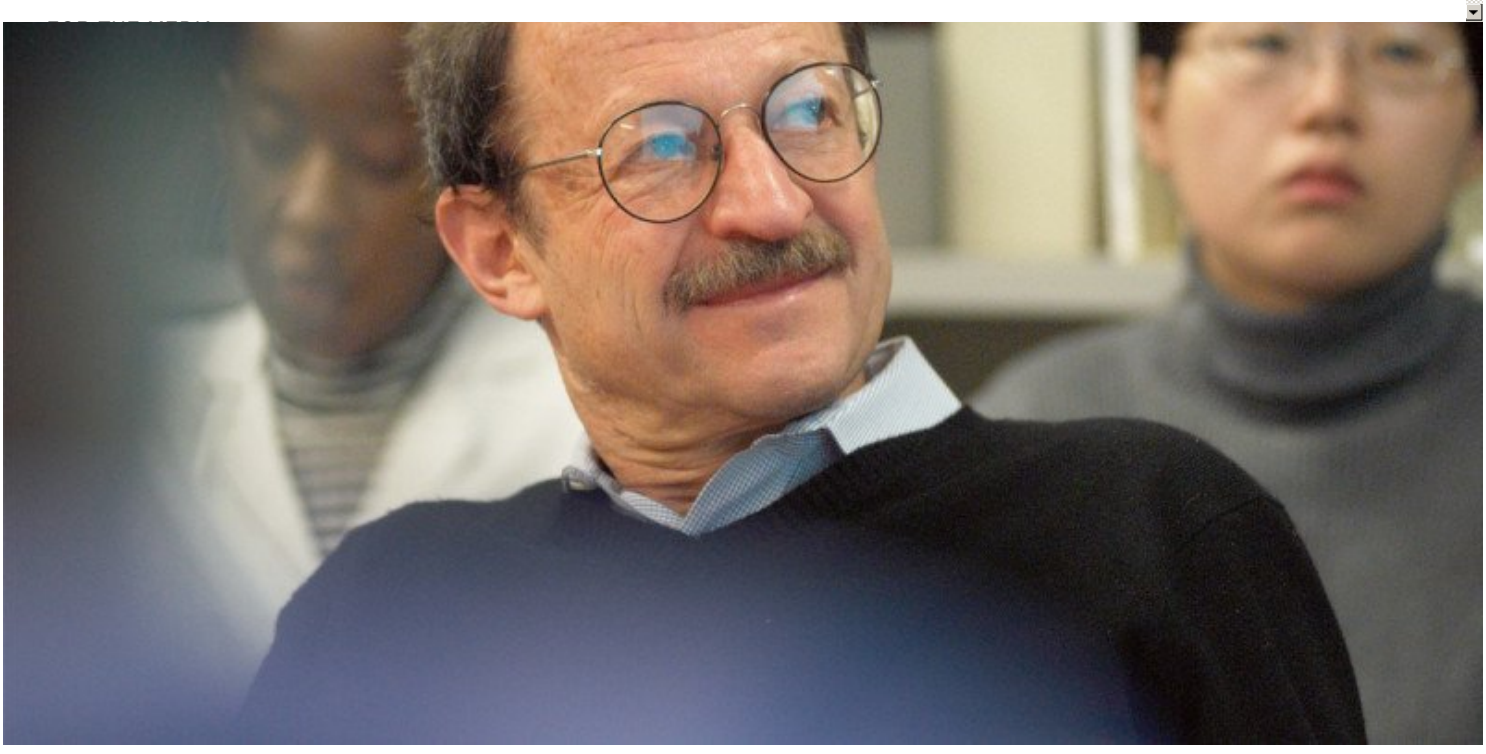


Three young investigators who have taken significant steps toward advancing the understanding of cancer will be the recipients of the 2009 Paul Marks Prize for Cancer Research, a prize awarded biennially since 2001 to scientists under the age of forty-six by Memorial Sloan Kettering Cancer Center.

