

## Center for Cancer Research

The MIT Center for Cancer Research (CCR) was founded in 1974, and is one of eight National Cancer Institute (NCI)–designated basic research centers. Our mission is to apply the tools of basic science and technology to determine how cancer is caused, progresses, and responds to treatment. Through this effort we have developed an increasingly complete understanding of the nature of cancer cells, which has led directly to improved treatments for the disease. Molecules identified by CCR research teams were targeted by two of the first few cancer-fighting drugs produced by molecular medicine to be approved by the Food and Drug Administration, in 1998 and 2001, respectively. Today, CCR continues to generate critical new insights into the basic mechanisms of cancer that are essential for advancing diagnosis and treatment of the disease. We remain committed to our founding vision that we can conquer cancer through research and technology.

The nature of basic cancer research has changed radically in the 30 years since CCR was founded. The sequencing of the human genome, as well as those of several other species, has broadened our focus from individual genes to gene networks and genome-wide approaches. Likewise, comprehensive proteomic methods and sophisticated computational tools are beginning to allow for the charting of intracellular signaling pathways with much greater refinement than could have been imagined just a few years ago. Meanwhile, it is now possible to manipulate gene function in cells in culture or in intact animals in unprecedented ways. CCR researchers have helped to affect these changes, and they remain extremely well positioned to take advantage of these developments and apply them to the study of cancer.

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

- An unmatched depth and breadth of intensely gifted researchers across the fields now crucial to advanced cancer research, from computer science and nanotechnology to chemical and biological engineering
- 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
- A deep commitment to training the next generation of leaders in cancer research.

Membership in CCR has steadily grown from its 13 dedicated faculty (housed in Buildings E17 and E18) to include 21 additional investigators from the departments of Biology, Biological Engineering, Chemistry, and Chemical Engineering as well as the Broad Institute, Whitehead Institute for Biomedical Research, and the Center for Environmental Health Sciences. This expansion has allowed CCR to incorporate the great strengths at MIT in genomic science, computational biology, biological and chemical engineering, and chemistry into its research programs while at the same time exposing MIT scientists and engineers more broadly to the problems and challenges of

cancer. The center has evolved to be both a physical entity and the organizing body for cancer research at MIT.

Funding support for CCR has also grown steadily in recent years and is currently at an all-time high. The center has maintained its designation as an NCI-designated Cancer Center following the successful competitive renewal of its center grant in 2005. Financial support for research in the center comes from many sources. The core of this support, which provides much of the funds for administration, core research facilities (i.e., biopolymers, flow cytometry, specialized laboratories, and partial support for new faculty), is a center core grant from NCI. In addition to the core grant, the center's resident faculty have a total of 47 fully funded projects. This competitive support comes largely from the National Institutes of Health and the Howard Hughes Medical Institute, industry, and a variety of foundations supporting research in particular disease areas, including the American Cancer Society and the Hereditary Disease Foundation. This latter type of support is particularly valuable for starting projects which later mature into federally funded grants. The center's success in attracting grant support is a reflection of the excellence of the research and educational activities of its faculty members. The FY2005 research volume was approximately \$16 million, which does not include \$2.7 million in additional support from the Howard Hughes Medical Institute.

CCR 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 two recent multi-investigator grants from NCI. The first is a grant in the Integrative Cancer Biology Program (ICBP), funded in fall 2004. This five-year grant will provide \$12.6M to ICBP investigators. The co-principal investigators on this grant are Richard Hynes and Doug Lauffenburger, and the grant includes several other MIT faculty from a range of departments. Likewise, over the past year, CCR was successful in becoming an NCI Center of Cancer Nanotechnology Excellence. The MIT-Harvard Nanomedical Consortium, of which CCR member Robert Langer and Massachusetts General Hospital faculty member Ralph Weissleder are co-principal investigators, is another multi-investigator grant that draws on the talents of MIT cancer biologists and experts in different areas of nanotechnology. This five-year \$20M grant is also administered through CCR.

In the last year, CCR faculty have made significant contributions in the following areas of research, which have broad impact on cancer research:

—*Normalcy of cloned embryonic stem cells.* Research in the Jaensich laboratory has demonstrated that mouse embryonic stem (ES) cells derived from nuclear transfer experiments are indistinguishable from ES cells derived from normal blastocysts. These results reduce concerns that ES cells made for therapeutic purposes by nuclear transfer might have inherent defects when used in vivo.

