

Impact. It is defined in the Merriam-Webster Dictionary as "the force of impression of one thing on another: a significant or major outcome." At the University of Massachusetts Medical School, we are committed to making an impact in health sciences education, research and public service both for the Commonwealth and the nation. This impact takes the form of training physicians, scientists and nurses; making research discoveries to prevent and cure disease; providing expertise to many state agencies; and enhancing our special relationship with UMass Memorial Health Care. This annual report describes examples of such impact.

Before the summer of 2002, most Americans read or heard the words "West Nile virus" and imagined an exotic disease restricted to the banks of the ancient river. But when people across the country began to contract the sickness and suffer its effects, the UMMS Center for Infectious Disease and Vaccine Research was already conducting important research on the molecular basis of West Nile virus in order to develop effective vaccines. In the pages of this report, you'll read about the center's impact on the efforts to combat illnesses that plague developing countries—and, because our world is indeed so small—threaten the U.S. as well.

Another example of our impact through research is the discovery of the genetic cause of a neuromuscular disorder called facioscapulohumeral muscular dystrophy, the third most common form of muscular dystrophy. This discovery was the result of long-term collaboration between a UMMS research team and colleagues in Italy. Program project grants and research consortia, both growing trends at our institution and further described in this report, are all about alliances we forge and how they drive our objective to understand the complexities of diabetes, cancer, HIV/AIDS, mental retardation and other afflictions.

What helps us make an impact in our research enterprise? Collaborative creativity, and it emanates from ongoing interactions between our faculty and students. Each year, UMMS encourages attendance from both groups at its Research Retreat, where science is shared and future directions are envisioned. As detailed in the following pages, the 2002 Retreat gave three Graduate School of Biomedical Sciences students the opportunity to enhance their scientific knowledge through face-to-face discussions with faculty from the institution's diverse research areas. In the words of one participant, "the Retreat provides a chance for all to make connections that promote interdisciplinary research and make this a superb academic institution."

Our medical students testify to the impact we are making every day in our mission of education, and nationally we have been recognized by *U.S.News & World Report* as fifth in the nation (out of 125 medical schools) in the 2002 Primary Care Rankings. The training of qualified and compassionate physicians and graduate nurses is critical to our core values.

Finally, we make an impact on the quality of care at our sister institution, UMass Memorial Health Care. Its affiliation with the Medical School attracts nationally distinguished physicians who are experts in the latest treatments and provide an educational atmosphere that brings out the best in our physicians and nurses. In this report, you'll meet the new leader of our clinical partner, John G. O'Brien, someone who shares my enthusiasm for the potential of our two great institutions. Together we know we can—and will—make an impact.

Aaron Lazare, MD

The Year in Review 2002



The University of Massachusetts Medical School and UMass Memorial Health Care have long-term plans for growth and development on the University Campus, essential to their complementary missions of education, patient care, research and service. Currently, facilities the institutions have outgrown, changes in health care delivery and the challenges of working in a structure that has seen a generation of continuous use limit the ability to perform as effectively and expansively as the region demands. To meet these current and future demands, UMMS and UMass Memorial initiated planning in 2002 for a complex array of projects that will change the face of the University Campus and its academic health center.

This Campus Modernization project represents critical capital

investments by the University and by UMass Memorial Health

Care, supported by the Commonwealth and the philanthropic

generosity of the people of the region. UMMS and UMass Memorial

are working together to encourage the successful integration and

coordination of these projects in order to minimize inconvenience

to patients, visitors, faculty, physicians and staff as much as possible;

and maximize the value of the capital investment, allowing them

to accomplish improvements neither institution could as effectively

complete alone. "The outcome will be a better facility than if work

Chancellor and Dean Aaron Lazare and UMass Memorial President

proceeded separately—an academic health sciences campus of

exceptional distinction, one in which we all can take pride and that the people of Central Massachusetts deserve," said UMMS

and CEO John G. O'Brien, in a joint statement in November.

and goodwill of thousands of UMass Medical School and UMass

Memorial employees, we'll do everything we can to minimize the impact on those who depend on the campus for education, care, employment and scientific

discovery. And, our commitment is that the safety of our patients, students and employees comes first."

An intensive period of analysis, planning and conceptual design began in the fall. This January, some interior space and structural changes to accommodate the expansion of clinical space were made. This spring, the façade and window system component will begin in earnest, and architectural conceptions of the new University Campus will be presented. Monitor the progress via the UMMS Web site at www.umassmed.edu/campusrevampus.

Through a carefully planned process, the assembly of a team of skilled construction and architectural/engineering experts and a committed leadership, the project's key elements will become reality between now and 2006. They include replacement of the exterior granite façade and window system; redesign and improvement of campus building entrances, walkways and exterior signage; expansion of the emergency department, catheterization labs, operating rooms and endoscopy suites; remodeling and expansion of space for diagnostic radiology, including on-site MRI; and construction of an additional parking garage. UMMS hired Bovis Lend Lease, one of the world's most experienced and well-respected construction management firms, to oversee Campus Modernization. Payette Associates, one of the nation's premier architectural/engineering firms experienced in health care and academic institutions, will design the facade, window system and entrance elements.

"Large and important changes are coming as a result of Campus Modernization," said Dr. Lazare and CEO O'Brien. "There will be inconvenience, but through the resourcefulness, patience

■ The Campus Modernization Project is the comprehensive renovation and expansion initiative of UMass Medical School and UMass Memorial Health Care.

Assistant Vice Chancellor for Commonwealth Medicine Patricia K. O'Day thrives on change. Attracted to the multitude of issues and opportunities that could arise from the potential number of health-related service programs to be offered by Commonwealth Medicine, she joined the endeavor in 1997. Five years later, her commitment to developing, implementing and growing those programs to benefit the state's most vulnerable populations has earned her one of the 2002 Manuel Carballo Governor's Awards for Excellence in Public Service. Presented annually to 10 state workers who exemplify

more than a decade with the Department of Public Welfare, where she improved office operations and developed performance measures that streamlined health care for over 600,000 Medicaid clients, she served as chief operating officer for the Lemuel Shattuck Hospital. There, O'Day was instrumental in efforts to refocus the institution's mission, transforming it into a primary provider of ambulatory and inpatient services for the Massachusetts Department of Public Health, offering a complete continuum of care to particularly vulnerable populations.

■ A commitment to developing, implementing and growing programs to benefit the state's most vulnerable populations has earned O'Day one of the 2002 Manuel Carballo Governor's Awards.

"the highest standards of public service through exceptional accomplishment, superior leadership, creativity and productivity," O'Day's Carballo Award is the fifth presented to a UMMS employee in the last seven years.

