at the Institute of Biophysics of the Russian Academy of Sciences. She completed her post-doctoral training in signal transduction at the Cardiology Research Center of the Russian

Academy of Sciences, and at the Department of Medicine at the University of Pennsylvania. In 2001, Dr. Krymskaya joined the faculty at the Pulmonary, Allergy, and Critical Care Division at the University of Pennsylvania.

Dr. Krymskaya's laboratory is investigating signaling mechanisms of smooth muscle cell proliferation and migration as it relates to the pathobiology of lymphangioleiomyomatosis (LAM), pulmonary arterial hypertension (PAH) and asthma. Dr. Krymskaya's group identified the function of the tumor suppressor gene tuberous sclerosis complex 2 (TSC2), a susceptibility factor for LAM, as a negative regulator of S6K1. She demonstrated that in primary human LAM cells mutations of TSC2 leads to the constitutive activation of S6K1 and abnormal LAM cell proliferation. Dr. Krymskaya has also advanced translational LAM research by demonstrating that rapamycin inhibits LAM cell proliferation. These results identified rapamycin as a promising therapeutic strategy for LAM patients, and paved the way for a rapamycin clinical trail at the Children's Hospital Medical Center in Cincinnati. For this achievement Dr. Krymskaya has honored by The Science Advancement Award from The LAM Foundation.

### Dr. David Kwiatkowski

dk@rics.bwh.harvard.edu

Dr. Kwiatkowski received a BSc from Caltech and his PhD from MIT, both in Mathematics, and then his MD from Columbia University in 1979. After training in Medicine and Hematology-Oncology at Massachusetts General Hospital, he has pursued laboratory investigation as a major activity for the past 20 years. His work has focused on TSC for the past 12 years, with major accomplishments in identification of the TSC1 gene, development of molecular genetic testing for TSC, analysis of genotype-phenotype relationships in TSC, development of TSC/ LAM mouse models, and analysis of signaling events and pathogenesis in TSC tumorigenesis in both mice and patients. He is currently an Professor of Medicine at Harvard Medical School, and a Senior Physician at Brigham and Women's Hospital and the Dana Farber Cancer Institute.

### Dr. Robert Langer

rlanger@mit.edu

Dr. Langer received his Bachelor's Degree from Cornell University in 1970 and his Sc.D. from the Massachusetts Institute of Technology in 1974, both in Chemical Engineering. Professor Langer completed a post-doctoral fellowship in the Folkman Lab at Harvard Medical School/Children's Hospital and joined the MIT faculty in 1977. Professor Langer has done pioneering work in the use of biomaterials for tissue engineering and drug delivery, most recently applying nanotechnology to cancer for developing novel targeted strategies for cancer therapy. Professor Langer has written over 840 articles and has over 500 issued or pending patents worldwide. Dr. Langer's patents have been licensed or sublicensed to over 100 pharmaceutical, chemical, biotechnology and medical device companies; a number of these companies were launched on the basis of these patent licenses. He served as a member of the United States Food and Drug Administration's SCIENCE Board, the FDA's highest advisory board, from

1995 – 2002 and as its Chairman from 1999-2002. Professor Langer is one of 14 Institute Professors at MIT and is one of very few people ever elected to all three United States National Academies and the youngest in history (at age 43) to ever receive this distinction.

### Dr. Sten Lindahl

sten.lindahl@karolinska.se

Dr. Lindahl has been Professor at Karolinska Insitutet since 1990. He has been Director of Research and Education at Karolinska University Hospital in Stockholm, Sweden since 2001.

Dr. Lindahl graduated from the Medical School at the University of Lund, Sweden in 1972.He was board certified as a Pediatrician and Anesthesiologist/intensivist in 1981. He received his PhD from the University of Lund in 1977. From 1986 to 1988 Dr. Lindahl was a Consultant at the Mayo Clinic in Rochester Minnesota, USA. He returned to Lund as a Pediatric anesthesiologist/intensivist in 1989.

Dr. Lindahl was appointed Professor in Anesthesiology and Intensive Care Medicine at Karolinska Insitutet, Stockholm, Sweden in 1990 and from 1990 to 2001 also served as clinical chair of Anesthesiology and Intensive Care Medicine at Karolinska Hospital. From 1993 to 2000 he also served as academic chair, Department of Surgical Sciences, Karolinska Institutet. Since 1996, Dr. Lindahl has been a permanent member of the Nobel Assembly for the Nobel Prize in Physiology or Medicine. He served as vice chair from 1999-2000 and chair from 2001-2002 of the Nobel Committee. Dr. Lindahl is currently still a member of the Nobel Committee and from 2006 also a member of the Board of Trustees of the Nobel Foundation.

