David H. Koch Institute for Integrative Cancer Research at MIT

The David H. Koch Institute for Integrative Cancer Research at MIT (KI) was announced on October 9, 2007, with a groundbreaking ceremony taking place the following March. By summer of 2010, the facility was nearly complete and final outfitting of the laboratories was well underway. Between November 2010 and January 2011, more than two dozen academic labs and 11 core technology facilities moved into the building from locations across campus. The move was considered a huge success, with many researchers reporting just two days of interruption in their experiments.

The faculty of the Koch Institute are drawn roughly equally from the schools of Science and Engineering. Fourteen faculty slots at the KI have been filled by School of Science faculty from the former MIT Center for Cancer Research (CCR), and 12 have come from the School of Engineering. Drawn from various departments, the KI continues MIT's tradition of scientific excellence and applied engineering ingenuity.

The new Koch Institute facility has been designed to support over 40 laboratories. In addition to 26–27 faculty laboratories distributed across five research floors, there will be up to six clinical fellows with laboratory space. The unique design of each research floor supports the technical needs of both scientists and engineers, while promoting interactions across disciplines. Also included in the new facility in the Swanson Biotechnology Center (SBC). The SBC facilities provide access to and training on highly sophisticated and diverse instrumentation. Included within the SBC infrastructure are nanomaterials technologies, genomics, proteomics, imaging, histopathology, preclinical testing, and others. Once fully operational, the SBC will employ approximately 60 full-time staff scientists working within one of 13 distinct technical units.

The intramural workforce at the KI has grown to approximately 650 individuals, including postdoctoral fellows, principal research scientists, clinical investigators, students, and staff. Interest in the KI's cancer research program from outside its walls has steadily increased as well, with the list of extramural faculty expected in the coming years. Extramural members reside in the departments, labs, and centers across campus, but have full access to the capabilities and programs provided by the KI. All told, the Koch Institute brings together over 1,000 researchers working in intramural and extramural laboratories.

Although the Koch Institute is a National Cancer Institute (NCI) designated center, is does not provide direct clinical care. The KI enters patients' lives through partnerships with clinical collaborators. By bringing MIT science from classrooms and laboratories into interdisciplinary, cross-institutional teams, the KI strives to serve as a conduit of medical innovation.

Research Focus Areas

Nano-Based Drugs

Most cancer drugs are blunt and toxic instruments, indiscriminately destroying both healthy and cancerous cells. We work at the molecular level to home in on cancer cells selectively. Our nanoscale cancer "smart bombs" deploy multiple emerging technologies from the realms of biology and bioengineering. First, we use antibodies, aptamers, or other means to detect cancer cells through the unique molecules they express. A toxin, antibody, or RNA interference (RNAi) molecule then disables the cancer cells. We package this payload in a liposome or other material so that it traverses the body efficiently. Our goal: a new generation of cancer therapies that eliminate cancer cells, but leave healthy cells alone.

Detection and Monitoring

The molecular differences that make cancerous cells lethal when left unchecked also provide the necessary clues to detect and identify them. We are developing highly sensitive cancer detectors through advances in molecular imaging and micro-electromechanical systems (MEMS) technologies. Implantable detectors combined with wireless data transmission technologies (telemetry) will enable continuous monitoring of cancer patients to immediately signal remission or relapse. And at the interface of detection and treatment, implantable detectors will one day trigger micro-scale drug delivery systems for automatic therapeutic interventions.

Metastasis

Primary tumors are seldom lethal—most cancer deaths are caused by metastasis. Cancer cells mutate and spread to far-flung regions of the body, where they are difficult to investigate and eradicate. Too little is known about the molecular and cellular changes that drive metastasis. Within our Ludwig Center for Molecular Oncology, we are identifying the genes that encourage metastatic spread and allow cancer cells to survive and thrive in disparate locations. We are also devising methods to identify and visualize sites of metastasis earlier in the disease. Armed with this knowledge, we aim to combat metastasis before it begins and destroy cancer cells wherever they may hide.

Personalized Medicine

Among the myriad genetic alterations observed in tumors, only some propel cancer cells to proliferate abnormally, survive inappropriately, and resist the drugs administered to destroy them. To know which alterations represent important therapeutic targets, we need to understand their place in the vast molecular network that underpins cellular function. We are using multiple genomic, proteomic, computational, and in vivo approaches to build a comprehensive "wiring diagram" for cancer cells and their molecular environment. This blueprint will lead us to better, more sophisticated strategies to control cancer and combat drug resistance.

