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

The David H. Koch Institute for Integrative Cancer Research was announced on October 9, 2007. By combining the faculty of the (now former) MIT Center for Cancer Research (CCR) with an equivalent number of distinguished engineers drawn from various MIT departments, the Koch Institute will continue CCR's tradition of scientific excellence while also seeking to directly promote innovative ways to diagnose, monitor, and treat cancer through advanced technology. Among the engineering faculty there will be remarkable diversity, as the Electrical Engineering and Computer Science, Materials Science and Engineering, Biological Engineering, Chemical Engineering, and Mechanical Engineering departments will be represented in the Koch Institute.

For three decades, CCR has been a mainstay of MIT's—and the nation's—efforts to conquer cancer. Its faculty has included five Nobel Prize winners, and the wealth of fundamental discoveries that have emerged under its aegis have helped shape the face of molecular biology. Under the banner of the Koch Institute, the future promises to hold even more astounding advances.

Within the Koch Institute we will not directly provide clinical care for cancer patients but discoveries made by Koch Institute scientists and engineers will have a broad impact on how the disease is detected and managed. Applying our great strengths in science and technology, and working closely with our clinical collaborators, Koch Institute researchers will be tireless in unraveling the complexities of this disease and bringing new discoveries—and new hope—to patients.

The Koch Institute includes more than 40 laboratories and more than 500 researchers located at our headquarters and across the MIT campus. This group includes cancer biologists, genome scientists, chemists, engineers, and computer scientists—all dedicated to bringing the most advanced science and technology to bear in the fight against cancer. In late 2010, we will move into a new state-of-the-art research facility.

Building 76, the new home of the Koch Institute, will feature roughly 180,000 square feet of laboratories, offices, and collaborative workspaces. The floor plans are specially designed to foster interaction and collaboration among biologists and engineers—both in terms of dedicated lab space and in the common areas, where informal talks will lead to new collaborations and spontaneous information sharing. Together, our diverse faculty members will create a new culture of interdisciplinary cancer science.

In addition to lab and meeting space, the building will feature a ground-floor exhibit gallery that will be home to a changing exhibit of art and technical displays that highlight MIT's leadership role in biomedical research.

Why Now and Why at MIT

In the Koch Institute, we see in this new era an exceptional opportunity to conquer cancer by capitalizing on the signature strengths of MIT:

- Intensely gifted researchers across fields now crucial to advanced cancer research, from computer science and nanotechnology to chemical and biological engineering—working together in teams
- A long tradition of working across the boundaries of traditional disciplines and of leaping past the barriers of conventional wisdom
- An entrepreneurial spirit that promotes not only the discovery of new knowledge but the creation of new techniques and technologies
- Powerful connections across Boston's unparalleled biomedical community and oncology centers of excellence across the United States and the world
- A deep commitment to training the next generation of leaders in cancer research

Funding support for the new Koch Institute has also grown steadily in recent years and is at an all-time high. The center has maintained its status as a National Cancer Institute (NCI) designated cancer center following the successful competitive renewal of its center grant in 2005. The center grant will be submitted for competitive renewal in 2009. Financial support for research in the center comes from many sources. The core of this support, which provides much of the funds for administration and core research facilities (biopolymers, flow cytometry, specialized laboratories, and partial support for new faculty) is a center core grant from NCI. In 2008, we announced the creation of the Swanson Biotechnology Center (SBC), named in honor of biotechnology pioneer Robert A. Swanson '69. Located on three contiguous floors, the SBC is instrumental to the Koch Institute's mission to become the world's foremost cancer research organization. Within the SBC, dedicated professional staff provide the expert technical tools and services that MIT life scientists and engineers require to understand and manipulate the complex biological functions that underlie cancer.

In addition to the NCI core grant, the center's resident faculty have a total of 110 fully funded projects, up from 59 reported in FY2007. This competitive support comes largely from the National Institutes of Health and the Howard Hughes Medical Institute (HHMI), industry, and a variety of foundations supporting research in particular disease areas, including the American Cancer Society, the Hereditary Disease Foundation, the Ludwig Foundation, and the Adelson Medical Research Foundation, among many others. The latter type of foundation support is particularly valuable for starting projects that later mature into federally funded grants. The Koch Institute's success in attracting grant support is a reflection of the excellence of the research and educational activities of its faculty members. The FY2008 research volume was approximately $24.5 million, up from $22.4 million reported in FY2007. In addition, the Koch Institute received about $2.9 million in support from HHMI, a number that is expected to further increase in 2008–2009 as a consequence of additional HHMI investigator appointments. Funds from foundations including the Ludwig Trust and private donations increase research volume by approximately four million dollars.