### Dr. Frank McCormack

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Dr. McCormack is Professor and Director of the Division of Pulmonary and Critical Care Medicine at the University of Cincinnati. He received his training in Internal Medicine at the University of Michigan and completed his Pulmonary and Critical Care Medicine Fellowship at the University of Colorado. He has an active NIH and VA Merit funded research program focused on the role of the alveolar epithelium in innate immunity and pulmonary fibrosis. His clinical interest is pulmonary fibrosis, especially as it relates to genetic lung disorders such as lymphangioleiomyomatosis. He co-directs the NCRR funded Rare Lung Disease Consortium. He has published approximately 80 peer reviewed papers, reviews and textbook chapters. He has been the Scientific Director of the Lymphangioleiomyomatosis Foundation since it was founded in 1995. Dr. McCormack is a Career Investigator of the American Lung Association and a member of the American Society for Clinical Investigation.

**Dr. Marsha Moses** Marsha.Moses@childrens.harvard.edu

Dr. Moses received a PhD from Boston University and completed a National Institutes of Health postdoctoral fellowship at Children's Hospital and MIT. She is the recipient of a number of NIH and foundation grants. Her awards and honors include the Cancer Research Foundation Award, American Cancer Society Research Award, the CaPCURE Research Award and the Science Scholar Fellowship Award, from The Mary Ingraham Bunting Institute of Radcliffe College. She is currently the Chair of the Cell Structure and Metastasis Peer Review Committee of the American Cancer Society. The Moses Lab has had a long-standing interest in identifying and characterizing the biochemical and molecular mechanisms underlying the regulation of tumor progression, from the angiogenic switch through metastasis. Dr. Moses and her group have discovered five different angiogenesis inhibitors, three of which are in clinical development for use against a variety of cancers. Significant efforts are now underway in the lab to identify the genes and proteins that they encode, that are responsible for the ''angiogenic switch". This critical checkpoint, during which time a tiny benign, avascular tumor acquires the vascular phenotype, is a prerequisite for subsequent tumor growth and progression.

The Moses Lab has recently identified and validated a number of genes which are differentially expressed during the angiogenic switch through metastasis. Dr. Moses and her group have discovered five different angiogenesis inhibitors, three of which are in clinical development for use against a variety of cancers. Significant efforts are now underway in the lab to identify the genes and proteins that they encode, that are responsible for the ''angiogenic switch". This critical checkpoint, during which time a tiny benign, avascular tumor acquires the vascular phenotype, is a prerequisite for subsequent tumor growth and progression. The Moses Lab has recently identified and validated a number of genes which are differentially expressed during the angiogenic switch and is currently developing molecular and biochemical interventions to prevent the switch from occurring by targeting some of these genes. In addition, the Moses Lab has, as part of their long term Urinary Proteomics Initiative, developed a number of sensitive and specific noninvasive urine tests for different cancers.These cancer tests are based on the lab's work focused on the detection of biomarker proteins purified from the urine of cancer patients.A number of these urine tests are currently in clinical testing as potential cancer diagnostics and prognostics.

**Dr. Joel Moss** mossj@nhlbi.nih.gov

Dr. Moss is Chief of the Pulmonary-Critical Care Medicine Branch, National Heart, Lung, and Blood Institute at the National Institutes of Health, Bethesda, Maryland, USA. He graduated from Brandeis University in 1967, summa cum laude with Honors in chemistry. In 1972, he received M.D. and Ph.D. degrees from New York University School of Medicine, with his dissertation on the regulation of lipid synthesis in the Department of Biochemistry under the mentorship of Dr. M. Daniel Lane. Following an internship and residency in medicine at the Johns

Hopkins Hospital, he completed post-doctoral and pulmonary fellowships in the National Heart, Lung, and Blood Institute (NHLBI) at the National Institutes of Health. Dr. Moss has coauthored over 500 scientific papers on basic and clinical research, edited or co-authored several books (including one on lymphangioleiomyomatosis [LAM]),and is a co-inventor of biotechnology patents. Dr. Moss is active in basic and clinical research; he has been a member of the NHLBI Institutional Review Board since 1988 (Chair since 1995) and is coauthor of a book on ethical considerations in clinical research. Dr. Moss has received multiple awards, including the Passano Foundation Young Investigator Award in 1981, the AFCR Young Investigator Award in 1987, and the LAM Foundation Award, 1999. Dr. Moss is a member of the American Society for Biochemistry and Molecular Biology, Association of American Physicians, American Thoracic Society and the American Society for Clinical Investigation (ASCI). He has been an ASCI Councillor and Vice President.

