

## Investing to Achieve

The research enterprise at UMMS continues to grow with unprecedented momentum, built upon extraordinary success.



As part of the explosive change in biomedical sciences in the past decade, the University of Massachusetts Medical School has responded with an ambitious investment in its research endeavors, including the recruitment of stellar faculty from around the world and the addition and upgrade of laboratory space across the campus.

## Building to Explore

In its pursuit of the next generation of medical research challenges, UMMS continues to invest in its facilities to promote a thriving research enterprise. In addition to the Aaron Lazare Medical Research Building, which added nine floors and 360,000 square feet of laboratory space to the Worcester campus when it opened in 2001, major renovations or additions to research space have been implemented in the campus's main building.

The most recent initiative, undertaken for the Department of Radiology's Neuroimaging and Intervention Division, includes the renovation of more than 8,000 square feet for a Radiology Imaging Research Suite featuring first-of-its-kind Philips

Growth is reflected in increased funding levels. Among all 125 medical schools in the nation, UMMS is in the top third in the rate of growth of grant funding and fourth in the number of grants awarded. Over the last seven years, total extramural funding has nearly doubled, from \$89 million in FY '98 to \$174 million in FY '05. Eighty percent of all research funding is received from the National Institutes

of Health, and National Centers of Research in AIDS, Diabetes, Chemical Biology, and Immunology and Biodefense are located at UMMS. The UMMS research enterprise has led to stimulating advancements in the treatment of disease and injury, as scientists investigate the causes of and cures for the most devastating diseases of our time, including diabetes, cancer, HIV/AIDS, heart disease, stroke, arthritis and neurodegenerative diseases. Breakthroughs in these areas are being successfully moved from the laboratory to the clinic, and UMMS efforts are reflected in the increasing number of invention disclosures, patent applications and awards and licensing agreements. In 2005, approximately \$5.7 million was generated from UMMS research faculty activity. RNAi technology is the top licensing revenue generator for UMMS at \$4.5 million through September 2005. (Read more about the revolution RNAi has sparked on page 1.)

Medical Systems MRI technology. The suite includes procedure rooms, reception and waiting areas and office space, as well as laboratories that support MRI research. The division's director is a world-renowned radiologist who has made pioneering contributions to the development of various endovascular procedures, which are now established treatments. This latest project complements a wave of renovation at UMMS over the past several years, in which virtually every academic department devoted to the basic sciences experienced extensive laboratory renovation. In addition, a new Clinical Trials Unit also opened, emphasizing the commitment to translate basic research breakthroughs into effective clinical applications.

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With a dramatic increase in external funding, a nationally renowned faculty and impressive laboratory facilities, UMMS is rapidly achieving its goal of national distinction in biomedical research.

# RESEARCH ENTERPRISE

AT THE UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL

FOURTH EDITION

## RNAi: A Scientific Tool with Broad Applications

RNA interference (RNAi) is considered the state-of-the-art method by which scientists can experimentally knock out the expression of specific genes in lab experiments to help define the biological functions of those genes. RNAi interrupts the way genes create proteins, the substances that activate and regulate the body's metabolic functions. It also has the ability to block the creation of harmful proteins produced by mutant genes—hence its use as a vital tool in research focused on specific diseases such as diabetes, HIV/AIDS and cancer.

Scientists theorize that RNAi has been turning off genes for millennia, working as a primordial immune system to protect our ancestral DNA. Yet, previous investigations of RNA (ribonucleic acid) focused on its role as a messenger in the cell, transporting genetic information from the DNA in the cell's nucleus to the ribosomes, the cell's protein factories. This changed in 1998, when Howard Hughes Medical Institute Investigator and Blais University Chair in Molecular Medicine Craig C. Mello, PhD, and Andrew Fire, PhD, then of the Carnegie Institution of Washington, jointly published the

results of an experiment in the journal *Nature* that dramatically enhanced the scientific community's understanding of RNA in biology.

The pair demonstrated that small pieces of double-stranded RNA, which comprise many viruses, had the unanticipated property of silencing—or

“It has been extremely exciting and rewarding to see RNA interference grow as a research tool and field of study—from a strange phenomenon in a simple microscopic worm into so many exciting new discoveries and a whole new research field.”

