SPRING 2009 DEAN'S UĂRTERLY Mount Sinai MOUNT SINA SCHOOL OF

ACCELERATING SCIENCE – ADVANCING MEDICINE

Sharpening Our Focus on Cancer

In 1971, President Nixon famously launched a war on cancer, challenging scientists to have a cure by our nation's bicentennial. We now know there will be no single cure for cancer. Rather, triumph over cancer will come from a broad range of treatments for the hundreds of diseases we call cancer.

With this new understanding, Mount Sinai is building a world-class cancer care center to unite research in cancer biology, developmental and molecular biology, stem cells, and pharmacology with multidisciplinary and comprehensive patient care under one roof and with one purpose-to advance human health.

This new center builds on our tradition of innovation for the treatment of liver, prostate, breast, head and neck, gynecological, and hematological malignancies. Mount Sinai discovered that a drug used to treat advanced kidney cancer helped patients live 44 percent longer; our surgeons are increasingly using robotic procedures to remove malignancies, significantly reducing hospital stays and recovery time; our physicians and researchers are also examining how to use the immune system to treat cancer.

One of the nation's leading immunologists and cancer specialists, Steven J. Burakoff, MD, joined Mount Sinai in 2007 to lead

a new era of cancer research and care. Mount Sinai Trustee James S. Tisch and his wife, Merryl H. Tisch, also committed \$40 million to establish The Tisch Cancer Institute, and we continue to recruit pioneering scientists and physicians to advance our programs.

Cancer touches everyone. Like many Americans, our new president has lost a loved one to cancer, and he has vowed to invest federal dollars in research and programs to help cancer patients and their families. President Barack Obama also strongly supports education about cancer prevention and management, and increased patient access to clinical trials.

This is a historic time in biomedical science-breakthroughs in genomics, protein chemistry, and molecular biology could potentially prevent disease and prolong life for cancer patients in ways we can only begin to imagine.



Dennis S. Charney, MD Anne and Joel Ehrenkranz Dean, Mount Sinai School of Medicine Executive Vice President for Academic Affairs, The Mount Sinai Medical Center

To learn more, visit www.mountsinai.org /Charney

DIANE E. MEIER, MD, NAMED A MacARTHUR FELLOW

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Diane E. Meier, MD, a pioneer in the field of palliative care, was named a 2008 MacArthur Fellow by the MacArthur Foundation. The MacArthur Fellowships, known as "genius grants," are given once a year to 25 US citizens who exemplify leadership and creativity. Each Fellow receives an unrestricted \$500,000 grant to support their work over the next five years.

Dr. Meier, Director of the Center to Advance Palliative Care and of the Hertzberg Palliative Care Institute, and the Catherine Gaisman Professor of Medical Ethics,

has revolutionized modern medicine by shaping the discipline of palliative care and bringing the issues of quality of care for the chronically and seriously ill, and their families, into the national spotlight. Her leadership of the Center to Advance Palliative Care, a national organization devoted to increasing patient access to quality palliative care, has positioned Mount Sinai as a leader in this field.

Palliative care is the medical subspecialty focused on pain relief and other symptoms of serious illness, helping patients make informed decisions to better manage their illness.

Medical Milestones

REVOLUTIONIZING SURGERY



The surgical team looks on as

Dr. Genden uses a robot to

remove the patient's tongue

tumor. Multiple robotic arms

are positioned over the pa-

Eric M. Genden, MD

Without touching the patient's head or mouth, Eric M. Genden, MD, Director of the Head and Neck Cancer Center and Chair of the Department of Otolaryngology, removed a tongue tumor from Gloria Deciucies, a 72-yearold nurse from Staten Island.

The surgery took less than two hours, and Ms. Deciucies went home the next day. The procedure is called Trans Oral Robotic Surgery (TORS), an experimental operation that involves removing benign and malignant tumors from the upper aerodigestive tract, which includes the tongue, voice box, and upper esophagus.

Mount Sinai is one of only three hospitals nationwide that offer TORS, which is still pending FDA approval. Dr. Genden performed the surgery robotically, sitting at a computer console using the da Vinci[®] Surgical System, which has been used at Mount Sinai to treat other conditions, including prostate cancer and uterine fibroids.

Traditional invasive surgery would have taken 12 to 15 hours, involved cutting the patient's lip and jaw to gain

access to the tumor, and required a two-week hospitalization. After surgery, Ms. Deciucies might have needed a feeding tube and suffered serious complications, such as difficulty swallowing. Instead, Ms. Decuicies was able to eat after the surgery and could be back at work in 10 days.