Cancer Immunology

When looking for a strong ally in the fight against cancer, perhaps none is better suited than our own immune system. Every day it is on the hunt for foreign invaders,

and it appears singularly effective at eliminating many nascent cancers before they even develop. Yet some cancers escape and turn lethal, for reasons that remain poorly understood. We are helping to illuminate the role of the immune system in fighting cancer using state-of-the-art protein engineering methods. Our goal is to create novel immunotherapies that augment and surpass the natural immune responses, for the cancers that get away.

Operating Within a Rapidly Changing Landscape

The launch of the Koch Institute brings new focus to emerging challenges in oncology while striving to capitalize on important new opportunities:

- The global impact of cancer continues to escalate, as does the cost of providing care. Controlling cost and providing patients with access will inevitably rely on new technologies.
- The convergence of life science and engineering is driving greater interest in—and funding for—interdisciplinary approaches.
- Conventional funding for basic cancer research is becoming increasingly constrained. Cross-disciplinary teams are competitively advantaged in their efforts to secure funding.
- Each cancer patient has a unique molecular fingerprint. Rapid advances and cost reductions in gene-profiling technologies are ushering in a new era of more personalized cancer care.
- New approaches to cancer diagnosis and treatment have generated a need for more scientifically sophisticated oncologists. Clinical investigators working at MIT can supply our faculty with clinical understandings of cancer and bring new scientific insights and creative approaches back to the clinic.

Working Closely with the National Cancer Institute and Other Supporters

Since 1974, MIT has maintained NCI-designated Cancer Center status. Prior to the launch of the Koch Institute, this center was operated as the Center for Cancer Research. Upon the launch of the KI, the Cancer Center Support Grant (CCSG) was resubmitted with an expanded faculty and mission statement. The results of resubmission were highly encouraging. In addition to obtaining an impressive increase in financial support, the study section applauded MIT and President Susan Hockfield for the visionary new organizational approach. NCI designation is important for several reasons. These monies provide critical support for administration and underwrite the operations of the SBC core research facilities (e.g., biopolymers, flow cytometry, histology, transgenics, bioinformatics). CCSG monies also provide important support for new faculty.

The Koch Institute is notable in part because of the broad range of disciplines represented among our membership. Indeed, this breadth of talent in science and engineering has been recognized in the form of multi-investigator grants from the NCI. In addition to a grant in the Integrative Cancer Biology Program initially funded

in 2004 (primary investigator Douglas Lauffenburger) and an NCI Center of Cancer Nanotechnology Excellence grant initially funded in 2005 and then renewed in 2010, the KI received a multimillion dollar grant to study tumor cell microenvironment in 2006 (PI Richard Hynes, renewed in 2011). The MIT-Harvard Center of Cancer Nanotechnology Excellence is a collaborative effort among MIT, Harvard University, Harvard Medical School (HMS), Massachusetts General Hospital (MGH), and Brigham and Women's Hospital. It is one of eight Centers of Cancer Nanotechnology Excellence supported by the NCI. It focuses on developing a diversified portfolio of nanoscale devices for targeted delivery of cancer therapies, diagnostics, noninvasive imaging, and molecular sensing. In addition to general oncology applications, the consortium focuses on prostate, brain, lung, ovarian, and colon cancer.

In October 2009, the KI was awarded a five-year grant from the NCI to start a new Physical Sciences-Oncology Center (PS-OC, PI, Alexander van Oudenaarden). The MIT PS-OC is a collaboration among MIT, Harvard University, University of California San Francisco, Harvard Medical School, Boston University, Hubrecht Institute, and Brigham and Women's Hospital. It is one of 12 Physical Sciences in Oncology Centers awarded by the NCI. The overarching goal of the center is to use both theoretical and experimental approaches inspired by physics and engineering to tackle important problems in cancer biology. The center is developing novel technologies and analytical and computational methods to track the dynamics of cancer at the single cell level. The funding, approximately $3.5M per year, supports four cancer research projects led by MIT physical scientists.

In March 2010, the KI received funding from the NCI to become a Center for Cancer Systems Biology. These centers are part of the NCI's Integrative Cancer Biology Program (ICBP)—its primary effort in cancer systems biology. The funding represents the continuation of our ICBP grant. Systems biology is rapidly emerging as an essential component of cancer research. Professor Lauffenburger, KI member and head of the Department of Biological Engineering, is the principal investigator for the new center.