— Howard Hughes Medical Institute Investigator and Blais University Chair in Molecular Medicine Craig C. Mello, PhD

CO-DISCOVERER OF RNA INTERFERENCE

interfering with—the expression of a gene whose coding sequence of DNA was similar to that of the RNA they tested. This discovery, hailed as the 2002 “Breakthrough of the Year” by the journal *Science*, was taken further by UMMS Professor of Biochemistry & Molecular Pharmacology Phillip D. Zamore, PhD, who shed light on how the phenomenon worked by indicating that it is small double-stranded RNA, the result of an enzymatic chopper he named “dicer,” which precisely guided the silencing reaction Mello and Fire identified.

Since Mello and Fire's seminal publication describing their breakthrough and Zamore's findings regarding its biochemical application, RNAi has revolutionized research in laboratories around the world. At UMMS, researchers are taking full advantage of RNAi technology to speed

investigation into a variety of diseases; outside UMMS laboratories, 49 companies at the forefront of pharmaceutical innovation have purchased licenses to RNAi technology, co-owned by UMMS and the Carnegie Institution. In 2005, the commercial market for RNAi-related products and services was prospected to reach \$450 million, according to *The BioWorld RNAi Report*.



For more information on the UMMS research enterprise contact: Office of Research, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA 01655-0002 508-856-1572 [www.umassmed.edu](http://www.umassmed.edu)

## Faculty Excellence

UMMS is home to a cadre of outstanding scientists who have realized the following prestigious accolades, appointments and achievements:



**Election to the NATIONAL ACADEMY OF SCIENCES; 2005 recipient of THE LEWIS S. ROSENSTIEL AWARD FOR DISTINGUISHED WORK IN BASIC MEDICAL RESEARCH, THE GAIRDNER INTERNATIONAL AWARD and THE MASSRY PRIZE**  
Craig C. Mello, PhD, Howard Hughes Medical Institute Investigator and the Blais University Chair in Molecular Medicine at UMMS, has been heralded along with colleague Andrew Fire, PhD, for the discovery of RNA interference (RNAi), which offers astounding potential for understanding and manipulating the cellular basis of human disease. Dr. Mello is a previous award winner of the Wiley Prize in Biomedical Sciences and the National Academy of Sciences Award in Molecular Biology.

### THE BANTING MEDAL FOR SCIENTIFIC ACHIEVEMENT

The Banting Medal is the highest scientific honor given by the American Diabetes Association in recognition of the recipient's long-term achievement in the study of diabetes. Aldo Rossini, MD, the William and Doris Krupp Professor of Medicine and director of the UMMS Division of Diabetes, received the honor for his efforts in the area of type 1 diabetes. Michael P. Czech, PhD, chair of the UMMS Program in Molecular Medicine, received the medal for his research focused on type 2 diabetes.

### A MEMBER OF THE ROYAL SOCIETY

Roger J. Davis, PhD, the H. Arthur Smith Chair in Cancer Research and a Howard

*UMass Medical School has experienced one of the highest growth rates of funded research in the country.*

Hughes Medical Institute Investigator at UMMS, is a member of the Royal Society, founded in Great Britain in 1660. The Society elects members for their contributions to fundamental research and in leading and directing scientific and technological progress in industry and research establishments. Past members include Sir Isaac Newton, Charles Darwin and Albert Einstein.

### HOWARD HUGHES MEDICAL INSTITUTE (HHMI) INVESTIGATORS

One of the most esteemed groups of scientists in the world, HHMI investigators are selected from among the faculties of the nation's finest universities and academic health centers. UMMS is home to three HHMI investigators: Roger J. Davis, PhD, the H. Arthur Smith Chair in Cancer Research; Michael R. Green, MD, PhD, the Lambi and Sarah Adams Chair in Genetic Research; and Craig C. Mello, PhD, the Blais University Chair in Molecular Medicine.