His clinical research is focused on destructive lung disease (e.g. LAM), with primary emphasis on the roles of infection/inflammation and susceptibility/ modifier genes on disease progression and severity. His LAM research centers on the abnormal smooth muscle-like cells (LAM cells) that proliferate in the lungs, lymphatics, and kidney, and are responsible for cystic lung destruction and abnormalities in the lymphatic system. Studies on a large cohort of LAM patients followed at the NIH have helped define the natural history of the disease, in particular, factors that are associated with disease progression. Additional, long-term basic research interests include guanine nucleotide-binding proteins, such as ADP-ribosylation factors (ARFs) and post-translational modification of proteins by ADP-ribosylation.

### Dr. David Sabatini

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David Sabatini is an Associate Member of the Whitehead Institute for Biomedical Research, Broad Institute, and MIT Center for Cancer Research as well as an Assistant Professor of Biology at the Massachusetts Institute of Technology. David is also a founding member of The RNAi Consortium of labs in the Boston area that is developing and using a genome-scale RNA interference (RNAi) library targeting human and mouse genes.

David and his lab, located at the Whitehead Institute, study the basic mechanisms that regulate cell growth, the process whereby cells and organisms accumulate mass and increase in size. The pathways that regulate growth are often deranged in human diseases, such as diabetes and cancer. His current focus is on a cellular system called the Target of Rapamycin (TOR) pathway, a major regulator of growth in many eukaryotic species. In addition to his work on growth control, David is developing and applying new technologies that facilitate the analysis of gene function in mammalian cells. He has developed 'cell-based microarrays' that allow us to look at the cellular effects of perturbing the activity of thousands of genes in parallel. His long-term goals are to identify and characterize these mechanisms and to understand their roles in the normal and diseased physiology of mammals.

David received his B.S. from Brown University magna cum laude and his M.D./Ph.D. from Johns Hopkins University in 1997. Later this same year, David was appointed a Fellow at the Whitehead Institute for Biomedical Research. This was followed in 2002 by a dual appointment to Associate Member at the Whitehead and Assistant Professor of Biology at the Massachusetts Institute of Technology.

Awarded the prestigious W. M. Keck Foundation Distinguished Young Scholar in Medical Research Fellowship in 2005, David has been the recipient of many awards and honors. He was named one of the "Worlds Top 100 Innovators in 2003" by Technology Review and his patented cell microarray process and identification of the component parts of cell growth protein implicated in diseases such as cancer have resulted in numerous publications in refereed journals. David was named both a Ross and Pew Scholar in 2003 and awarded a Rita Allen Fellowship in 2004.

### Dr. Cheryl Walker

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Dr. Cheryl Lyn Walker is currently the Ruth and Walter Sterling Professor of Carcinogenesis in the Department of Carcinogenesis of the UT MD Anderson Cancer Center. She received her Ph.D. in Cell Biology in 1984 from the University of Texas Southwestern Medical School in Dallas. Prior to joining the faculty at MD Anderson, Dr. Walker was a scientist at the Chemical Industry Institute of Toxicology and did post-doctoral research at the National Institutes of Health. She has been a Professor in the Department of Carcinogenesis for over 10 years and also holds joint academic appointments in the College of Pharmacy at the University of Texas at Austin and in the College of Veterinary Medicine at Texas A&M University. She also directs the Molecular Genetics and Environmental Carcinogenesis Research Core of the National Institute for Environmental Health Sciences Center for Research on Environmental Disease.

Dr. Walker's research interests are aimed at understanding the molecular basis of disease. Her research is focused on the role tumor suppressor genes in cancer and proliferative smooth muscle diseases such as uterine leiomyoma and lymphangioleiomyomatosis (LAM). Her laboratory is actively investigating how signal transduction pathways, such as the PI3K pathway, become perturbed as a result of loss of function of tumor suppressor genes involved in kidney and uterine cancer including TSC-2, VHL and PTEN. She has developed several unique animal models for studying the molecular defects that contribute to the development of uterine and kidney cancer, which are widely used for preclinical studies to identify new therapeutic interventions for these diseases. Dr. Walker also has research interests in the area of mechanisms by which chemicals in the environment cause cancer, and has recently identified developmental programming as a new type of gene-environment interaction that can influence cancer risk.

