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The Robert Dawson Evans

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DEPARTMENT OF MEDICINE

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Annual Report 2007

Boston University Medical Center

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# CHAIRMAN'S REPORT



*David L. Coleman, M.D.*

CHAIRMAN  
DEPARTMENT OF MEDICINE  
JOHN WADE PROFESSOR

*Jack Ansell, M.D.*

PROFESSOR OF MEDICINE  
VICE CHAIR, CLINICAL AFFAIRS

*David Battinelli, M.D.*

PROFESSOR OF MEDICINE  
VICE CHAIR, EDUCATION

*Barbara Corkey, Ph.D.*

PROFESSOR OF MEDICINE  
VICE CHAIR, RESEARCH

*John F. Keaney, M.D.*

PROFESSOR OF MEDICINE  
VICE CHAIR, RESEARCH

*Jeffrey Samet, M.D.*

PROFESSOR OF MEDICINE  
VICE CHAIR, PUBLIC HEALTH

*Douglas Faller, M.D., Ph.D.*

PROFESSOR OF MEDICINE  
VICE CHAIR, CANCER CENTER

*Thomas Barber, M.D.*

ASSOCIATE PROFESSOR OF MEDICINE  
CHIEF OF MEDICINE, QUINCY MEDICAL CENTER

*Jay Orlander, M.D., M.P.H.*

ASSOCIATE PROFESSOR OF MEDICINE  
ASSOCIATE CHIEF, MEDICAL SERVICE  
BOSTON VETERANS ADMINISTRATION  
HEALTHCARE SYSTEM

*Alan Weitberg, M.D.*

PROFESSOR OF MEDICINE  
CHAIRMAN, DEPARTMENT OF MEDICINE  
ROGER WILLIAMS MEDICAL CENTER

The Department of Medicine is pleased to welcome David Coleman, M.D., F.A.C.P., Wade Professor of Medicine, to the Department as its Chairman this year. The Department has continued to grow and develop in multiple areas with the boundless energy and enthusiasm of its new Chair.

Barbara Corkey, Ph.D., Professor of Medicine and Biochemistry and Director of the Obesity Research Center, assumed the role of Vice Chair for Research from John Keaney, M.D., Professor of Medicine and faculty member of the Section of Cardiovascular Medicine. Under both of their stewardships, the research efforts of the department continue to grow. Overall research funding from federal and other sources increased to an all time high of over \$165 million for the Department. We continue to rank very highly among departments of medicine in overall funding from the National Institutes of Health. In addition, we continue to complete successfully for major program grants from many sources.

The John Joseph Moakley Ambulatory Care building, named in honor of the late Congressman, who was a devoted champion of Boston Medical Center, was completed and opened for clinical care this year. The building brings together many programs of clinical excellence and specialty services in one location, streamlining access to care and providing patients with the latest in technology and treatment. The Solomont Center for Hematology and Medical Oncology, the Belkin Breast Health Center, and the Dempsey Center for Digestive Disorders all found new homes in the multispecialty focused building. The Endoscopy Center was also moved into the new clinical space housed between the outpatient Digestive Disorders practice and the Menino Pavilion inpatient facility.

Accentuated by the opening of the Moakley building, the Department's clinical activity

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continued to grow, as it has consistently done in recent years. The ambulatory activity increased to a total of 218,691 visits this year (3.9% increase over last year), with growth occurring largely in the subspecialty practices. The largest growth in volume was experienced in the Endocrinology and Diabetes program (20.7%/5523 visits) followed closely by the Cardiology practice (22.7%, 4996 visits). The newly created Belkin Breast practice saw 2609 visits in its first partial year of operations. Inpatient admissions to the medical service at Boston Medical Center totaled 18,353 (3.0%) this year with an average length of stay of 5.15 days. The number of ambulatory visits and inpatient admissions are again at all-time highs for the Department. The Hospitalist service continued to expand with the ongoing addition of physician assistant teams to the traditional house staff and faculty team structure. There are ongoing efforts to right size the medicine teams to preserve optimal educational and patient care experience for house staff and students.

The 2006-2007 academic year was the eighth year of the Graduate Program in Molecular Medicine. Forty-one students participated in the program, 13 in the combined M.D./Ph.D. track and 28 in the Ph.D. track; two of these 12 already have their M.D. degree and are clinical fellows pursuing research training. Twenty one students have graduated from the program to date. The Graduate Program in Molecular Medicine provided a total of twelve credit hours of upper level graduate teaching for about 84 students in the Division of Graduate Medical Sciences, with a total of more than 300 credits awarded in all classes. This success was possible through the participation of many faculty in the Department of Medicine.

The Internal Medicine Residency Training Program continues to attract a large number of candidates from across the United States and abroad. The most recent match was particularly strong and included an incoming class of 58 house officers representing over 41 different medical schools. The 154 total

house officers are drawn from over 60 medical schools across the country. In addition to academic strength, house officers are also very diverse and include 22% under-represented minorities. In an effort to improve the scholarly component of our program, we introduced our first Senior Resident Academic Day. Here, over 40 residents presented their scholarly work in the form of poster presentations, abstracts, and lectures. We also enjoyed one of our strongest fellowship matches in many years and our house officers will be pursuing training in some of the most prestigious fellowship programs in the country.