> Each of the researchers we are honoring has already built a body of work that has advanced the field of cancer research.
>
> Memorial Sloan Kettering Cancer Center President Harold Varmus

This year's winners are Arul M. Chinnaiyan at the University of Michigan, who discovered chromosome rearrangements that lead to prostate cancer; Matthew L. Meyerson at the Dana Farber Cancer Institute, who discovered mutations in lung cancer cells; and David M. Sabatini at the Whitehead Institute, who discovered a pathway that helps regulate the growth of cancer cells.

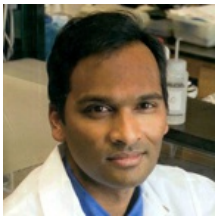
"Each of the researchers we are honoring has already built a body of work that has advanced the field of cancer research," said Memorial Sloan Kettering Cancer Center President Harold Varmus when announcing the winners.

The winners were selected by a committee made up of prominent members of the cancer research community and chaired by Titia de Lange, a professor at The Rockefeller University and a former Marks Prize winner. "Although all three winners are focused primarily on working in the laboratory, the translational aspect of their discoveries has already begun to influence the treatments that cancer patients receive," Dr. de Lange said.

The prize is named for Paul A. Marks, President Emeritus of Memorial Sloan Kettering, who led the Center for 19 years, from 1980 to 1999. It was created by Memorial Sloan Kettering's Boards of Overseers and Managers at the time of Dr. Marks' retirement to honor his many contributions as a distinguished scientist, teacher, and leader.

This year's winners will each receive an award of $50,000 and will speak about their work at a public symposium held at Memorial Sloan Kettering's Rockefeller Research Laboratories Auditorium on Thursday, December 3, 2009.

Arul Chinnaiyan



Arul M. Chinnaiyan

Dr. Chinnaiyan is S. P. Hicks Endowed Professor of Pathology and a professor in the Department of Pathology and Urology at the University of Michigan Medical Center. He is also a Howard Hughes Medical Institute (HHMI) investigator and an American Cancer Society Research Professor. His most important discovery to date is the finding that more than half of all prostate cancers are the result of a gene fusion known as *TMPRSS2-ETS*. Oncogenic gene fusions result when pieces of chromosomes break apart and reconnect in such a way that they encode for a cancer-causing protein.

Dr. Chinnaiyan made the discovery while studying the genetic changes in a large collection of prostate tumor samples from patients. "At the time, gene fusions were thought to occur only in blood cancers such as leukemias and lymphomas, but not in solid tumors," Dr. Chinnaiyan explained. (The best-known oncogenic fusion gene was *BCR-ABL*, the cause of chronic myeloid leukemia, which is the target of the drug imatinib [Gleevec®].) "We were not looking for these types of genes, so the finding was serendipitous."

Today researchers believe that the *TMPRSS2-ETS* fusion drives the formation of many prostate cancers, but so far they have been unable to target it and block its activity. Finding small-molecule drugs to inhibit cancer growth is now an important focus of Dr. Chinnaiyan's work. He is also initiating new research projects to look for cancer-causing gene fusions in other solid tumors, including breast cancer.

Dr. Chinnaiyan has been active in the wider research community as well, as co-creator of the Oncomine Research Platform, an online database containing cancer gene expression analysis information for academic researchers. He is also a board-certified pathologist and spends part of his time developing and implementing new molecular tests for the diagnosis and prognosis of cancer.

"Arul's discovery of this unique fusion in prostate cancer has opened up numerous opportunities for the development of novel diagnostic and therapeutic approaches," said David Ginsburg, a professor at the University of Michigan Medical School and an HHMI investigator, who nominated Dr. Chinnaiyan for the award. "There are no more than a handful of physician-scientist cancer researchers at this phase of their careers who could even be compared to his level of research accomplishment and promise for the future."

Dr. Chinnaiyan received his MD degree and a PhD degree in pathology from the University of Michigan Medical Center.

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Matthew Meyerson

Dr. Meyerson is Director of the Center for Cancer Genome Discovery at Dana-Farber Cancer Institute, a professor of pathology at Harvard Medical School, and a senior associate member of the Broad Institute of MIT and Harvard. He is a leader in the field of cancer genomics, especially in the area of lung cancer. A major focus for his work has been determining the role that mutations in the epidermal growth factor receptor (*EGFR*) gene play in lung cancer, especially its response to the targeted therapies erlotinib (Tarceva®) and gefitinib (Iressa®).

