The David H. Koch Institute for Integrative Cancer Research at MIT

The launch of the David H. Koch Institute for Integrative Cancer Research at MIT (KI) was announced on October 9, 2007, and the groundbreaking for the new institute's research facility occurred in March 2008. By summer 2010, the facility was nearing completion and final outfitting of the laboratories was well under way. KI's technical contributions have been fast-tracked by its drawing on current MIT faculty members. Thirteen faculty slots have been contributed to the new institute from the School of Science faculty of the (now former) MIT Center for Cancer Research (CCR), and an equivalent number have been contributed from the School of Engineering. Drawn from various MIT departments, the Koch Institute continues MIT's tradition of scientific excellence and applied engineering ingenuity.

The new Koch Institute facility has been designed to support over 40 laboratories. Approximately 26 of these are faculty laboratories that will be distributed across five floors. Each research floor of the facility has been designed to support the technical needs of both scientists and engineers. Also included in the new facility is the Swanson Biotechnology Center (SBC). Once fully operational, SBC will employ approximately 70 full-time staff scientists working within one of 13 distinct technical units. The SBC facility provides 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 other research facilities. Collectively, the intramural workforce inside KI is approximately 650 individuals. Interest on campus in KI's cancer research program has continued to grow. At the end of FY2010, 20 additional MIT faculty laboratories had joined as extramural members and this number is expected to grow. Extramural members reside in departments, labs, and centers across campus but have full access to the capabilities and programs provided by KI.

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

Research Focus Areas

Nanotechnology Therapy

Most cancer drugs are blunt and toxic instruments, indiscriminately destroying both healthy and cancerous cells. KI's researchers work at the molecular level to home in on cancer cells selectively, using nanoscale cancer "smart bombs" that deploy multiple emerging technologies from the realms of biology and bioengineering. First, antibodies, aptamers, or other means are used to detect cancer cells through the unique molecules they express. A toxin, antibody, or RNA interference (RNAi) molecule then disables the cancer cells, and this payload is packaged in a liposome or other material so that

it traverses the body efficiently. The goal: a new generation of cancer therapies that eliminate cancer cells but leave healthy cells alone.

Detection and Monitoring

To arrest cancer before it kills, it is necessary to find it early and track its progress. The molecular differences that make cancerous cells lethal when left unchecked also provide the necessary clues to detect and identify them. KI is developing highly sensitive cancer detectors through advances in molecular imaging and microelectromechanical systems 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 microscale 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 the Ludwig Center for Molecular Oncology, KI researchers are identifying the genes that encourage metastatic spread and allow cancer cells to survive and thrive in disparate locations. Methods are also being devised to identify and visualize sites of metastasis earlier in the disease. Armed with this knowledge, the aim is to combat metastasis before it begins and destroy cancer cells wherever they may hide.

Pathways and Resistance

What makes cancer cells different, and dangerous? 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, it is necessary to understand their place in the vast molecular network that underpins cellular function. Using multiple genomic, proteomic, computational, and in vivo approaches, KI researchers are building a comprehensive "wiring diagram" for cancer cells and their molecular environment. This blueprint will lead to better, more sophisticated strategies to control cancer and combat drug resistance.

Immune System

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

Emerging Challenges and New Opportunities

The launch of the Koch Institute underscores emerging challenges in oncology research and the importance of capitalizing on important new opportunities:

- The global impact of cancer continues to escalate as does the cost of providing care—controlling cost and providing access will inevitably rely on technology.
- The convergence (and interdependence) of life sciences and engineering is driving up interest in and funding for interdisciplinary approaches.
- Conventional funding for basic cancer research is becoming increasingly constrained—cross-disciplinary teams are competitively advantaged.
- The molecular fingerprint of cancer patients is highly individualized—rapid advances and reductions in cost of gene profiling technologies are ushering in a new era in personalized medicine.
- Diagnosis and treatment of cancer is pushing the need for more scientifically sophisticated oncologists—clinical investigators working at MIT are bringing the clinical problems of cancer into the minds of our faculty and bringing back to the clinic scientific insights and creative approaches.

National Cancer Institute and Other Supporters

Since 1974, MIT has maintained an NCI-designated cancer center status. Prior to the launch of the Koch Institute, this center was operated as the CCR. Upon the launch of KI, the NCI-center grant was resubmitted during its five-year competitive renewal 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 (i.e., biopolymers, flow cytometry, and specialized laboratories). NCI-center monies also provide important support for new faculty.