The new Koch Institute is notable in part because of the broad range of disciplines represented among our membership. This breadth of talent in science and engineering has been recognized in the form of multi-investigator grants from NCI. In addition to a grant in the Integrative Cancer Biology Program funded in 2004 and an NCI Center

of Cancer Nanotechnology Excellence funded in 2005, the center received a $6 million grant to study tumor cell microenvironment in 2006. Richard Hynes is the principal investigator with coinvestigators Tyler Jacks, Robert Weinberg of the Whitehead Institute, and Ralph Weissleder of Massachusetts General Hospital (MGH).

Collaboration is integral to the mission of the Koch Institute

In 2007, Alnylam Pharmaceuticals, Inc., a leading RNA interference (RNAi) therapeutics company, signed an agreement to sponsor a five-year research program focused on the delivery of RNAi therapeutics. Koch Institute coinvestigators Robert Langer and Daniel Anderson are working closely with Alnylam, which provides research funding for approximately 10 postdoctoral researchers annually over the five-year term. In 2008, this research team published exciting in vivo results that were featured on the cover of *Nature Biotechnology*.

In May 2008, the Koch Institute began a collaboration with Microsoft under which new bioinformatics training modules will be developed. The program is fully underwritten by a gift from Microsoft and will support individuals in the SBC Bioinformatics & Computing Facility and help to acquire additional informatics resources. The new training modules will be designed to improve the computational competence of Koch Institute students and postdocs and illustrate key experimental requirements important in subsequent data analysis. These new training methods will be shared broadly within the research community, and Koch Institute researchers have begun to participate in training workshops hosted by Microsoft. This one-year program has the potential for renewal and, if successful, could lead to additional collaborative projects between Koch Institute researchers and Microsoft.

In July 2008, the Koch Institute finalized a collaboration agreement with the MGH Cancer Center. Historically many of MIT's faculty have participated in collaborations involving researchers from MGH. The new collaboration agreement seeks to expand on these successes and to provide additional resources to support interdisciplinary and interinstitutional partnerships. The program intends to specifically support research teams working on metastasis and detection/monitoring; both are areas of high unmet need and both are central to the Koch Institute's research mission. An ignition grant was obtained from an anonymous foundation to launch this program and project teams are being formed. This new agreement will also establish formal mechanisms to stimulate information exchange and collaboration between the Koch Institute and MGH investigators. The Koch Institute intends to build similar partnerships with other centers of clinical oncology excellence in Boston and beyond.

Awards and Honors

MIT professor Angelika Amon and Todd R. Golub of the Broad Institute of MIT and Harvard will share the 2007 Paul Marks Prize for Cancer Research, an award of $150,000, along with Gregory J. Hannon from Cold Spring Harbor Laboratory.

In January, professor Robert A. Weinberg of MIT's Department of Biology became the first recipient of a new Swedish science prize, in recognition of his cancer research. The 20,000 Euro prize, sponsored by a foundation set up by Swedish scientists Georg and

Eva Klein, was presented by Sweden's Crown Princess Victoria at a January 29 ceremony in Stockholm.

Tyler Jacks, director of the Koch Institute, became president-elect of the American Association for Cancer Research (AACR) in April. AACR promotes the flow of information between research scientists and clinicians, thus affecting the lives of cancer patients. Jacks previously served on the board of directors and the nominating committee.

In May, two more Koch Institute faculty members were named HHMI investigators: Sangeeta N. Bhatia, professor of electrical engineering and health sciences and technology, and Darrell J. Irvine, Eugene Bell career development associate professor of tissue engineering and associate professor of biological engineering and materials science and engineering. A biomedical engineer, one of Bhatia's long-term goals is to generate a complete implantable liver. Another major effort in Bhatia's lab is the development of nanoparticles designed to diagnose and treat cancer. Irvine is an engineer focused on delivering drugs and vaccines to the immune system more effectively. The goal is to create materials that, once in the body, can attract and be taken up by immune cells and then spur them to seek out pathogens or tumor cells. Bhatia and Irvine join the current Koch Institute HHMI investigators Angelika Amon, Stephen Bell, H. Robert Horvitz, Richard Hynes, and Tyler Jacks.