O'Day's career has been characterized by efforts to employ creativity in the challenging environment of public service agencies. After

From promoting qualitative, cost-effective and comprehensive disability determinations through Disability Evaluation Services to encouraging specialized case management to individuals with developmental disabilities who reside in nursing homes through the Nursing Home Initiative, O'Day has helped guide Commonwealth Medicine toward meeting its goal of partnership



with the state's human service agencies to optimize efficiency, increase the value and quality of health care expenditures. and improve access and delivery of care. According to Chancellor and Dean Aaron Lazare, "In all of the programs that Patty has administered, she has successfully promoted quality and efficiency, even in the face of seemingly impossible odds. Patty has been able to perform these 'miracles' because she is nothing short of a visionary who brings private-sector thinking to public-sector programming."



Anthony Carruthers, PhD, was appointed the new dean of the Graduate School of Biomedical Sciences in December. Dr. Carruthers, a member of the UMMS faculty since 1983, replaces Thomas B. Miller Jr., PhD, who retired in June.

A highly regarded professor in the Department of Biochemistry & Molecular Pharmacology and internationally recognized for his research of glucose transport across membranes, Carruthers received his doctoral degree in physiology from King's College London. He served as a visiting scientist with the Marine

Biological Association of the United Kingdom and as a postdoctoral research associate in the Department of Physiology at King's College before joining UMMS in 1982 as a research associate. He became assistant professor of biochemistry in 1983, associate professor of biochemistry and physiology in 1990, and professor in 1996. He served as interim chair of biochemistry & molecular pharmacology from 1997-2001.

Leslie Berg, professor of pathology and chair of the search committee that identified Carruthers, said, "As Tony has been at UMMS for most of his academic career, he has a deep understanding of the institution and is committed to the graduate program.'

As dean, Carruthers will lead a vibrant and valued part of the educational and research components at UMMS. The GSBS attracts a select group of students each year, who benefit from the continual growth of a research enterprise currently receiving \$135 million annually and faculty recognized throughout the

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world for their innovative investigations on the cutting-edge of biomedical science. Carruthers' NIH research has led to significant revision and expansion of the understanding of glucose transport. "My research remains a life-motivating interest," said Carruthers. "I am delighted to share my passion for research with the student body.'

Vitae 2 Vitae Annual Report 2002 Annual Report 2002

The Year in Review



Drs. Majno, Wheeler and O'Donnell

The Worcester District Medical Society (WDMS), representing over 1,400 physicians and medical students in Central Massachusetts, chose UMass Medical School faculty for all three of its major awards presented at its Fall District Meeting in November.

The A. Jane Fitzpatrick Community Service Award honored H. Brownell Wheeler, MD, the Harry M. Haidak Distinguished Professor of Surgery *Emeritus*, who has served his patients as a caring, highly skilled surgeon; UMMS as founding chair of surgery; and the WDMS as both founding chair of its End-of-Life Committee and president from 2000-2001. Dr. Wheeler has mentored countless students, residents and young faculty, and built a fledgling academic department of surgery into one of national and international distinction. He has also helped to bring together Worcester's community of physicians and its existing hospitals in long-lasting partnerships.

The President's Award, given only when physicians of exceptional stature are nominated, recognizes individuals for their extraordinary contributions to the health of the community. Recipient Guido Majno, MD, professor *emeritus* and former chair of pathology, who retired after 30 years at UMMS in fall 2002,

☐ The Worcester District Medical Society recognizes physicians who go above and beyond to serve humanity and contribute to our community.

has achievements on multiple fronts. He is revered as a teacher by his students; distinguished as a research scientist; and noted as a clinical diagnostician who advanced understanding of health and disease at the cellular, molecular and genetic levels.

The Career Achievement Award honors a member who has demonstrated compassion and dedication to the medical needs of patients and the public, and has made significant contributions to the practice of medicine. Recipient Daniel O'Donnell, MD, assistant professor of family medicine & community health, shows his commitment to individuals and communities from all socioeconomic levels as medical director of Worcester's Great Brook Valley Health Center. Dr. O'Donnell blends an active clinical practice with his administrative duties, and integrates quality care for individuals with improving care for the community through clinical research.

Chancellor and Dean Aaron Lazare spoke before an international audience of 500 in August at the Centre for Initiatives of Change in Caux, Switzerland. His Caux Lecture topic was on the healing power of apology, an especially appropriate one for the annual conference, which includes an Agenda for Reconciliation program for people from regions currently in conflict. According to Initiatives of Change, the organization credited with enhancing relations between Germany and France follow-



ing World War II, "durable peace depends on genuine processes of healing the past. When people have been at war or have suffered at the hands of others, building trust takes courage and is often painful. It involves a process of acknowledging past wrongs, and expressions of apology leading, when possible, to explicit acts of both restitution and forgiveness."

Dr. Lazare, a national authority on the subject of shame and humiliation in medical encounters and an expert on the apology process, described the offering and

acceptance of apologies as "one of the most profound interactions of civilized people. Apology is the only cure for a humiliation, to break the circle of grudges and vengeance." Apologies have grown in importance, he theorized, because the turn of the millennium called for "a fresh start, soul searching, a clean slate, a moral reckoning," that contributed to an "explosion of apologies in the 1990s," including that made by Pope John Paul II for the so-called wrongs of the Catholic Church. "All of a sudden, apology became important—and I believe it will stay that way," Lazare noted.

Outlining the four parts to an apology—acknowledgment of the offense; communicating remorse, forbearance and shame; offering an explanation for the offense; and making reparations—Lazare said that even a gesture can be enough, citing the Pope's visits to the Wailing Wall and Yad Vashem, the memorial to the Holocaust in Jerusalem. He gave examples of a false apology—using the passive phrase "mistakes were made" instead of saying

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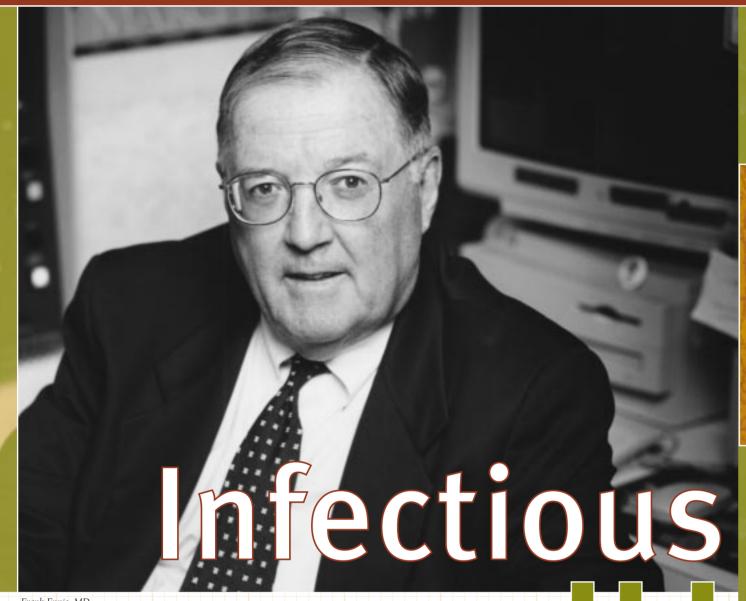
"I made mistakes"—and discussed instances of genuine apology, including from a German president for his country's crimes in World War II, and the head of the U.S. Bureau of Indian Affairs for the suffering of Native Americans.