Dr. Genden has been leading an investigator-initiated clinical trial, with nearly 50 patients enrolled, examining robotic surgery for head and neck tumor removal with his colleagues. "The results have been so encouraging that the FDA is interested in having us submit our data as part of its approval process," Dr. Genden says.

Other potential uses for TORS include treatment of sleep apnea and skull-base surgery. Dr. Genden's goal is to make robotic surgery a viable option for the treatment of head and neck tumors that are difficult for surgeons to reach. "If I can use a procedure that takes less time, decreases complications, and opens up the operating room for other surgeries, it benefits both patients and the hospital," says Dr. Genden.

To learn more, visit www.mountsinai.org/Genden



DIANE E. MEIER, MD, NAMED A MACARTHUR FELLOW (CONTINUED)



Diane E. Meier, MD

Today, about 1,500 hospitals now have palliative care teams, up from fewer than 100 just five years ago.

In 1982, Mount Sinai became the first American medical school to open a geriatrics department, the Brookdale Department of Geriatrics and Adult Development. Dr. Meier joined the Mount Sinai faculty the following year and spent the next 25 years working to improve the care of seriously and chronically ill patients. Dr. Meier's research has examined how palliative care programs improve symptoms and satisfaction with care for both patients and their families, and how hospitals can best integrate this model into modern medicine.

In 1998, Dr. Meier established the Hertzberg Palliative Care Institute at Mount Sinai, a model program that assists patients and families in navigating the complexities of illness and devises strategies for managing pain and other symptoms.

Dr. Meier also received the 2009

Clinical Excellence Award at the Castle Connolly Medical Ltd. National Physician of the Year Awards. She is one of only three physicians to receive the award, which recognizes excellence in clinical medical practice. Currently, she is the Principal Investigator of a National Cancer Institute–funded study on the outcomes of hospital palliative care services in cancer patients.

To learn more, visit www.getpalliativecare.org and www.mountsinai.org/Meier.

INVESTIGATING TRANSPLANT REJECTION

Peter S. Heeger, MD, Director of the Transplant Immunology Research Program and Professor of Medicine in the Division of Nephrology, was awarded a five-year, \$2 million National Institutes of Health (NIH) study to investigate the mechanisms that underlie the rejection of transplanted organs.

A long-term goal of the project is to use information obtained from animal models to design therapies that prolong transplant survival in patients. Fifty percent of kidney transplant patients will experience organ failure within ten years. Heart transplants fail within five to seven years, and lung transplants have even shorter lives. Late organ loss can be caused by toxic side effects from medications, undertreated immune reactions, infections, and recurrent disease. Dr. Heeger's studies focus on understanding a certain component of the immune response, called complement, and how it contributes to the long-term injury of the transplanted organ. Dr. Heeger and his colleagues hope to design new treatments to block complement activity and potentially lengthen transplanted organ survival. Dr. Heeger also runs a multicenter NIH-supported grant testing the utility of biomarkers that could predict transplant rejection before it is clinically evident.

"Findings from these two studies," says Dr. Heeger, "will hopefully permit transplant physicians to individualize treatments for each patient so we can minimize side effects, prolong graft survival, and improve patient health."



Peter S. Heeger, MD

To learn more, visit www.mountsinai.org/TRP and www.mountsinai.org/Heeger.

PICTURE THIS

The Translational and Molecular Imaging Institute has received a \$2 million high-end instrumentation grant from the National Institutes



Zahi A. Fayad, PhD

of Health National Center for Research Resources. The grant will be used to purchase a state-of-theart micro MRI scanner that will help researchers better understand disease pathology and molecular mechanisms in vivo.

"This high-performance, smallanimal magnetic resonance imaging system allows us to study the fundamental mechanisms of biological function, ultimately leading to new advances and treatments for diseases," says Zahi A. Fayad, PhD, Interim Director of the Translational and Molecular Imaging Institute and Professor in the Departments of Radiology and Medicine (Cardiology).

Called a 7 Tesla large-bore MRI, the new scanner allows for the imaging of live animals or human specimens up to 16 centimeters in diameter. It is also equipped with coils and anesthesia accessories. The unique imaging instrument is also compatible with the clinical scanners currently used at The Mount Sinai Hospital, so it will enhance and accelerate the ability to share critical information from the laboratory with physicians and patients.

"From bench to bedside, protocols and molecular technologies developed on this system can immediately be transported to current clinical scanners for human use," explains Cheuk Ying Tang, PhD, Principal Investigator on this project, Director of the In-Vivo Molecular Imaging Shared Facility, and Assistant Professor of Radiology and Psychiatry.