MIT institute professor Robert Langer won the Millennium Technology Prize in June, the world's largest award for technology innovation. Langer was chosen "for his inventions and development of innovative biomaterials for controlled drug release and tissue regeneration that have saved and improved the lives of millions of people," according to Technology Academy Finland, which gives the award every other year. Langer was chosen from three finalists considered for the award. Langer also received the National Medal of Technology during a ceremony at the White House. In addition, Langer was chosen as one of two winners of the 2008 Max Planck Research Award, a prize funded by the German government

Faculty Growth

Paul Chang joined the Koch Institute this year as assistant professor. Professor Chang came to the Koch Institute and MIT from Harvard Medical School. His lab is interested in understanding the mechanism of poly(ADP-ribose) function in cells and organisms as well as in identifying novel molecules required for mitotic spindle assembly. The lab is taking a global approach to understanding the cellular mechanism of poly(ADP-ribose) function. Poly(ADP-ribose) is implicated in a number of critical biological processes and in cancer. A number of companies are developing new classes of cancer drugs that target this pathway.

Research Mission

Over the course of 2008, the faculty, students, fellows, and staff have made important progress in each of the Koch Institute targeted research areas:

Developing nanotechnology-based cancer therapeutics: Using nanoscale particles loaded with chemotherapeutic agents—and covered with homing molecules that allow

them to selectively bind to cancer cells—our investigators are building a new class of "smart bombs" for cancer. These functionalized nanoparticles hold the promise of both reducing toxicity and improving the efficacy of a wide range of existing anticancer agents. Nanotechnology is also being applied to RNAi, which can be used to silence genes in many biological systems. RNAi could be used to inhibit the function of virtually any cancer-causing gene.

Creating novel devices for cancer detection and monitoring: Better detection is key to achieving better outcomes. We are creating nanoscale imaging agents and other sensors and developing highly sensitive molecular and cellular detection methods using microelectromechanical systems. These tools and devices can also be deployed to monitor tumors. By combining implantable detection technologies with telemetry, we can monitor whether a cancer is in remission or undergoing relapse. In time, such devices may incorporate microscale drug delivery systems that automatically release therapeutic drugs when cancer cells are detected.

Exploring the molecular and cellular basis of metastasis: Roughly 90% of all cancer deaths are due not to the primary tumor but to the effects of the metastatis of the disease. Yet virtually nothing is known about this process. How do cancer cells leave their primary site? How do they traverse the blood system and take up residence elsewhere? In our Ludwig Center for Molecular Oncology we are identifying the genes that encourage metastatic spread and the pathways that allow cancer cells to survive and thrive in distant sites in the body.

Conducting systematic analysis of cancer pathways and drug resistance: Because cancer cells mutate, they are able to proliferate, survive, and, in some cases, resist efforts to destroy them. Using genomic and proteomic analyses, computational modeling, and functional testing in sophisticated animal models, Koch Institute investigators are working to uncover the key pathways that allow cancer cells to keep dividing and remain alive. When this "wiring diagram" of cancer cells is complete, it will be possible to develop new strategies to control the disease and combat acquired resistance.

Engineering the immune system to fight cancer: Cancer cells are fundamentally different from normal cells; therefore, the immune system ought to be able to recognize them as foreign and destroy them. Clearly, however, either the immune system is not equipped to recognize the changes that occur in cancer or tumors evolve mechanisms to elude the immune response. Believing that the immune system can play a role in the fight against cancer, a team of immunologists and biological engineers is exploring how tumors evade immune recognition and how to develop methods to overcome these mechanisms.

Training the Next Generation of Research Leaders

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

has a major impact both on the fundamental understanding of cancer and on its translation to and from the clinical arena. To further the center's goal of bringing cutting-edge research to the cancer research community in the Boston area, on June 27, 2008, the Koch Institute hosted its seventh annual scientific symposium, "Nanotechnology and Cancer: The Power of Small Science." Koch Institute faculty, along with leading cancer nanotechnology scientists from around the country, provided their latest research findings during the annual symposium. The event included more than 1,100 registered participants from 87 cancer-focused companies and 47 academic universities or institutions. Participants traveled from 15 states and six countries to participate. The one-day technology program was filmed and shared with the world from the Koch Institute website.

To get a new result, you need a new equation. MIT is accomplishing this with the world's first institute dedicated entirely to cancer research that brings more than two dozen biologists and engineers together in a fully collaborative, multidisciplinary effort. The Koch Institute will achieve progress in the quest to control cancer by attacking the disease from a number of innovative new angles. With a state-of-the-art cancer research and technology facility, the Koch Institute is clearly—and quickly—changing the landscape and shifting the paradigm for cancer research.

Tyler Jacks
Director
Koch Professor of Biology

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