KI is notable in part because of the broad range of disciplines represented among its membership. Indeed, this breadth of talent in science and engineering has been recognized in the form of multi-investigator grants from NCI. In addition to an Integrative Cancer Biology Program (ICBP) grant funded in 2004 and an NCI Center of Cancer Nanotechnology Excellence grant funded in 2005, CCR received a multi-million dollar grant to study tumor cell microenvironment in 2006. In October 2009, KI investigators were awarded a five-year grant from NCI to fund projects by physicists to start a new physical science–oncology center. The funding, approximately $3.5 M per year, will support four cancer research projects led by MIT physical scientists.

In March 2010, KI received funding from NCI to become a Center for Cancer Systems Biology. These centers are part of NCI's ICBP program, which is NCI's primary effort in cancer systems biology, a field that is rapidly seen as an essential component in the future of cancer research. Douglas Lauffenburger, KI member and head of the Department of Biological Engineering, will be the principal investigator for the new center.

The sponsored research volume for KI totaled $30.5M in FY2010, up 15.4 percent from $25.8M reported in FY2009. An increase of 8 percent has been projected, to $33.2M, for FY2011. This represents only funding administered directly by KI, and is only a portion of the total research portfolio. It does not include support for sponsored fellowships, gifts, and direct funding for investigators from the Howard Hughes Medical Institute (HHMI). If these items are included, funding for KI faculty is considerably higher. This competitive support comes largely from the National Institutes of Health and HHMI, industry, and a variety of foundations, including the American Cancer Society, the Hereditary Disease Foundation, and the Ludwig Foundation, along with a broad base of philanthropic donors and partners. KI's success in attracting grant support is a reflection of the excellence of the research and educational activities of its faculty members. Of particularly high impact is HHMI, with nine investigators affiliated with KI: Angelika Amon, Stephen Bell, Sangeeta Bhatia, H. Robert Horvitz, Richard Hynes, Darrell Irvine, Tyler Jacks, Susan Lindquist, and David Sabatini. As of June 30, 2010, the Cancer Research Initiative has raised $232.5M in philanthropic support.

Collaborative and Cross-institutional Initiatives

In February 2010, a collaborative initiative in translational cancer research between MIT and Massachusetts General Hospital (MGH) began its second phase. This novel inter-institutional alliance is organized into four teams, with members from both institutions.

Some highlights include:

- encouraging pharmacodynamic properties demonstrated for a new drug delivery system being developed for ovarian cancer patients
- successful use of next-generation sequencing and proteomic technologies to characterize the molecular nature of metastatic lesions
- expansion of genetically defined murine cohorts to begin new lung cancer (siRNA) drug trials
- further advances using tuned gold nanorods for less invasive tumor ablation.

The MIT-MGH collaborative initiative shows that the distance between investigators, either in physical location or in technical background, can be overcome by increased interaction through seminars, meetings, and sharing of resources. By providing financial support and aggregating technical objectives, this program has enabled 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 (with an option to renew) sponsored research effort involving KI's interdisciplinary faculty, students, and staff. The teams will begin the collaboration by working in the areas of cancer diagnostics, cancer biology pre-malignancies, and genetic models of disease, studying profiles of the tumor microenvironment. A joint scientific steering committee composed of MIT faculty members and Ortho-McNeil-Janssen employees will jointly oversee TRANSCEND.

Another excellent example of cross-institutional science is Stand Up To Cancer (SU2C), the Entertainment Industry Foundation's charitable initiative supporting groundbreaking research aimed at getting new cancer treatments to patients in an accelerated timeframe. SU2C reached a significant milestone this year, awarding the first round of three-year grants—totaling $73.6M—to five multidisciplinary, multi-institutional research "dream teams." Sangeeta Bhatia and colleagues were awarded a part of this funding. Professor Bhatia's team will focus on bioengineering and clinical applications of circulating tumor cells, with Daniel A. Haber, director of the MGH Cancer Center, and Mehmet Toner, professor of biomedical engineering, Harvard Medical School, as co-leaders.

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 KI from the School of Engineering.