To learn more, visit www.mountsinai.org/TMII.

Young Pioneers

UNDERSTANDING THE KLF6 GENE

As a medical student at Mount Sinai, Goutham Narla, MD, PhD, Assistant Professor of Medicine and of Genetics and



Goutham Narla, MD, PhD

Genomic Sciences, discovered the KLF6 gene in the laboratory of Scott L. Friedman, MD, Professor of Medicine and Chief of the Division of Liver Diseases. As a faculty member, he continues to make new discoveries about the role of KLF6 that have laid the groundwork for improving the diagnosis and treatment of malignancies like breast, prostate, and lung cancer.

The breakthrough, which was published in *Science*, is now being used by Dr. Narla for potential applications in the treatment of metastatic cancer. Dr. Narla received the Howard Hughes Medical Institute Physician-Scientist Early Career Award for his research last year.

Dr. Narla's team identified a splice variant of the KLF6 gene, known as KLF6-SV1, which causes cancerous cells to grow out of control. The group found that a small RNA molecule can inhibit this splice variant that serves as an accelerator for cancer growth and decrease tumor size in mice. These results were published in the *Journal of Clinical Investigation*.

While Dr. Narla is hopeful to move to a Phase 1 trial in patients soon, some of his discoveries can already be translated from bench to bedside. He says, "If a tumor is aggressive, we should treat it with chemotherapy and follow it more closely. If it isn't, we would spare patients the side effects of these drugs. KLF6-SV1 helps tell us that."

To learn more, visit www.mountsinai.org/Narla.



Vivek Y. Reddy, MD

VIVEK Y. REDDY, MD

Vivek Y. Reddy, MD, one of the nation's leading cardioelectrophysiologists, joined The Mount Sinai Medical Center as Director of Electrophysiology Laboratories. Dr. Reddy leads a renowned team of physician-scientists who are developing definitive therapies for cardiac arrhythmias to obviate the need for ongoing medications.

Under Dr. Reddy's leadership, the team has conducted many breakthrough studies of novel technologies, such as the first use of a balloon cryoablation catheter to treat patients with atrial fibrillation and the first use of an endoscopic balloon ablation catheter to visually guide ablation of atrial fibrillation in patients.

As the Director of Cardiac Electrophysiology and Associate Professor of Medicine at the University of Miami, Miller School of Medicine, Dr. Reddy built a world-class cardiovascular team. Dr. Reddy also worked at Massachusetts General Hospital in Boston for seven years and most recently as Director of the Experimental Electrophysiology Lab at Massachusetts General Hospital. After earning his medical degree from the University of Michigan in Ann Arbor, Dr. Reddy completed a residency in internal medicine at Yale-New Haven Hospital in Connecticut. He then completed a clinical cardiology fellowship at the University of Chicago Hospitals in Illinois and a clinical and research cardiac electrophysiology fellowship at Massachusetts General Hospital in Boston.



Wayne K. Goodman, MD

WAYNE K. GOODMAN, MD

Wayne K. Goodman, MD, joined Mount Sinai School of Medicine as Chair of the Department of Psychiatry, where he will incorporate advances in neuroscience into the clinical care of patients and the education of trainees. He will study major neuropsychiatric disorders, bring new technologies and innovations in drug discovery, and emphasize the role of neurodevelopmental factors in the pathogenesis of psychiatric disorders.

One of the nation's leading researchers and clinicians for obsessive compulsive disorder (OCD), Dr. Goodman directed some of the most important clinical trials that led to new therapies. He developed the leading evaluation instrument for OCD and co-founded the Obsessive Compulsive Foundation. An expert psychopharmacologist, currently serving as Acting Chair of the Food and Drug Administration's Psychopharmacologic Drug Advisory Committee, he has published several hundred scientific papers and received numerous prestigious honors, including the Mysell Lecture Award from Harvard University.

Dr. Goodman served as Director of the Division of Adult Translational Research and Treatment Development at the National Institute of Mental Health from 2007 to 2009. Prior to that, he was Chairman of the Department of Psychiatry at the University of Florida (UF) College of Medicine. During that time, he received numerous federal grants, including one to study deep brain stimulation in refractory OCD. He first joined UF as a Professor in 1993.

Dr. Goodman is a native New Yorker who attended the Bronx High School of Science and graduated from Columbia University with a degree in electrical engineering. He then received his medical degree from Boston University School of Medicine and completed his residency and fellowship in psychiatry at Yale University. He joined the faculty in the Department of Psychiatry at Yale University School of Medicine, where he rose to the rank of Associate Professor.