Lazare answered questions from audience members, who had traveled from Ivory Coast, Burundi, Angola and India, among some 70 other countries. "I was moved to see how completely this diverse audience had understood and accepted the major points of the talk: that the management of dignity is perhaps the greatest challenge to interpersonal and international relations, and that apology is the best—and perhaps only—cure for humiliation," Lazare noted after his return to UMMS.



The Lamar Soutter Library celebrated completion of renovations in December. "Some people come into the library to use the computers, while others wish to get away from the day-to-day grind and read the current journals or browse the stacks. We needed a combination of spaces that would not only provide areas to sit and do work, but also allow people some space to relax," explained Elaine Russo Martin, MSLS, the Library's director. "In the end, although we have the same number of workstations, computers and seating, the more comfortable and efficient arrangement enhances our services." Changes include the reconfiguration of computers into individual cubicles to promote privacy; a new circulation desk, which makes all library loan and circulation services more accessible; the relocation and reconfiguration of the reference desk and disbursement of photocopiers throughout the library to improve customer access; and the purchase of lighted work tables, sofas and chairs to improve patron comfort.

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Frank Ennis, MD

Lavesdrop on the weekly two-hour staff meeting of the UMMS Center for Infectious Disease and Vaccine Research (CIDVR), and you might forget you're in a laboratory in the cold northern hemisphere where mosquitoes die each fall and public health policies keep our water potable and our children immunized.

The eight faculty and 30 postdoctoral fellows, graduate students and research staff of the CIDVR regularly tangle with viral pathogens such as West Nile virus, hantavirus, Japanese encephalitis, dengue fever, yellow fever and smallpox, in addition to more familiar infectious diseases like hepatitis C, HIV and influenza. Although some of these viruses haven't crossed our borders recently with significant impact, their history of devastation in developing countries makes them a serious concern. The World Health Organization (WHO) predicts environmental and social determinants of infectious disease transmission will only expand in

the coming decade: another billion people in the world, continued urbanization, and changes in global climate and local weather patterns increase the likelihood that these emerging and re-emerging viruses will become more familiar.

"Although still largely unseen in our country, many of these diseases are commonplace elsewhere," said Francis A. Ennis, MD, professor of medicine and molecular genetics & microbiology, and director of the CIDVR. "The developing world simply doesn't have the resources needed to combat disease and create vaccines." That task falls to researchers like those in the CIDVR.

who have dedicated their careers to understanding the molecular basis of human diseases caused by infectious agents and to the development of safe and effective vaccines against these agents. CIDVR faculty and staff focus on the disease process itself, scrutinizing the molecular mechanisms of the human T lymphocytes that dictate the immune response—or overresponse—to infection. The researchers employ clinical research, cell culture and molecular biology approaches and call upon their colleagues in immunology, pathology and molecular genetics in other UMMS departments.

By Alison M. Duffy

Members of the UMMS Center for Infectious Disease and Vaccine Research study the minutiae of molecules to create vaccines for global impact.

> With a budget of nearly \$4.5 million, both in the U.S. and around the world, have overseen clinical trials since the late to serve on key committees of the WHO, with the New York State Department of

million subcontract as part of an NIH initiative to understand itself with flu-like symptoms.

regions to obtain blood samples from

Similarly, fears of an intentional release of and domestic debate about the possible CIDVR is at the forefront. Faculty are currently studying the efficacy of diluted inadequate should there be a smallpox examining the human memory in T-lymreceived in infancy, indicating that immunity might last far longer than originally whether it might render revaccination

Such research is fueled by the active interest of not only the CIDVR faculty, but also graduate students and fellows involved the training component exposes physicians, and creative, which is critical in this field." In the last two decades, more than 30 CIDVR, innovative thinkers who then fan out across the globe to battle the viral pathogens threatening the population. 'Through our training and our research UMass Medical School," said Ennis, "I believe we're making a difference."

Progression in immunology has resulted recently from better understanding of how in Medicine in 1996. Additional data have lead to better understanding about the

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A major NIH grant to UMMS and four other prestigious institutions accelerates type 2 diabetes research.

Gaining from the _____ Genome

By Andrea L. Badrigian

ncredible excitement surrounded the announcement in June 2000 that a "rough draft" of the human genome had been produced. An overarching objective of the worldwide Human Genome Project (HGP) — begun over a decade ago to identify all of the genes in human DNA and ascertain the sequence that makes up that DNA—the draft's unveiling meant that 90 percent of the sequence was complete, with a "finished manuscript" just over the horizon, now expected sometime this year.

The fields of genomics and proteomics are, simply, the study of the DNA words that instruct the making of proteins, the actual building blocks of the cell. Both fields have accelerated dramatically in the wake of the successful HGP. Researchers have, of course, for some time realized the fundamental role genes play in disease development and progression—but now they are gaining access to genetic information on a grand scale that allows for the molecular pinpointing of "mistakes" made by genes as they direct human cells how to act, or act out. The National Institutes of Health (NIH) has responded quickly, supporting research endeavors aimed to mine the wealth of information provided by the HGP. One such effort is the Diabetes Genome Anatomy Project, funded in October 2002 with \$10 million over five years, and granted to a consortium comprising UMass Medical School, Joslin Diabetes Center, Dana-Farber Cancer Institute, Children's Hospital and Massachusetts Institute of Technology.

The project's principal investigators at UMMS are Michael P. Czech, PhD, chair of the Program in Molecular Medicine, and Silvia Corvera, MD, professor of molecular medicine. They feel an excitement not unlike that experienced at the time of the "rough draft" announcement. "Each partner in this consortium brings unique capabilities and technologies to take advantage of the spectacular revolution in gene discovery so that we can further understand type 2 diabetes," said Dr. Czech. "We are truly at the frontier of great discovery."

"It is an extraordinary privilege and incredibly inspiring to be a part of a consortium such as this in which each scientist realizes that attacking a problem as complex as diabetes is beyond the capabilities of a single lab," Dr. Corvera added. "We've all been friendly competitors; now the data from this project will be presented without thoughts of authorship, and with a conviction that our

best bet is to work together. UMass Medical School is honored that the NIH has given this concept a shot."