Daniel Anderson is an expert in novel material chemistries used for improving drug delivery. Prior to joining KI, Professor Anderson was a senior research fellow in the laboratory of Institute Professor Robert Langer. Professor Anderson's laboratory is pioneering the use of robotic methods for the development of smart biomaterials for drug delivery and tissue engineering. His lab has developed methods allowing rapid synthesis, formulation, analysis, and biological testing of large libraries of biomaterials for use in medical devices, cell therapy, and drug delivery. Professor Anderson obtained his PhD from the University of California, Davis, in 1997.

The newest faculty member to join KI is J. Christopher Love, who comes to KI 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. Professor Love's broad research objective is to improve the design and implementation of quantitative bioanalytical processes in order to maximize the knowledge gained about the heterogeneities and dynamics of individual cells within a complex population. Professor Love obtained his PhD from Harvard University in 2004.

The 2009 Linus Pauling Medal was awarded to KI faculty member Stephen J. Lippard, the Arthur Amos Noyes Professor of Chemistry, for his outstanding contributions to chemistry. The medal is given annually by the American Chemical Society and is named after the American chemist and two-time Nobel Laureate Linus Pauling—one of the most influential scientists in history. Professor Lippard is the 44th awardee of the Linus Pauling Medal.

In 2010, Angelika Amon, professor of biology, was elected to the National Academy of Sciences (NAS) for her distinguished and continuing achievements in cancer research. NAS members from MIT have increased to 2,097, with 409 active, non-voting foreign associates. Professor Amon's election to NAS brings to 17 the number of Koch Institute members who have been elected to NAS and/or the National Academy of Engineering.

Also in 2010, KI member and Institute Professor Phillip A. Sharp received the fourth annual American Association for Cancer Research Margaret Foti Award for Leadership

and Extraordinary Achievements in Cancer Research. This award recognizes an individual whose leadership and extraordinary achievements in or in support of cancer research have made a major impact on the field overall.

Koch Institute Clinical Investigator Program

The Koch Clinical Investigator (KCI) program is an important new component of the interdisciplinary design of KI. Koch 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 clinical samples and settings that can be catalytic for important research advances.

KCI's goal is to provide "top of their class" physician-scientists 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 frontline view of clinical challenges in cancer treatment.

Candidates for the KCI program must:

- be subspecialty 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 KI. Holding a three- to five-year appointment, Koch Institute clinical investigators spend 10–50 percent 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 lab-bench to patient-bedside.

The first clinical investigator, Alice T. Shaw, MD, PhD, was appointed in August 2009. KI funding covers a stipend as well as personnel, equipment, and research costs. At full capacity, the KCI program hopes to host up to six investigators.

Dr. Shaw is an attending physician in the Center for Thoracic Cancers at MGH and an assistant professor of medicine at Harvard Medical School. In addition to caring for patients with lung cancer, she also performs clinical and translational research in major collaboration with KI faculty-led research teams. Dr. Shaw's major research interests include studying anaplastic lymphoma kinase translocations in non-small cell lung carcinoma (NSCLC), 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 Koch Institute faculty members Daniel G. Anderson and Robert Langer on a project titled "Aerosolized nanoparticles for siRNA delivery to lung cancers."

With the opening of KI's new facility, additional KCI appointments will be made in 2011.

Training the Next Generation of Research Leaders

In addition to its strengths in basic research, KI performs an important role in training future researchers in biomedical science, including undergraduate and graduate students and postdoctoral and clinical fellows. KI faculty fulfill critical roles in the educational programs of the Department of Biology and in various engineering departments. Extensive collaborations exist with medical schools, hospitals, and the biotechnology/pharmaceutical industries.

In 2009, the Wellcome Trust, MIT, and KI launched a new interdisciplinary research fellowship program that will fund postdoctoral fellows to do research at the interfaces between 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 Koch Institute 2010 summer symposium, "Integrative Approaches to Cancer," was the institute's ninth annual event and was held on June 10 and 11, 2010. Over the two-day program, top cancer researchers from around the world shared insights and updates on their work. This year's KI annual oncology symposium and CCR reunion event drew more than 1,300 attendees from across the globe.

Focused on developing new solutions to complex challenges of cancer, MIT has assembled the world's first interdisciplinary institute dedicated entirely to cancer research, bringing together more than 650 individuals. With a state-of-the-art cancer research and technology facility opening in December 2010, the Koch Institute is clearly—and quickly—changing the landscape and shifting the paradigm for cancer research.

Tyler Jacks
Director
David H. Koch Professor of Biology

More information about the Koch Institute can be found at http://ki.mit.edu/.