Under the direction of Robert Weinberg, the Ludwig Center for Molecular Oncology was established through grants from the Virginia and D. K. Ludwig Fund for Cancer Research. It unites members of the Koch Institute and MIT's extended cancer research community in a mission to unravel the mysteries of metastasis.

In FY2011, KI's research volume totaled $35.9M, up from the $30.5M (approximately 15%) reported in FY2010. This represents an increase that is primarily attributable to our larger faculty pool but these numbers represent only the funding directly administered by the KI, which is only a portion of the total research portfolio. The research portfolios of many of the KI's faculty members are still managed by their home departments. Also not included in this figure are sponsored fellowships, gifts, and direct funding for investigators from the Howard Hughes Medical Institute (HHMI), which collectively represent considerably greater funding. In addition to the NIH and HHMI, the KI's competitive support comes largely from industry and foundations, including the American Cancer Society, the Hereditary Disease Foundation, and the Ludwig Foundation, along with a broad base of philanthropic donors and partners.

The KI's success in attracting grant support is a reflection of the excellent research and educational activities generated by its faculty members. Of particularly high impact is HHMI, which counts nine KI faculty (five intramural and four extramural) members among its 330 investigators: Angelika Amon, Stephen Bell, Sangeeta Bhatia, H. Robert Horvitz, Richard Hynes, Darrell Irvine, Tyler Jacks, Susan Lindquist, and David Sabatini. As of June 31, 2010, the MIT Cancer Research Initiative has raised $232.5M in philanthropic support.

Collaboration Is Integral

In 2011, we began the final phase of the MIT-MGH Collaborative Initiative in Translational Cancer Research, a novel inter-institutional alliance. The program is organized into four teams made up of members from both institutions.

The primary program focus areas are:

- A drug delivery system under development for ovarian cancer patients
- Use and proteomic technologies to characterize the molecular nature of metastatic lesions
- New lung cancer (siRNA) drug trials in novel animal models
- Optimizing gold nanorods for less invasive tumor ablation

The MIT-MGH Collaborative Initiative shows that distances between investigators, either in physical location or in technical background, can be overcome through increased interaction. By providing financial support and aggregating technical objectives, this program has enables researchers to tackle difficult problems together.

In June 2010, MIT and the Ortho-McNeil Janssen division of Johnson & Johnson announced the TRANSCEND collaboration. The partnership began with a five-year sponsored research effort (with an option to renew), involving the interdisciplinary faculty, students, and staff from the KI. Teams have begun working in the areas of cancer diagnostics, cancer biology pre-malignancies, genetic models of disease, and profiles of the tumor microenvironment. A Joint Scientific Steering Committee composed of MIT faculty members and Ortho-McNeil Janssen employees oversees the TRANSCEND program. By the end of FY2011 nine separate MIT labs had begun projects supported by the TRANSCEND program.

Another excellent example of cross-institutional science is Stand Up To Cancer (SU2C), the Entertainment Industry Foundation's charitable initiative to support groundbreaking cancer research SU2C reached a significant milestone in 2009, awarding the first round of three-year grants totaling $73.6M to five multidisciplinary, multi-institutional research "dream teams." Sangeeta Bhatia and colleagues were selected as a "dream team" with the focus of detecting and isolating circulating tumor cells (CTCs) in pursuit of new diagnostic and therapeutic strategies. Dr. Daniel A. Haber, director of the MGH Cancer Center, and Mehmet Toner, professor of biomedical engineering at HMS, are co-leaders of the team.

Finally, the Bridge Project is a collaboration between the KI and the Dana-Farber/Harvard Cancer Center (DF/HCC), designed to bring bioengineering and clinical oncology together to solve today's most challenging problems in cancer research and care. Through seed funding for collaborative research teams comprised of both MIT and DF/HCC investigators, the Bridge project is designed to reach beyond existing individual networks to establish new ties between unmet clinical needs and technological solutions that have not traditionally been connected.

Faculty Growth and Honors

Following the addition of Paul Chang in 2007 and Matthew Vander Heiden in 2009, two new faculty members were recruited to join the KI from the School of Engineering.

Professor Daniel Anderson is an expert in novel material chemistries used for improving drug delivery. Prior to joining as a faculty member, Professor Anderson was a senior research fellow in the laboratory of Institute Professor Robert Langer. Professor Anderson's lab is pioneering the use of robotic methods for the development of smart biomaterials for drug delivery and tissue engineering.

The newest faculty member to join the KI is J. Christopher Love. Professor Love comes from the Department of Chemical Engineering and is an expert in the use of analytical tools and devices to study the dynamic behavior of immune cells.