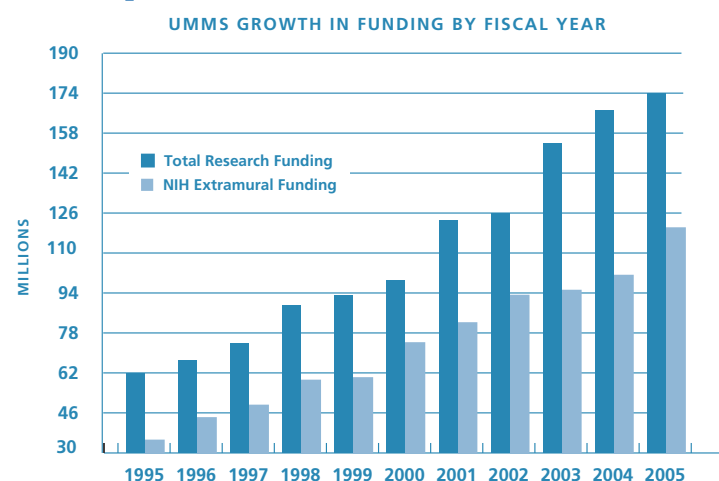
### PEW SCHOLAR IN BIOMEDICAL SCIENCES

Launched in 1985 by the Pew Charitable Trusts, the Scholars program provides crucial support to investigators in the early- to mid-stages of their careers who show outstanding promise in the basic and clinical sciences. Lambertus (Bert) van den Berg, PhD, UMMS assistant professor of molecular medicine, was one of 15 scholars chosen in 2005 from a national pool of candidates; he receives \$240,000 to support his research over a four-year period.

### RAPID ACCESS TO INTERVENTION DEVELOPMENT AWARD (RAID)

Chair of the Department of Cancer Biology Dario C. Altieri, MD, received the award from the National Cancer Institute for the clinical development of an anti-cancer agent called shepherdin (details at right). Dr. Altieri's was the only accepted proposal in the project cycle, testament to shepherdin's promise.

## Explosive Growth



## Research Accomplishments

During the last three decades, UMMS researchers have aggressively pursued the most complex medical challenges. The following list represents recent milestones in the research enterprise:

- **A unique new HIV vaccine approach that incorporates DNA from multiple strains of the virus shows promise for generating antibody and T-cell responses in otherwise healthy people.** These preliminary findings, presented by UMMS scientists and Advanced BioScience Laboratories, Inc. at the AIDS Vaccine 2005 International Conference, resulted from a Phase I clinical trial designed to test the safety of the vaccine and to monitor its ability to generate immune responses.
- **UMMS investigators have redefined human cell division.** The investigators found that when a cell divides, one of the new "daughter" cells actually causes the separation by blasting away from the other; the "older cell" is then marked as such with a protein-packed ring structure. This finding could lead to new research on cell aging and potentially, stem cell division.
- **UMMS investigators, working with colleagues from the University of Toronto, discovered that a known marker for Alzheimer's disease is abnormally low in spinal fluid at least 4 to 12 years before the expected onset of symptoms** in a group of subjects with a gene mutation that almost guarantees they will develop the early-onset familial form of the disease. The findings may have an impact on the development of therapies that could be initiated years before high-risk individuals develop symptoms.
- **A research development by the UMMS Massachusetts Biologic Labs and Medarex, Inc. may lead to an effective treatment for C difficile-associated diarrhea**—an ailment that afflicts more than 300,000 hospitalized patients every year. The investigators have initiated a Phase II clinical trial of CDA-1, a novel, fully human monoclonal one-dose antibody developed to inhibit *Clostridium difficile* Toxin A, an endotoxin present in hospitalized patients diagnosed with the disorder.
- **A licensing agreement between UMMS researchers and SpermaTech AS of Oslo will lead to the production of a promising drug target for a male birth control pill**—without any apparent side effects. The target is a protein found only in sperm cells that regulates the sperm's motility.
- UMMS researchers have also introduced the following breakthroughs in biomedical science over the past four decades:
  - **Discovery of the link between the immune system and type 1 diabetes**, regarded as the pivotal moment in determining the disease's origins;
  - **Discovery of cancer detection technology** that may predict the onset and severity of certain cancers before a tumor actually forms;
  - **Discovery of a genetic cause that underlies the third most common form of the muscular dystrophies**; the finding may ultimately lead to the first effective treatments;
  - **Discovery that HIV is fundamentally different from other types of retroviruses** due to its ability to infect the macrophage, a sentinel of the immune system.
- **UMMS investigators, in collaboration with colleagues in Italy and at the Moffitt Cancer Center in Florida, created a molecular anti-cancer agent that selectively kills tumor cells while sparing normal cells nearby.** The agent, named shepherdin, interferes with a protein that aids in unchecked proliferation and growth of cancer cells and is active on a variety of cancer types, making it suitable for broad therapeutic applications.
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- **A novel human monoclonal antibody that can neutralize multiple variants of the rabies virus has been developed by a team of scientists at the UMMS Massachusetts Biologic Laboratories and the U.S. Centers for Disease Control and Prevention.** Worldwide, rabies remains a significant problem; monoclonal antibodies can be produced in large quantities at lower costs than blood products and are easier to distribute to remote sites.