

2005 LAM SUMMIT PARTICIPANTS

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Dr. Joe Avruch avruch@molbio.mgh.harvard.edu

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 signalling 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. Myles Brown myles_brown@dfci.harvard.edu

Dr. Brown received his MD from Johns Hopkins University in 1982, followed by an internal medicine residency at Brigham and Women's Hospital and a fellowship in medical oncology at Dana Farber Cancer Institute. He conducted postdoctoral research at the Massachusetts Institute of Technology from 1987 to 1990. In 1989, he joined the staff of DFCI, where his molecular studies focus on the role of the estrogen receptor in breast cancer and the androgen receptor in prostate cancer. Estrogen plays a critical role in the development of the normal breast and in breast cancer. The biochemical mechanisms underlying these processes, however, remain largely unknown. The overall aim of current research is to build on recent advances in the molecular understanding of estrogen receptor (ER) action to better define the role played by estrogen in the normal breast and in breast cancer.

During the past few years, several laboratories, including the Brown Lab, have identified many important coregulatory molecules that play a central role in mediating the transcriptional activity of ER. The Brown Lab's current hypothesis is that the differential expression of these molecules accounts in part for the tissue-specific activity of selective ER modulators, such as tamoxifen and raloxifene. In addition, the gene encoding one of these ER coactivators, AIB1, was cloned as a gene amplified in breast cancer cells, raising the possibility that altered expression of an ER coactivator may play a central role in estrogen-stimulated breast cancer growth. Androgen receptor (AR) plays an analogous role in the prostate. Recent work in the Brown Lab is aimed at extending studies of the importance of coregulators to prostate cancer.

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 till 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 throughput optimization of these conjugates in vitro.

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.

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. Frank McCormack frank.mccormack@uc.edu

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 lymphangiomyomatosis. He co-directs the NCCR 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 Lymphangiomyomatosis 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 angiogenesis

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during 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 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 non-invasive 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 lymphangioliomyomatosis [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.