Philippe M. Soriano, PhD

PHILIPPE M. SORIANO, PHD

Philippe M. Soriano, PhD, an expert in the genetic analysis of mouse development and cancer research, has joined Mount Sinai as Professor of Developmental and Regenerative Biology and of Oncological Sciences.

Dr. Soriano studies mouse genes to learn their functions during embryonic development and the causes, origins, and nature of cancer and other diseases. Dr. Soriano's laboratory focuses on genes implicated in signaling pathways and focuses on two main areas, growth factor signaling and cell guidance cues. His research utilizes advanced mouse molecular genetic techniques, including gene targeting and gene trapping.

His recent research has zeroed in on the postnatal activation of the PDGF pathway, which leads to phenotypes reminiscent of systemic scleroderma, a disease that affects 300,000 patients in the United States. Dr. Soriano also studies mutations in ephrin-B1, which in humans leads to craniofrontonasal syndrome (CFNS). CFNS is a peculiar X-linked syndrome characterized by body asymmetry, neurological defects, midline defects, skeletal abnormalities, and dermatological abnormalities.

Dr. Soriano has worked for the past 15 years at the Fred Hutchinson Cancer Research Center in Seattle studying the genetic mysteries in processes relevant to cancer development.

Philanthropy

\$40 MILLION DONATION ESTABLISHES CANCER INSTITUTE

Mount Sinai Trustee James S. Tisch and his wife, Merryl H. Tisch, have committed \$40 million to The Mount Sinai Medical Center to establish The Tisch Cancer Institute, a state-of-the-art, patient-oriented, comprehensive cancer care and research facility.

The Tisch Cancer Institute, which will be directed by Steven J. Burakoff, MD, Professor of Medicine and Oncological Sciences, will enhance Mount Sinai's basic science and clinical research programs as well as its programs in cancer control and prevention to develop comprehensive approaches to prevention, detection, and treatment. The Tisch Cancer Institute is one of 12 new multidisciplinary institutes that will become a model for 21st-century medicine.

The Institute will bring together highly trained clinicians across a variety of disciplines to promote seamless, integrated care from initial diagnosis through follow-up, including medical, surgical, and radiation treatments; pain management; palliative care; behavioral medicine; physical therapy; and psychosocial services. The Institute will advance translational research efforts by fostering collaboration and synergy among physicians and basic scientists so that patients receiving care will also have access to innovative clinical trials of new treatments; this will particularly benefit individuals at high risk for brain,

breast, head and neck, liver, prostate, and thoracic cancers.

The Institute will be located in the Medical Center's new translational research building, the Center for Science and Medicine, of which four floors, two for basic research and two for clinical care and clinical research, will be devoted solely to cancer. Comprising nearly half a million square feet, the Center for Science and Medicine is expected to be completed in 2011.

"Cancer is one of the most pressing health concerns of our time. It transcends geographic and socioeconomic borders and touches us all," says Mr. Tisch, a Trustee of Mount Sinai since 1988. "With The Campaign for Mount Sinai, the Medical Center is building upon its tradition of translational medicine and making a major commitment to enhancing clinical and research programs to accelerate the development of novel cancer therapeutics. Merryl and I believe this Institute will enable Mount Sinai to revolutionize how we diagnose and treat cancer, and



also set a new standard for the care of cancer patients."

Mr. Tisch is President and Chief Executive Officer of Loews Corporation, a holding company that is one of the largest diversified financial corporations in the United States. Its principal subsidiaries are CNA Financial Corporation (NYSE: CNA), Merryl H. Tisch and James S. Tisch

Boardwalk Pipeline Partners, LP (NYSE: BWP), Diamond Offshore Drilling, Inc. (NYSE: DO), HighMount Exploration & Production LLC, and Loews Hotels. Dr. Merryl H. Tisch is the Chancellor of the New York State Board of Regents.

For more information, visit www.mountsinai.org/Tisch.



LEFT TO RIGHT: Kenneth L. Davis, MD; Eva Dubin; and George Raptis, MD, MBA

DUBIN GROUNDBREAKING

Mount Sinai Hospital recently celebrated the latest addition to campus—the Eva and Glenn Dubin Breast Care Center, which will be directed by George Raptis, MD, MBA, Associate Chief for Solid Tumors in the Division of Hematology-Oncology and Associate Professor of Medicine.