In 2011, Michael Cima, David H. Koch professor of engineering, and Linda Griffith, professor of biological engineering and mechanical engineering, were named to the National Academy of Engineering (NAE). These selections bring to 18 the number of KI faculty members who are members of the NAE and/or the National Academy of Sciences.

The 2012 Priestly Medal—the American Chemical Society's most prestigious award—will be awarded to KI faculty member and Institute Professor Robert Langer. Langer was recognized for cutting-edge research that helped create the controlled-release drug industry and the field of tissue engineering.

A broad-based faculty search is currently under way.

Clinical Investigators Program

The KI Clinical Investigator (KCI) program is an important new component of the interdisciplinary design of the KI. KI clinical investigators work side by side with MIT scientists and engineers to invent new solutions to the problems of cancer. They bring to these collaborations insights and direction that are drawn directly from their clinical focus, and provide access to the clinical samples and settings that can be catalytic for important research advances.

The KCI program's goal is to provide "top-of-their-class" physical scientists with a unique opportunity to participate in cutting-edge cancer research while maintaining clinical activity at Boston-area oncology treatment centers. The investigators' dual

role ensures that they remain involved in clinical practice, which in turn benefits KI researchers by providing a front-line view of clinical challenges in cancer treatment.

Candidates for the KCI program must:

- Be sub-specialty board-certified and eligible for licensure by the Massachusetts Board of Medical Examiners
- Be at the postdoctoral, instructor, or assistant professor level
- Have a record of productivity in clinical, translational, and basic research

The selected individuals receive dedicated lab space and research support and work closely with faculty mentors at the Koch Institute. Holding a three-to five-year appointment, KI clinical investigators spend between 10 and 50% of their time treating patients at their respective treatment facilities. This ensures that the investigators' clinical capabilities are maintained and fosters the timely transfer of discoveries from Institute lab-bench to patient bedside. KI-provided funding covers a stipend, personnel, equipment, and research costs. At full capacity, the KCI program hopes to host up to six investigators.

The first KI clinical investigator, Alice T. Shaw, MD, PhD, was appointed in August 2009. Dr. Shaw is an attending physical in the Center for Thoracic Cancers at MGH and an assistant professor of medicine at HMS. In addition to caring for patients with lung cancer, Dr. Shaw also performs clinical and translational research in collaboration with Koch Institute faculty-led research teams. Dr. Shaw's major research interests include studying anaplastic lymphoma kinase (ALK) translocations in non-small cell lung carcinoma (NSCLS), developing targeted strategies to treat NSCLCs harboring activating KRAS mutations, discovering new targets in NSCLC using both genetic and phosphoproteomic strategies and developing novel nanoparticle-based siRNA delivery systems to target genetically defined subsets of lung cancer.

Dr. Shaw is already collaborating with KI faculty members Daniel G. Anderson and Robert Langer on a project titled, "Aerosolized nanoparticles for siRNA delivery to lung cancers." She also collaborated with KI director Tyler Jacks on a 2011 publication that established oxidative stress pathways as potential therapeutic targets in KRAS mutant forms of cancer.

With the opening of the new facility, additional KI clinical investigators are being selected.

Training the Next Generation of Research Leaders

In addition to its strengths in basic research, the KI performs an important role in training future researchers in biomedical science, including undergraduate and graduate students and postdoctoral and clinical fellows. Koch Institute faculty members fulfill critical roles in the education programs of the Department of Biology and in various Engineering departments.

In 2009, the Wellcome Trust, MIT, and the KI launched a new interdisciplinary research fellowship program that will fund postdoctoral fellows to do research at the interfaces of biology, medicine, computation, the physical sciences, and engineering. Postdoctoral researchers in this program are funded for two to three years at MIT, followed by one to two years in the United Kingdom. The program has enrolled four scientists thus far.

The 10th annual Koch Institute Summer Symposium, titled "Fueling Cancer: New Advances in Metabolism and Disease," was held on June 10, 2011. Top cancer researchers from around the world shared insights and updates on their work related to cancer metabolism. The event drew more than 1,300 attendees from across the world.

With an intense focus on developing new solutions to the complex challenges of cancer, MIT has assembled the world's first interdisciplinary institute dedicated entirely to cancer research. As a state-of-the-art cancer research and technology facility, the Koch Institute is clearly—and quickly—changing the landscape of cancer research.

Tyler Jacks
Director
David H. Koch Professor of Biology

More information about the Koch Institute is available at http://ki.mit.edu/.