In 2004, Dr. Meyerson's team was one of three groups to report that *EGFR* mutations in tumor cells were linked to patients'

responses to gefitinib. His group also found that these mutations were more common in the lung tumors of nonsmoking women and people of East Asian descent. Molecular testing for *EGFR* mutations is now a standard part of lung cancer diagnosis at most hospitals, and the test's results determine which therapies individual patients will receive.

Matthew L. Meyerson

Dr. Meyerson has been active in the study of other cancer-related genes, including *JAK2*, which is a factor in some types of leukemia; *ALK,* which is activated in lung cancer and neuroblastoma; and *FGFR2,* which is activated in endometrial cancer. His laboratory has made other discoveries regarding the lung adenocarcinoma genome, including activation of the *NKX2-1* and *TERT* genes. He is also a leader in the Cancer Genome Atlas (TCGA) project, which was initiated by the National Cancer Institute in 2006 to improve the understanding of the molecular basis of cancer. Last fall, he was one of two lead authors of TCGA's first major paper, a comprehensive characterization of the genes and pathways that are important in glioblastoma brain tumors. Finally, Dr. Meyerson's laboratory has developed a new approach to find cancer-causing microbes.

"With the ongoing revolution in genome technology, we need complete characterization of the cancer genome and all the genetic alterations that cause cancer," Dr. Meyerson said. "We're at a point where it's possible, and this goal is very much in sight."

"Matthew's findings have changed the treatment of adenocarcinomas of the lung," said James D. Griffin, Chairman of the Department of Medical Oncology at Dana-Farber, who nominated Dr. Meyerson for the prize. "This work and his ongoing work characterizing other genomic changes in lung cancers have placed him at the forefront of developing personalized therapy for patients with this deadly disease."

Dr. Meyerson received his MD degree from Harvard Medical School and his PhD degree from Harvard University.

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David Sabatini

Dr. Sabatini is an associate professor of biology at the Massachusetts Institute of Technology and a member of the Whitehead Institute for Biomedical Research. He is also an HHMI investigator. While he was still in graduate school, Dr. Sabatini identified the mTOR protein kinase, a key protein in regulating cell growth, proliferation, and survival. He has continued to study the protein and its signaling pathway for much of his career, characterizing other related proteins and helping to determine how the mTOR pathway relates to cancer.

David M. Sabatini

"All cells, including cancer cells, need to generate mass and ramp up production of all of their components in order to grow and divide," Dr. Sabatini explained. "We now know that mTOR is the master regulator of that. The mTOR pathway can sense an outside or internal stimulus related to growth, and the pathway has to be turned on for the cell to grow."

Dr. Sabatini discovered mTOR when he was studying the small molecule rapamycin, a compound that was known to have immunosuppressive and anticancer properties. (mTOR stands for mammalian target of rapamycin.) Two derivatives of rapamycin, temsirolimus (Torisel®) and everolimus (Afinitor®), both of which target the mTOR pathway, are now approved for the treatment of kidney cancer.

His work with mTOR required him to develop many new technologies that are now being used in laboratories around the world to study signaling pathways, including cell-based microarrays and tools related to RNA interference (RNAi). He has been a leader in the RNAi Consortium, a multi-institutional effort to generate a library of RNAi reagents targeting every human gene.

Because the mTOR pathway is regulated by nutrients, much of Dr. Sabatini's current work is focused on how metabolism, including the restriction of calories in the diet, affects cancer. He is developing mouse models with gene mutations that mimic the effects of extremely low-calorie diets by restricting the mTOR pathway.

"David seizes opportunities, embraces collaborations, and is not daunted by the complexity of cellular regulation of metabolism," said Robert A. Weinberg, a member of the Whitehead Institute and Director of the MIT Ludwig Center for Cancer Research, who nominated Dr. Sabatini. "I strongly believe that he is on the trajectory to becoming one of the most influential scientists in the field of cellular energy metabolism and its multiple intersections with cancer research."

Dr. Sabatini earned his MD and PhD degrees from the Johns Hopkins University School of Medicine.

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