The Diabetes Genome Anatomy Project, or DGAP as it is called by its investigators, takes the Human Genome Project further, with the goal to reveal "the sets of genes and gene products involved in insulin action and the predisposition to type 2 diabetes, as well as the secondary changes in gene expression that occur in response to the metabolic abnormalities present in diabetes," according to the grant submission. Six projects and four cores form the DGAP; Czech heads Project 3—the anatomy of gene expression—while Corvera directs the Proteomics Core for Project 3 with UMMS colleague John D. Leszyk, PhD, another leader in the field. Three additional UMMS researchers, Sarah Coulter, Varsha Patki, PhD, and Sabina Semiz, MD, add to the complement of 12 other scientists and labs making up the consortium. Their findings will be used to create an interactive database, protocols for gene expression and proteomic analysis and "gene chips," all for use by researchers in the field.

"One of the most exciting aspects of this consortium is that the data will get a fast track into the public domain through a Web site providing information from all five sites, in some cases before publication," explained Czech. "The consortium members are presenting this data to each other literally as it is coming off the instrumentation—this results in a great acceleration of the discovery process because we are talking at early stages of our thinking."

Corvera explained that the free and immediate flow of information is an imperative of the NIH. "The data must be made available to research enterprises as quickly as possible. This helps avoid duplication worldwide, something that has been a problem. In addition, we will establish a common language for diabetes research.



Michael Czech. PhD

We'll explain these experiments in a way that they can be compared and from which conclusions can be easily drawn."

The DGAP will use "gene chips" to analyze the activities of massive numbers of genes simultaneously. Approximately the size of a fingernail, each chip will be infused with sequences from as many as 12,000 genes to allow analysis of their function. "We'll be able to read very quickly gene functions that differ, for example, in the various states of diabetes," noted Czech, "providing us snapshots of the genes at particular points in time, revealing their activity or inactivity, their defectiveness or responsibility for different aspects of the disease."

The DGAP is a revolutionary result of the Human Genome Project, itself a spectacular accomplishment that we look forward to applying to the disease of diabetes," Czech concluded. "We have our mandate and the expertise, equipment and energy to see it through."



Silvia Corvera, MD

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A Strong Bond

By Mark L. Shelton

he new president and chief executive officer of UMass Memorial Health Care, John G. O'Brien, speaks plainly about the partnerships he envisions—and has already begun to nurture—with the Medical School, the medical staff, the department chairs and the community:

"We simply have to have a relationship that will develop and flourish, because our interdependence is our strength. My first and last word about the school and the chairs is that 'we're partners.' The successes of the Medical School in research, in teaching, in training and recruitment, in outreach, match up perfectly with our future prospects. In a way, it's like an epoxy: two compounds that, when combined, form a strong bond—far stronger than either on its own. That's the future of UMass Memorial."

O'Brien's gift for not only speaking plainly, but for his ability to lead, his ability to manage and—notably, after 25 years at Cambridge Health Alliance (and more than 15 years as its chief executive)—his ability to achieve, are well-known regionally and nationally. Under his leadership, a once small, financially ailing city hospital was transformed into the fiscally viable, integrated Cambridge Health Alliance health care system. In 1993, on behalf of the staff of Cambridge Hospital, O'Brien accepted the Foster G. McGaw Prize, a coveted award given by the American Hospital Association to a single hospital in the United States each year that displays its utmost commitment to improving the health status of its community. And what he sees when he looks at UMass Memorial is "tremendous opportunity."

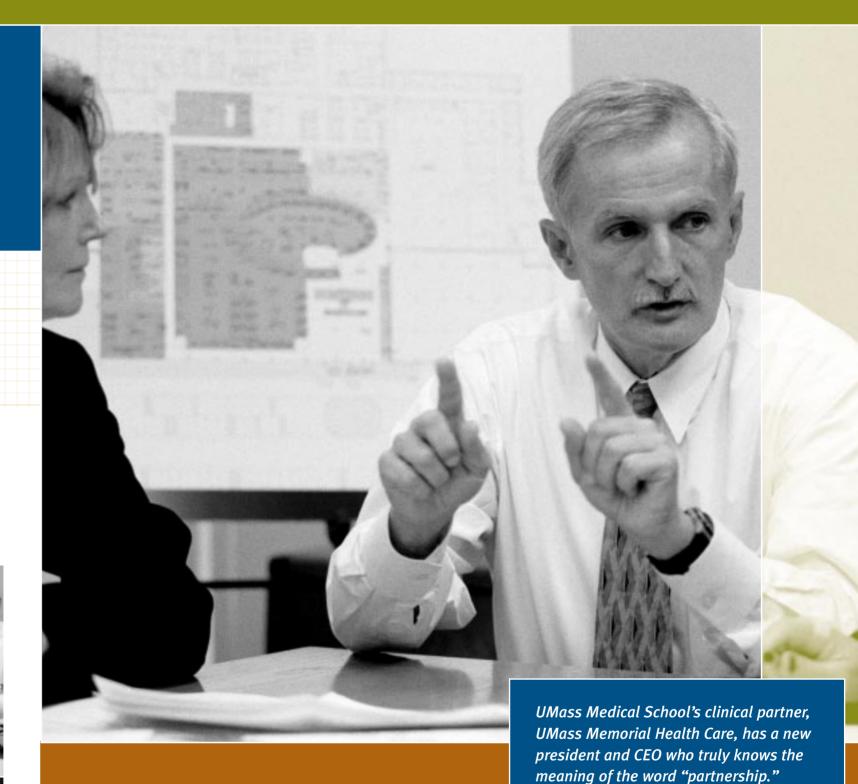
"This is a health care system that has been in some distress," he observed, "but that distress doesn't obscure its potential. As we do our work here, as we invest in the facilities and in the workforce, as we develop better access, better models for care and better systems to serve the patients, people will see just how much we can accomplish. The department chairs and the leadership of the medical staff will have significant responsibility to be more prominent and more active in the clinical administration of the institution, much as they have been with the Medical School. And we're going to work closely with Dr. Lazare and the leadership of the Medical School to facilitate strong relationships that will enhance both of these great institutions."

As O'Brien settles in, he has already become a familiar face around the campus and around Worcester, where he moved during his first week on the job. "It's a challenge," he tells everyone, "there really is so much to do." But as he says this, he's not only doing it, but smiling about it, as well.

John O'Brien with UMass Memorial Medical Center-University Campus President Rita Battles (top) and with Christine Klucznik, vice president for Ambulatory Services at UMass Memorial (bottom).







strong bond

"There is so much work going on here: the research, the medical student and resident training, the role in the community. Some of it, such as the research in the new research building, is brand new to me. Most of it, however, I'm well familiar with. UMass Memorial and its partner, the Medical School, have a great future, and I can't adequately say how excited I am to be a part of it."

