

Center for Cancer Research

The year 2004 marked the 30th anniversary of the founding of the Center for Cancer Research (CCR). The center was established to study fundamental biological processes related to cancer. The goals of the center's research can be generally stated as developing an understanding of the genetic and molecular basis of cancer, how alterations in cellular processes affect cell growth and behavior leading to cancer and other diseases, and how the immune system develops and recognizes antigens. These goals are related to the center's major research programs in cancer-associated genes and mammalian genetics, molecular, cellular, and developmental biology, and immunology.

Approximately 248 people work in the center, distributed among the research laboratories of 13 faculty. In addition, seven faculty members in the Whitehead Institute, four in Biology, two in the Broad Institute, one in Chemistry, one in Chemical Engineering, and four in the Division of Bioengineering and Environmental Health Sciences are affiliate members of the CCR. The center is therefore both a physical entity and the organizing body for cancer research at MIT.

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, etc.), specialized laboratories, and partial support for new faculty), is a center core grant from the National Cancer Institute. The current term extends to April 30, 2005, and the competitive renewal is presently under review. In addition to the core grant, the center's 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, from industry, and from a variety of foundations supporting research in particular disease areas (American Cancer Society, Hereditary Disease Foundation, Muscular Dystrophy Association, National Neurofibromatosis Foundation, CaPCURE, Arthritis Foundation, etc.). This latter type of support is particularly valuable for starting projects that 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 FY2004 research volume was approximately \$17 million, which does not include \$2.7 million in additional support from the Howard Hughes Medical Institute.

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 many 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 effect these changes, and they remain extremely well positioned to take advantage of these developments and apply them to the study of cancer.

Animal Models of Cancer

Using gene targeting in the mouse, several CCR investigators have developed powerful mouse models of tumorigenesis. These models are being used both to elucidate the contributions of individual genes to tumor initiation and progression and to study the interactions between normal cells and the emerging tumor (including tumor-stromal interactions, tumor vasculature, and tumor immunology). Increasingly, such models will be used for developing and screening novel anticancer agents as well as improved methods for early detection and cancer prevention. The postgenomic tools being developed in the Broad Institute will be very useful in the investigation of these models. CCR investigators Jacks, Hynes, Lees, Jaenisch, Housman, Chen, Gertler, Sorger, Samson, Lander and Weinberg are all engaged in the development and/or characterization of mouse models of cancer.

Stem Cells, Development, and Cancer

Tumorigenesis is intimately linked to normal embryonic development and homeostasis of adult tissues. Such links have been strengthened with the discovery and characterization of embryonic and adult stem cells. CCR researchers have performed fundamental research in this area to date, and the further elucidation of the relationship between stem cell biology, normal developmental processes, and tumorigenesis will be an important theme in the center in the future. Several CCR investigators have active research programs in this area, including Jaenisch, Lodish, Hopkins, Horvitz, Hynes, Sherley, Lees, and Jacks.

RNAi Technology

The discovery of RNA interference (RNAi) and related processes has led to the development of powerful new methods to manipulate gene function. Almost overnight, RNAi methods have revolutionized the ways in which the functions of individual genes and pathways are being interrogated, both in cell-based systems and, increasingly, in the whole animal. RNAi-based technologies are being used to study many biological processes and diseases, including cancer. CCR investigators have been critical to the development and deployment of these technologies, and they will remain a cornerstone of our investigation of cancer-associated pathways in the future. The following CCR investigators have active programs in RNAi and related processes: Sharp, Sabatini, Gertler, Lander, and Horvitz.

Integrative Analysis of Cancer Pathways

The availability of genome sequences from human, mouse, and other organisms, plus the development of sophisticated postgenomic, proteomic, and biocomputational tools, has greatly accelerated the pace of discovery in cancer research. However, while much has been learned about the component parts of relevant pathways and processes, the challenge remains to translate the flood of new information into a more complete and integrated understanding of normal and transformed cells. Such insight will be critical to efforts in basic cancer biology as well as for understanding the basis of existing cancer

therapeutics and for designing improved therapies. A key to addressing this challenge is to apply mathematical and computational modeling methods to biological problems. Within their own research programs and through interactions with the Broad Institute and the Computational and Systems Biology Initiative, CCR investigators are actively pursuing both the acquisition of large data sets and the development of new approaches to interpret and utilize the information. These activities currently include gene expression array analysis, systematic genetic and proteomic approaches to the cell cycle and other cell biological processes, transcription factor profiling, and signal transduction network analysis. CCR investigators involved in these projects include Lander, Yaffe, Lauffenburger, Sorger, Young, Jaenisch, Samson, Amon, Bell, Jacks, Lees, and Hynes.

In addition to its strengths in basic research, the CCR performs an important role in training future researchers in biomedical science, including undergraduate and graduate students, as well as 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 and pharmaceutical industries. Thus, research in the CCR has a major impact both on the fundamental understanding of cancer and on 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 18, 2004, the CCR hosted its third annual scientific symposium on the molecular basis of cancer, entitled "The Small RNA Revolution: Biology, Technology and Disease," featuring nine renowned researchers, including Phillip Sharp, CCR founding member and winner of the Nobel Prize in physiology or medicine.

A major strength of the center remains its attractiveness as an environment for the training of young scientists. The center has 41 graduate and undergraduate students and 59 postdoctoral fellows/associates.

Faculty Awards

It is a pleasure to report the following honors and awards to faculty of the center during this past year: Nancy Hopkins received the Radcliffe Institute Graduate Medal and became a member of the National Academy of Sciences; Phillip Sharp received the University of Illinois Alumni Achievement Award and was made an honorary member of the National Academy of Sciences, Republic of Korea; and Jacqueline Lees and Jianzhu Chen were promoted to professor.

Tyler Jacks

Director

Koch Professor of Biology

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