—*Nanoparticles for cancer drug delivery.* The Langer laboratory has developed new nanoscale particles to improve delivery of anti-cancer agents to tumors. These particles can be coupled to peptides that allow them to home in on cancer cells and loaded with potent anti-cancer agents. To date these materials have been tested in preclinical models,

but these successes should hasten their use in prostate cancer patients and, in time, other cancer patients.

—*New model of ovarian cancer developed.* The Jacks laboratory has created a powerful new model of epithelial ovarian cancer that mimics many of the hallmarks of this deadly disease. This model will aid in the search for markers of ovarian cancer that can be used in early detection and in the search for more effective therapies to control the disease.

—*A new twist on metastasis research.* Approximately 90% of cancer deaths are due to metastasis, and yet this phase of the disease remains poorly understood. The Weinberg laboratory has performed genetic screens to identify factors that control the metastatic potential of cancer cells. They have shown that the Twist transcription factor is critical in this process through its ability to induce cancer cells to adopt more invasive and migratory behavior.

—*Genome sequence of the domestic dog.* Eric Lander and colleagues have sequenced the genome of the domestic dog. They have also carried out studies to determine the degree of relatedness among different dog breeds and between the dog and its ancestor, the wolf. These studies are important to lay to groundwork to understand the genetic basis for the many varied traits in dogs as well as to understand the breed-specific predisposition to diseases, including cancer.

—*Activation of cancer pathways triggers a cellular sensor.* The Lees laboratory has demonstrated that the Arf tumor suppressor is finely regulated to detect changes in the activity of different oncogenic pathways. Their work identified key factors that keep Arf repressed in normal cells and allow it to become active in cells that have suffered oncogenic insults.

—*Understanding cell death pathways through reverse engineering.* The Yaffe, Sorger, and Lauffenburger laboratories have collaborated to use computational and mathematical modeling to decipher the intricate control of cell death, or apoptosis. By measuring thousands of data points over a time course of cell death and then feeding the data to high-speed computers, these investigators were able to discern new pathways that had eluded investigators using more traditional methods. This paper represents an important step forward in applying “systems biology” to solve key problems in cancer.

—*Loss of imprinting induces cancer.* The Jaenisch laboratory has linked the loss of regulation of imprinted genes with tumor predisposition in mice. Using mouse strains that are unable to perform imprinting, this group has shown that proper imprinting is required to prevent tumor development in various tissues. This work furthers the importance of epigenetic control of gene expression as a source of critical defects in cancer.

—*Making more blood cells.* The Lodish laboratory has developed methods for greatly expanding the development of hematopoietic stem cells in culture. Given the importance of these cells in reconstituting the blood system in transfusions in cancer patients,

including those undergoing autologous blood transfusions, this method could improve the efficacy of such transfusions.

—*Metastasis without lymphangiogenesis*. The Hynes laboratory has directly tested the importance of production of new vessels of the lymphatic system for the spread of prostate cancer. These vessels had previously been suggested to be critical for initiating metastasis in this organ, but based on genetic manipulation of prostate cancer cells in a mouse model of the disease, the Hynes group concluded that travel through the blood, and not the lymphatic system, is the operative route. This work is important for understanding the details of metastatic spread, which is responsible for the vast majority of cancer deaths.

In addition to its strengths in basic research, CCR performs an important role in training future researchers in biomedical science, including undergraduate and graduate students and postdoctoral and clinical fellows. The faculty of the center fulfill critical roles in the educational programs of the Department of Biology. Extensive collaborations exist with medical schools, hospitals, and the biotechnology/pharmaceutical industries. Thus, the research in CCR 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 24, 2005, CCR hosted its fourth annual scientific symposium, The New Science of Cancer Therapy. President Susan Hockfield welcomed 1,100 individuals from MIT, other area academic institutions, and industry. The symposium featured speakers from academia and industry, including Philip Beachy, Brian Druker, Pearl Huang, Daniel Haber, William Kaelin, Robert Langer, Victoria Richon, Susan Hellmann, and Frank McCormick. By all accounts, it was a highly successful and informative meeting.

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*More information about the Center for Cancer Research can be found online at <http://web.mit.edu/ccr/>.*