The Dubin Breast Cancer Center will house a comprehensive, integrated program that brings together the best minds in breast radiology, medical oncology, surgery, radiation oncology, pathology, clinical genetics, psychosocial support, and clinical translational research to provide patients with seamless care.

The groundbreaking symbolizes this major initiative for the new Tisch Cancer Institute as it develops the clinical and research infrastructure necessary for a National Cancer Institute Cancer Center designation. It also demonstrates the determination of the Boards of Trustees and the institution's leadership to the success of cancer program development, which is a major focus of Mount Sinai's strategic plan.

For more information, visit www.mountsinai.org/BreastCancer.

Photo Essay



WATCHING CELLS TALK

These images show experiments that allow researchers to see communication within a living cell. The experiments were conducted by Susana Neves, PhD, a postdoctoral fellow.

The upper left panel shows a cell before it receives a signal from the drug adrenaline. When adrenaline communicates with the cell, it raises the levels of a messenger within the cell, seen as the orange circle (lower left panel).

This messenger activates an enzyme (lower middle panel) that goes to and stimulates proteins in the nucleus that turn on genes, shown here as green dots (lower right panel). The upper middle and right panels show the nucleus of cells before they receive signals. Thus, information flowing through this bucket brigade allows a cell to respond to drugs. Such studies are required for both drug discovery and understanding the action of known drugs.

For more information, visit www.mountsinai.org/Iyengar and www.mountsinai.org/ETI.

PHOTO: The laboratory of Ravi lyengar, PhD, Co-Director of the Experimental Therapeutics Institute and Professor and Chair of the Department of Pharmacology and Systems Therapeutics

RECALCULATING CANCER

This year, 562,340 people—more than 1,500 each day—will die from cancer in the United States, and 1.5 million will be diagnosed.

Cancer is often described by very large numbers like these. But such figures obscure that a fundamental shift in thinking has taken place in cancer research, one that needs wider understanding by the public and policy makers.



Steven J. Burakoff, MD

There is no one denominator for cancer; it is hundreds of different diseases and each must be evaluated—and treated—on its own.

One early example of this was our success in treating childhood leukemia. This condition represents a small fraction of all cancer patients—only 3,540 cases were diagnosed in the United States in 2008—but within this, the cure rate is 90 percent, up from 40 percent 25 years earlier. When the denominator includes all cancers, however, the cure rate amounts to less than a quarter of one percent.

Much of this gain against childhood leukemia came from aggressive chemotherapy, a treatment that galvanized a new beginning in cancer treatment when it was first developed 60 years ago. We are now at another watershed moment in cancer research.

Combination therapies and new enzyme-targeting treatments have turned many deadly cancers—certain adult leukemias and gastrointestinal stromal cell tumors among them—into chronic diseases.

Genetic research has also put us on the path to targeted therapies that could have significant success. Consider that DNA decoding has identified a certain gene mutation in 10 percent of people with lung cancer, which accounts for a third of all cancer deaths. Nearly 100 percent of these patients respond to a small-molecule drug that focuses on the mutation.

This is a clear victory over one disease, but a smaller achievement when the denominator expands to all lung cancers, and all cancers.

Developing vaccines to prevent cancers is another attainable goal that requires more emphasis. Cancer cells evade detection by the immune system—and the most sensitive diagnostic tools—in many insidious ways. We are working on ways to engage the patient's immune defenses to recognize and withstand these stealthy cells. Early data indicate that vaccines could have considerable impact on renal cancer and melanoma, which is on the rise.

There is great need to build an arsenal of targeted approaches. Certain diseases, such as ovarian and lung cancers, are rarely detected early. And our nation's increase in life expectancy—79 years for people born today, up from 63 in 1940—further expands the pool of vulnerable populations since cancer risk increases with age.

Even as the nation faces other health challenges – from H1N1 flu virus to health care reform—we must strengthen our commitment to cancer research. The pledge to increase federal funding for cancer research is encouraging, but of the \$10 billion in stimulus money allocated for health care, only \$1.3 billion will go to cancer, and this must be spent in two years.

Already, the number of grant applications has far outstripped the available funding. To capitalize on the promise of targeted treatments, we must recalculate budgets for the hundreds of diseases we call cancer.

There is no one denominator for cancer; it is hundreds of different diseases and each must be evaluated— and treated—on its own.

- Steven J. Burakoff, MD

To learn more, visit www.mountsinai.org/Burakoff. This commentary was first published in *The New York Times* on June 2, 2009. Steven J. Burakoff, MD, is Director of The Tisch Cancer Institute.



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