Mind Meld

By Sandra L. Gray

The whole is greater than the sum of its parts. That is the simple but powerful premise behind National Institutes of Health (NIH) program project grants. At UMMS, 11 projects gather the collective minds of some of the best and the brightest in their respective departments (and, in some cases, other institutions) to bring their combined expertise and state-of-the-art technological tools to bear on important biomedical questions.









Top, left to right: John Sullivan, MD, and Celia Schiffer, PhD Bottom, left to right: Firoze Jungalwala, PhD, and Gary Stein, PhD

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Program project grants bring out the best in UMMS research expertise, equipment and effort.

Totaling over \$58 million in 2002, the dramatically increasing volume of these grants acknowledges the growth of the UMMS research enterprise as the institution continues to accelerate its expansion. "Project grants are a measure of a maturing research institution, one which has depth and breadth in multiple areas of biomedical research," explained John L. Sullivan, MD, professor of pediatrics and molecular medicine and director of the UMMS Office of Research.

"Our program is a good example of one that cannot be tackled in the context of a single grant format," said Michael P. Czech, PhD, chair of molecular medicine. He is principal investigator of *Membrane topography of cell signaling complexes*, which brings together diverse but equally powerful technologies, from X-ray protein crystallography to four-dimensional microscopy, to understand basic cellular functions that have enormous implications for understanding diseases such as diabetes. "There is a remarkable openness and excitement about other people's work here—a lot of cheerleading goes on among laboratories."

Gary S. Stein, PhD, the Gerald L. Haidak, MD, and Zelda S. Haidak Professor and chair of Cell Biology is principal investigator for two separate but related programs, *Nuclear structure and gene expression* and *Bone cell structure and gene expression*. "On a state-of-the-art campus like ours, with not a single instrument lacking, we can address any problem if people get together," he said. Both projects seek to understand cellular processes involved in cancer and skeletal disorders, in the process expanding investigators' own horizons along with those of the institution. "Bringing many people together expands individual as well as collective knowledge, enhancing each scientist's understanding," Dr. Stein added.

A longstanding project grant, established over 30 years ago at the Eunice Kennedy Shriver Center in Waltham, which merged with UMMS in 2000, exemplifies how such grants help refine research over time. Firoze Jungalwala, PhD, professor of biochemistry & molecular pharmacology at the Shriver Center, was a project leader for many years before becoming the principal investigator of Biochemical & genetic aspects of mental retardation. Recent discoveries under Dr. Jungalwala's direction include identification of molecular signals and mechanisms that regulate and guide neuronal cells to their target during development of the brain and defects in neuronal migration that could cause mental retardation. "Different teams and projects have come into the mix. The flavor of the grant has changed over the years as our research has become more sophisticated and focused," he said.

The most recent UMMS project grant is its first to bring laboratories from several other institutions together with those here. Celia A. Schiffer, PhD, assistant professor of biochemistry & molecular pharmacology, is principal investigator and program director for *Targeting ensembles of drug-resistant HIV proteases*. The multidisciplinary collaboration, which has expertise ranging from patient therapy to organic chemistry, affords Dr. Schiffer and colleagues from Stanford University Medical Center, the University of North Carolina School of Medicine, the University of Maryland/Center for Advanced Research in Biotechnology and the Massachusetts Institute of Technology, the means to make strides against drug-resistant HIV.

Core laboratories are integral to first getting program project grants, then realizing their potential. Dr. Sullivan proudly enumerates the full spectrum of core facilities at UMMS that enable investigators to approach virtually every realm of biomedical inquiry with the best tools and technology available: proteomics, genomics, tissue culture, chemical biology, nucleic acid, to name a few. The UMMS laboratory of Professor Tariq M. Rana, PhD, director of the Program in Chemical Biology, for example, will serve as the Schiffer program's core facility with a combinatorial chemical library of hundreds of thousands of potential drug compounds that can be rapidly and efficiently screened for their therapeutic effects on HIV. The UMMS Biomedical Imaging Group, which invented a unique, four-dimensional microscopy technique and serves as a major contributor to the Czech program, is another example of a core laboratory.

NIH program project grants maximize valuable research dollars while optimizing intellectual as well as technological capital, fostering the evolution of scientific inquiry, refining ever more focused investigations, and developing scientists individually and collectively. "We expect to see more growth in program grants as we expand our research enterprise," said Dr. Sullivan. "They will be instrumental in fulfilling our research mission."

Current UMMS Program Project Grants and Principal Investigators

Gary Stein, PhD, Bone cell structure and gene expression and Nuclear structure and gene expression

John Sullivan, MD, Ontogeny and maintenance of virus-specific T-cells

Michael Czech, PhD, Membrane topography of cell signaling complexes

Celia Schiffer, PhD, Targeting ensembles of drug-resistant HIV proteases

Francis Ennis, MD, Mechanisms of immunopathology in DHF/DSS

Aldo Rossini, MD, Viral infection influence on transplantation tolerance and Mechanisms of islet transplantation tolerance

Lawrence Recht, MD, Neural stem cells and neuro-oncology

Firoze Jungalwala, PhD, Biochemical and genetic aspects of mental retardation

William McIlvane, PhD, Stimulus control in mental retardation

Vitae

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It's all about

the Science

By Kelly A. Bishop

The UMMS Research Retreat provides an annual opportunity for students, fellows and faculty to share their excitement for science.

As one pursues answers to the most complex of scientific problems, bench research can too often become a solitary practice. At UMass Medical School, however, the merits of scientific collaboration are enthusiastically promoted.



With an appreciation for the great potential of individual and interdepartmental relationships to advance scientific inquiry, UMMS has continued to encourage the transfer of ideas at its annual Research Retreat. This year's Retreat, held during the first week of October at the Marine Biological Laboratory in Woods Hole, provided attending Graduate School of Biomedical Sciences students, faculty, postdoctoral fellows and staff the opportunity to share insights, information and intriguing questions related to the basic sciences.

The three-day event organized by the UMMS Office of Research and made possible by the active participation of both clinical and basic science departments, featured faculty and student presentations on a wide range of contemporary and progressive topics. From discussions on survival checkpoints in cancer to the activation of the immune response in the fruit fly, the Retreat's scientific sessions were enhanced by an informal setting and a diverse audience of individuals at various educational and professional levels. This year's Retreat also featured the inaugural Dan Mullen Poster Awards for Scientific Achievement. Honoring the late Dan Mullen, a 30-year veteran of both the Department of Physiology and the former Department of Pharmacology & Molecular Toxicology, the awards recognize students who demonstrate exceptional creativity, quality of science and overall excellence in their poster presentations at the Retreat. This year's inaugural winners—Joshua Fischer,

Alejandro Murad and Todd Pearson—commend the Retreat as a highlight of the academic year.