Dr. Walker serves on the editorial boards of several of the leading journals in the areas of cancer research, carcinogenesis and environmental health. These include *Molecular Cancer Research* (for which she is a Senior Editor), *Environmental*

*Health Perspectives, Toxicological Sciences, Cancer Research,* and *Molecular Carcinogenesis*. She has published over 100 primary research papers and review articles in the area of cancer and environmental health, in addition to numerous book chapters and monographs on these topics.

### Dr. Vicky Whittemore

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Vicky Holets Whittemore, Ph.D. is Vice President and Director of Science for the Tuberous Sclerosis Alliance in Silver Spring, MD. She has been associated with the organization since her nephew was diagnosed with Tuberous Sclerosis Complex (TSC) in 1985. Vicky and her son, Andrew, were both diagnosed with TSC in 1990. She served on the Board of Directors from 1987-1993, serving as Chairman of the Board from 1988 – 1992, and Chair of the Research Committee from 1992-1993. She joined the staff of the TS Alliance in 1994.

Dr. Whittemore received a B.S. in Zoology from Iowa State University in 1977 and a Ph.D. in Anatomy from the University of Minnesota in 1982. She completed a postdoctoral fellowship at the University of California-Irvine in 1984, and a Fogarty Fellowship at the Karolinska Institute in 1986 before joining the faculty at the University of Miami School of Medicine in the Departments or Neurological Surgery and Cell Biology & Anatomy, working in the Miami Project to Cure Paralysis. In 1994, she left the position of Associate Professor at the University of Miami to join the staff of the Tuberous Sclerosis Alliance, where she has worked to build the interest and support of TSC research. She is the co-editor with Manuel Gomez and Julian Sampson of the third edition of Tuberous Sclerosis Complex and the author of more than 30 peer-reviewed publications. She currently serves on the Review Committee for the Collaboration, Education, Testing and Translation (CETT) Program through the Office of Rare Disorders at the National Institutes of Health, and serves on the Board of Directors of the National Coalition of Health Care Professionals in Genetics (NCHPEG).

### Dr. Amy Farber

amy_farber@hms.harvard.edu

Amy Farber is trained as a social scientist focused on the study of law, medicine and society. She is a member of the Department of Social Medicine at Harvard Medical School (HMS) and Executive Director of the LAM Treatment Alliance.

Dr. Farber received her BA in political science from U.C. Berkeley and her PhD from Harvard University. Following her doctorate she received additional training in law at Northeastern University and medical ethics at Harvard University. Her doctoral work focused on physician decision-making within American and South African healthcare systems and was sponsored by the National Institutes of Health. Throughout her career, Dr. Farber has been involved in advocacy around to address health disparities and access to basic healthcare for the poor and those with HIV/AIDS in the US and abroad. Dr. Farber is an active member of the Institutional Review Board of Brigham and Woman's Hospital and the Massachusetts General Hospital.

Since her diagnosis with LAM in April 2005, with the support of researchers, clinicians, loved ones, colleagues and friends, she has dedicated herself to research advocacy and fundraising to find a treatment for Lymphangioleiomyomatosis or LAM in the fastest time possible. Dr. Farber is currently founder and Executive Director of the LAM Treatment Alliance, a 501(c)3 non-profit exclusively dedicated to accelerating the pace of LAM treatment research.

**Dr. Michael Nurok** mnurok@partners.org

Michael Nurok is a member of the Department of Anaesthesia and the Department of Social Medicine at Harvard Medical School. His area of specialty is Cardio-thoracic care. Dr. Nurok graduated medical school from the University of Cape Town in South Africa in 1997 after which he performed doctoral research at the Ecole des Hautes Etudes en Sciences Sociales and the Intensive Care service of the University of Paris, Hopital Necker Enfants Malades in Paris, France as recipient of a Bourse Présidentielle d'Excellence from the French Ministry of Foreign Affairs. His research focuses on the social, ethical, and philosophical implications of treating critically ill patients with particular emphasis on cultural considerations. He is an active member of the Brigham and Women's Hospital Ethics Committee and the Partners (Massachusetts General and Brigham and Women's Hospitals) Institutional Review Board. Dr. Nurok is a founding member of The LAM Treatment Alliance and actively serves on the Board of Directors.