For Fischer, a third-year doctoral student whose research interests include understanding the mechanisms of Lyme disease that allow the bacterium to affect different physical systems in varied infected organisms, the Retreat showcases the diverse programs that initially attracted him to UMMS. "Every year the focus changes a bit to highlight some of the programs that are lesser known to students as well as expose them to the investigations of other labs. It is an invaluable advertisement for students who are just starting to think about which labs they want to choose."

Now in his second year of GSBS study, Murad credits the casual, amicable atmosphere of the Retreat with fostering meaningful conversations between students and faculty. For Murad, a native of Argentina who chose UMMS for its emerging Department of Neurobiology and its experts on circadian rhythms, such opportunity is particularly valuable. "It is a very comfortable environment because everyone seems to love science and truly enjoy what they do. With so many people attending, you can meet and talk with students and principal investigators that you rarely see on campus."

According to C. Robert Matthews, PhD, the Arthur F. and Helen P. Koskinas Professor and chair of Biochemistry & Molecular Pharmacology, the exposure to others in the research community is invaluable for faculty as well. "The Retreat is a terrific opportunity for our students, postdoctoral fellows and faculty to share their discoveries and their excitement for science. The breadth of activities, the very high quality of the work and the dramatic increase in the faculty cadre are evident in the posters and presentations. The Retreat also provides a chance for all to make connections and build friendships that promote interdisciplinary research and make this a superb academic institution."

Deeply involved in his thesis research into the genetic basis of autoimmune processes and the individual contributions of the dozens of genes that control diabetes, Pearson reiterates Dr. Matthews' sentiments, acknowledging the Retreat for informing him on the continuing growth and success of the UMMS research enterprise. "After your first year of graduate school, you tend to find your own specialty and not pay as much attention to what everyone else is doing. But, especially in the last eighteen months, there has been such an explosion in new investigators that when I went to the Retreat, I was amazed at who is here now and the really great things that they are doing." As a member of the lab of Aldo A. Rossini, MD, the William and Doris Krupp Professor of Medicine, Pearson was especially intrigued by recently appointed Professor of Surgery Giacomo Basadonna, MD, PhD, and his presentation, "Operational Tolerance in Transplantation."

"Dr. Basadonna is doing a lot of the same diabetes research that we are doing. In fact, after the Retreat he came to our lab and gave a seminar. I think the Retreat definitely opens your eyes to the possibility of collaboration within the institution."

Ioshua Fischer, Todd Pearson and Alejandro Murad



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Facts and Figures



20 Million

The number of Americans newly affected by depression each year. In May, the Robert Wood Johnson Foundation awarded a one-year planning grant of \$100,000 to UMMS and the Massachusetts Division of Medical Assistance to develop approaches that improve treatment of depression in primary care. Depression is a significant dimension of illness for many who suffer from chronic conditions such as diabetes, asthma, heart disease, cancer and pain. For many, it is the primary care provider rather than a psychiatric specialist who is on the front line in treatment for depression; primary care providers therefore must have the knowledge and systems to effectively manage this widespread condition. If the grant's planning phase is successful, UMMS will be eligible for additional funding to launch two-year pilot intervention projects to test improved screening, assessment, treatment and management of chronic depression in primary care settings statewide.

2 Million

The number of individuals who will die from tuberculosis worldwide this year. In the slums of Lima, Peru, for example, Multidrug-Resistant Tuberculosis is of grave concern among health care providers, including UMMS alumnus Michael L. Rich, MD '93, MPH, who returned to Worcester as keynote speaker for Commencement exercises in June. A former member of Doctors Without Borders, which received the Nobel Peace Prize in 1999, and a current physician with Partners in Health, a charitable organization based at Harvard Medical School. Dr. Rich also assists the World Health Organization (WHO) as it takes a systematic approach to TB prevention by obtaining political commitment from national governments to reduce the spread of the disease in affected areas. Rich reported in his Commencement address that through the WHO effort, today most of the MDR-TB patients in Peru receive effective treatment and the cure rate has achieved 80 percent.



Million



20,000

The number of completed patient flights the UMass Memorial Life Flight air ambulance program has performed over its 20-year existence, celebrated in September. From the first flight on September 17, 1982, through each of the 34,000 calls and 20,000 completed flights, the program has been a crucial link for accident victims and critically ill patients needing life-saving emergency medical care. The program marked its 20,000th patient mission on June 28 and has trained more than 300 physicians in the latest advances in emergency



The number of genes that cause the most common form of polycystic kidney disease. In a study published in a June issue of the journal Current Biology, a research team led by Gregory Pazour, PhD, assistant professor of cell biology, and George B. Witman III, PhD, the George F. Booth Chair in the Basic Sciences, described new results that provide insight into the cause of the disorder that affects over 12.5 million people worldwide. The Current Biology paper reported that a protein called polycystin-2, previously shown to cause polycystic kidney disease when defective in humans, is present on tiny hair-like structures called cilia that extend from the surfaces of human kidney cells. The findings yield important new clues about how polycystic kidney disease develops. The Pazour-Witman team reported two years ago that defects in kidney cilia assembly could cause polycystic kidney disease in mice. The new discovery demonstrates a link between the cause of kidney disease in mice and humans, and reveals at least one function of the kidney cilia: relaying signals that control cell growth.

The number of physicians trained in geriatrics for every 4,000 Americans over age 65. Less than one percent of the nation's nurses are certified in geriatrics. To better address the health care needs of the aging here in the Commonwealth, the Health Resources and Service Administration of the U.S. Department of Health and Human Services awarded \$645,000 to the UMMS Graduate School of Nursing in September. With the three-year federal training grant, the GSN will enhance its current adult acute care and adult ambulatory nurse practitioner programs with a geriatric specialty. Specificially, the project will expand access to the GSN's gerontological nurse practitioner programs; recruit minority graduate students interested in geriatric care; enhance the curricula of the master's program by focusing on acute and primary care of older adults; develop the cultural competence of program graduates; and promote the health of older residents via clinical preventive service.

FY '02 FUNDING AND REVENUE

State appropriation to schools	\$ 34.1 million
State contracts*	26.7 million
Public service	97.4 million
Research (sponsored activity)	126.3 million
Other revenue sources**	88.6 million

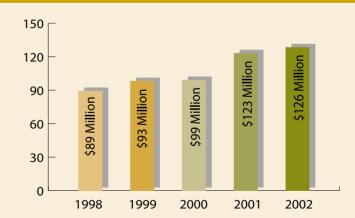
Total \$373.1 million

FY '03 FUNDING AND REVENUE (PROJECTED)

State appropriation to schools	\$ 33.1 million
State contracts*	26.1 million
Public service	100.9 million
Research (sponsored activity)	143.4 million
Other revenue sources**	94.2 million

Total \$397.7 million

RESEARCH FUNDING INCREASE – LAST FIVE YEARS



TECHNOLOGY MANAGEMENT

For Fiscal Year	1997	1998	1999	2000	2001	2002
Invention disclosures	56	42	49	49	49	48
U.S. patent applications	29	30	24	27	50	44
Licensing agreements	6	13	17	14	15	17
Sponsored research agreements	\$3,397	2,494	4,509	2,117	2,450	442
Licensing revenue	\$742	1,897	6,724	8,801	11,678	14,516

(\$ in thousands)

0

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^{*}Provide mental health and pediatric services for those who cannot afford private care.

^{**}Examples are continuing education and student fees, biologic labs and newborn screening programs and other non-state revenue sources.

Facts and Figures (continued)

TEACHING PARTNERS AND AFFILIATES

UMass Memorial Health Care

UMass Memorial Medical Center (Hahnemann, Memorial and University campuses)

UMass Memorial-Clinton Hospital

UMass Memorial-HealthAlliance Hospitals

UMass Memorial-Marlborough Hospital

UMass Memorial-Wing Memorial Hospital and Medical Centers

Berkshire Medical Center

Milford-Whitinsville Regional Hospital

St. Elizabeth's Hospital

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St. Vincent Hospital at Worcester Medical Center

Additional Teaching Affiliates

Barre Regional Family Health Center Community HealthLink Community Health Connections/ Family Health Center–Fitchburg Day Kimball Hospital Fallon Community Health Care Family Health Center-Queen Street Hahnemann Family Health Center Harrington Memorial Hospital Heywood Hospital Holyoke Health Center Holyoke Hospital Hubbard Regional Hospital Lawrence Family Health Center Metrowest Medical Center Noble Hospital South County Pediatrics Tri-River Family Health Center Westboro State Hospital Worcester State Hospital

EDUCATION

Number of Faculty

Full-time 827

Part-time **92**

School of Medicine

MD students 407 PhD/MD students 14 Alumni 2,387

Residents & fellows 532 in UMMS programs

Graduate School of

Biomedical Sciences PhD students 224

PhD/MD students 21

PhD Biomedical Engineering/

Medical Physics (a joint program with WPI) 7

Alumni **190**

Graduate School of Nursing

MS students 59 Post master's students 6 PhD students 32 Part-time students **72**

Alumni **501**

Continuing Medical Education Certificates 19,015

Allied Health Program students 648

The Year In Philanthropy

The Campaign for Research (1999-2002)

The Campaign for Research, the University of Massachusetts Medical School's first major capital fund-raising effort, closed on June 30, 2002, having raised \$41.6 million in cash, pledges and eligible planned gift intentions from approximately 1,300 generous donors. According to Campaign Chair Nancy Edman Feldman, this eclipsed the campaign goal of \$38 million, and the planned timetable of five years.

Highlights of the Campaign for Research include:

- the University's largest-ever charitable gift, \$21 million, from Jack and Shelley Blais to name the new Aaron Lazare Medical Research Building;
- an increase in the endowment by more than \$5 million, including the establishment of seven new named endowed chairs and professorships; and
- ten leadership gifts received representing \$1 million or more, along with 27 gifts of amounts in the six-figures.

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Celebrating Hope, Building Knowledge, Changing Lives

The Center for Adoption Research at the University of Massachusetts is the only university-based center in the nation dedicated solely to the study of adoption and foster care. By developing innovative research and educational programs, analyzing and helping develop practices and policies, and expanding public awareness and understanding, the center is making significant strides toward improving the lives of children and families who are touched by foster care and adoption. UMMS Chancellor and Dean Aaron Lazare, who with his wife Louise has adopted eight children of several races, leads the center as executive director.

In January 2002, the center celebrated its accomplishments and recognized distinguished individuals who have helped advance critical issues in adoption and foster care at its first major fund-raising event in Boston. Proceeds from the gala dinner held at the Fairmont Copley Plaza Hotel support the center's ongoing research programs and its initiatives aimed at affecting change and breaking down barriers to adoption and to improving foster care. Among those honored for their service to children were:

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The Year In Philanthropy (continued)

U.S. Congressman William D. Delahunt for his tireless efforts promoting enlightened federal policy on adoption (Champions for Children Award); Massachusetts Representative John H. Rogers for his role in policy formulation in the state (Commonwealth Award); and Valora Washington, executive director of the Unitarian Universalist Service Committee for her efforts to ensure that permanent homes are found for all children in foster care (Heart and Home Award). Boston DMA Wendy's Marketing Cooperative received the Corporations That Care Award.

In the last two years, the Center for Adoption Research, established in 1997, has undertaken some 30 research projects including: Analysis of foster care caseload dynamics; Clinical treatment models for adopted children and families; Understanding the link between ADHD and adoption; Ethical issues in adoption; Access to records in adoption and guidelines for the courts; Search in adoption; and K-12 curricula models for adoption and foster care.

The Mission of the UMass Memorial Foundation

The UMass Memorial Foundation serves as the advocate for the University of Massachusetts Medical School and UMass Memorial Health Care by working with donors to facilitate advancements in medical research and patient care and to educate tomorrow's medical professionals. Contact the Foundation at 508-856-5520 or at giving@umassmed.edu.

From Trustee to Test Tubes, Alumnus Has Spanned the UMMS Experience



As a student trustee to the University of Massachusetts Board in 1993, Eric W. Dickson, MD '95, was instrumental in the vote to make Emergency Medicine its own department within UMMS—one of the first in the country. Today, the associate professor and director of emergency medicine research continues to contribute to the department's pioneering methods by positioning it at the forefront of basic science research.

"What drew me to emergency medicine, in addition to its distinction as a new discipline, was its research promise. We see a new patient every eight minutes with a totally different complaint; I can investigate many areas and never leave the field of emergency medicine." He added, "When I started in the field, there were five National Institutes of Health grants *total* in emergency medicine nationwide; today we hold four at the Medical School—only two other programs in the country have achieved this level of funding."

Dr. Dickson attributes success in two distinct research areas to not only good fortune but also to the mentorship he received during his medical and graduate education at UMMS. The first research area, which he pursued with Interim Chair of Anesthesiology Stephen O. Heard, MD, involved liquid ventilation, or the use of pure perfluorocarbon to improve the breathing capability of patients with acute respiratory distress. According to Dickson, he and Dr. Heard began investigating the technique using mouse models in the early 1990s and, several years ago, were involved in some of the first human clinical trials. "It is the ultimate thrill for a clinician-scientist to take what has been learned in the lab and use it to help a critically ill patient."

The second research success story, initiated with Professor of Medicine Richard C. Becker, MD, involved the investigation of a molecular mechanism underlying the phenomenon of "preconditioning," in which individuals who

experience chest pain or angina prior to heart attack may have less permanent damage to their heart than those who experience a heart attack without warning. Following submission of a paper on the topic, Dickson was indirectly contacted by one of the

journal's associate editors, new Professor of Emergency Medicine Karin Przyklenk, PhD, about the research. Dickson and Dr. Przyklenk began a long-distance collaboration on the topic that helped Dickson garner initial funding as well as a 2002 Young Investigator Award from the Society for Academic Emergency Medicine. "One of my greatest achievements was hiring my mentor, Karin, to serve as lab director here. She is an incredible scientist." He also commended Department of Physiology Chair Maurice Goodman, PhD, and his faculty for providing the mentors necessary for him to receive his first NIH grant.

Given Dickson's preference for variety in his work, it's not surprising that his route to UMMS was atypical. A former Army combat medic, Dickson was trained as a respiratory therapist and began his career at UMMS in this field. "I had worked in several Boston hospitals and often felt that we were looked upon as a separate class by the physicians, residents and medical students. But here, everyone treated each other with respect. Already in pre-med classes and intermittently working here, I decided to go for admission to the Medical School. It's the best career decision I've made."

While in his second year of medical school, Dickson was urged by Michael Foley, MD '76, former University board member, to pursue a one-year position as a student trustee. "As a gastroenterologist at the first community hospital I worked in, Dr. Foley was my model in terms of becoming a physician. When I first worked at UMass Medical School and saw how everyone worked together, it was clear to me that Dr. Foley practiced what he had learned here."

Today's Trustee

A full decade after Dr. Eric Dickson's tenure as a University trustee, School of Medicine student Doreen DeFaria '03 has taken on the mantle to represent the Worcester campus.

A student who immediately enrolled in UMMS following receipt of her bachelor's degree in biology and neuroscience from Duke University, DeFaria admits that she initially chose the institution for its close proximity to her family, focus on primary care and cost-effectiveness. As she wraps



up her fourth year, however, DeFaria affirms that her time as a student here has given her a full appreciation for the Medical School's unique stature among its fellow institutions. "The faculty are outstanding and all of the students are so impressed with the dedication they have to making us excellent physicians," said DeFaria. "This great experience, coupled with the excellent clinical exposure and a desire to learn about governance, inspired me to pursue a position on the University board."

Elected by their peers, student trustees attend the quarterly University board meetings, as well as serve on a committee of their choice. DeFaria sits on the Administration, Audit and Finance Committee and finds that the experience is providing her with an appreciation of how the University functions, as she observes where appropriations are allocated throughout the five-campus system.

In addition to the University board, DeFaria serves on the board of UMass Memorial Health Care. In this capacity, she meets monthly with board members and serves on the Patient Care Assessment Committee. "I find this committee particularly interesting since we actually look at how the hospital is run in terms of quality, something I would never have had exposure to as a student."

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The Last Moral

By Mario Stevenson, PhD
the David I. Freelander Professor of AIDS Research at UMMS

In July 2002, the journal *Nature* published significant findings from research conducted by Michael Malim of King's College London and colleagues at the University of Pennsylvania School of Medicine. It described their discovery of a viral gene in humans—CEM15—that defends against attack from HIV, the virus that causes AIDS. According to the research, CEM15 would normally halt HIV infection, but is suppressed by an HIV protein called virion infectivity factor, or Vif. Overcome Vif, and CEM15 could potentially become a form of natural resistance to viral activity, leading to the establishment of new drug treatments for HIV or AIDS. This is an important finding and one that is especially appealing to me because it is the result of investigations focused on answering a single basic research question—what are the functions of viral genes? While over seven years in the making, the discovery of CEM15 underscores the inspiring potential of basic research.

Mind you, we still have a very superficial understanding of how HIV works. We read in newspapers about the degree to which HIV is studied—we must, therefore, know everything about it. That is not the case. To illustrate, HIV has nine genes that likely require dozens of distinct interactions to occur in order to perpetuate itself. Specifically, these nine genes use cellular processes to complete certain stages of the virus' life cycle. If we determine what those processes are, we can block them with drugs. The advantage to targeting cellular processes is that those processes don't change; they don't mutate. On the

other hand, the current targets, viral proteins, mutate so quickly that today's drug regimens become useless in a matter of months for some patients. That's because the virus uses evolution millions of times faster than we do; it adapts to its new environment easily and precisely when it senses change. In the case of the CEM15 gene, for example, at some point HIV directed Vif to combat it. We must discover how we can help the innate CEM15 come out on top again.

A breakthrough of this magnitude in HIV research could come soon, or years from now. I often tell people who come through the lab that, as far as I'm concerned, the only characteristic one needs to work with HIV is stubbornness, with a supporting layer of thick skin. Persistence is key as each day brings disappointments in this field of investigation. The virus does not act according to human logic—just when we think we might have some aspect figured out, HIV throws a counter-intuitive wrinkle into the mix. I do believe that one day this virus will be beaten. I hope in my lifetime. Meanwhile, 4,000 babies are infected every day in Africa. As a point of comparison, at the height of the epidemic in this country, 4,000 U.S. babies were being infected—in a year. Africa's horror is well known; India's situation is probably just as bad, but its government isn't recognizing it as such. In China, the government is mobilizing now to do something about an impending human disaster.



death sentence in our country because drugs—albeit ones with complicated side effects—have been aggressively develsince our government declared war on budget is \$1.5 billion, the money is spread quite thin. Project-oriented of funds—the rest is spent on education, for drugs and other essential components that make up the huge AIDS continuum. Thankfully, because of the support UMMS ratory facilities and mentorship, we were able to establish a Center for AIDS Research. This reflects a proven commitment to the field and encourages us to continue to be stubborn and persistent, doing the best we can in our efforts to combat this disease.

Dr. Stevenson and his colleagues were the first to demonstrate that HIV is fundamentally different from other types of retroviruses due to its ability to infect non-cycling cells. This property is what enables the virus to infect macrophages, which are supposed to recognize foreign pathogens and stimulate the immune system. Infection of macrophages may be essential to the replication of the virus; HIV likely uses them as a "transport" mechanism to disseminate the virus throughout the body. Stevenson's research explores strategies to interrupt the virus' ability to use macrophages in this way. When this transport mechanism is better understood, he believes it will give his team a target to exploit for new drug therapies. Because of this research, UMMS was awarded funding as one of 15 Centers for AIDS Research across the U.S. in 1998, sharing \$20 million awarded by the National Institutes of Health.