The medical student programs including the third year medicine clerkship, the fourth year advanced acting internship, and the biology of disease course continue to receive some of the highest evaluations in the medical school. In addition to faculty, Medicine residents play a key role in the education of medical students.

The Department continues to support resident/faculty teaching development through our intern and junior resident leadership retreats. In an effort to further enhance the bedside teaching curriculum, we have implemented a new faculty development program specifically focusing on improving physical diagnoses and bedside communication skills.

The fellowship training programs continue to be very competitive and attract strong candidates from prestigious residency programs from around the country. These fellows strengthen our environment through the patient care they provide and the research they perform. In addition, they play an important role in teaching our house officers and students.

Overall, this academic year has been very productive for the Department in every domain. In the coming year, we look forward to continued growth and success.

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## ORGANIZATIONAL OVERVIEW

### DEPARTMENT OF MEDICINE

#### CHAIRMAN

David Coleman, M.D.

#### VICE CHAIRS

Vice Chair, Clinic Affairs  
Vice Chair, Cancer Center  
Vice Chair, Education  
Vice Chair, Public Health  
Vice Chair, Research

Jack Ansell, M.D.  
Douglas Faller, M.D., Ph.D.  
David Battinelli, M.D.  
Jeffrey Samet, M.D., M.P.H.  
Barbara Corkey, Ph.D.

#### SECTIONS

Cardiovascular Medicine  
    Vascular Biology Unit  
Clinical Epidemiology Research and Training Unit  
Endocrinology, Diabetes, and Nutrition  
    Weight Management Center  
Gastroenterology  
General Internal Medicine  
    Community Medicine Unit  
    Medical Information Systems Unit  
    Women's Health Unit  
Geriatrics  
Hematology and Medical Oncology  
    Comprehensive Program in Sickle Cell Disease  
Hypertension  
Infectious Diseases  
    Center for HIV/AIDS Care and Research  
Molecular Medicine  
    Biomolecular Medicine Unit  
    Genetics Program  
    Immunotherapy Unit  
    Molecular Genetics Unit  
    Obesity Research Center  
    Whitaker CVI Digital Imaging Microscopy Center  
Nephrology  
Preventive Medicine and Epidemiology  
Pulmonary, Allergy, and Critical Care Medicine  
Rheumatology  
    Vasculitis Center

Wilson Colucci, M.D.  
Richard Cohen, M.D.  
David Felson, M.D.  
Shalender Bhasin, M.D.  
Caroline Apovian, M.D.  
Michael Wolfe, M.D.  
Jeffrey Samet, M.D.  
Christopher Shanahan, M.D.  
Robert Friedman, M.D.  
Karen Freund, M.D.  
Rebecca Silliman, M.D., Ph.D.  
Jack Ansell, M.D., (*ad interim*)  
Martin Steinberg, M.D.  
Haralambos Gavras, M.D.  
Paul Skolnik, M.D.  
Paul Skolnik, M.D.  
John Murphy, Ph.D.  
John Murphy, Ph.D.  
Lindsay Farrer, Ph.D.  
Jianlin Gong, M.D.  
Vassilis Zannis, Ph.D.  
Barbara Corkey, Ph.D.  
Michael Kirber, Ph.D.  
David Salant, M.D.  
R. Curtis Ellison, M.D, D. Sc.  
David Center, M.D.  
Robert Simms, M.D. (*ad interim*)  
Peter Merkel, M.D.

#### CENTERS

Arthritis Center  
Cancer Center  
Center for Primary Care  
Pulmonary Center  
Whitaker Cardiovascular Institute

Robert Simms, M.D. (*ad interim*)  
Douglas Faller, M.D., Ph.D.  
John Noble, M.D.  
Jerome Brody, M.D.  
Karen Antman, M.D. (*ad interim*)

#### AFFILIATED HOSPITALS

Boston Veterans Administration Healthcare System  
Quincy Medical Center  
Roger Williams Medical Center

Jay Orlander, M.D., M.P.H.  
Thomas Barber, M.D.  
Alan Weitberg, M.D.

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# EVANS MEDICAL FOUNDATION HISTORY

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**BOSTON UNIVERSITY MEDICAL CENTER  
DEPARTMENT OF MEDICINE**

**HISTORY**

The Boston University School of Medicine (BUSM) was established in 1873 when the University assumed responsibility for the New England Female Medical College. Among its historic distinctions are its commitment to equal education for women and men and the development of the nation's first academically affiliated Home Medical Service. In more recent decades, the School developed an extensive program of biomedical research based in several major research facilities. Department of Medicine faculty are important contributors to the research programs of the School and are able to take full advantage of the School's research facilities and core research support centers.

Boston University Medical Center Hospital (BUMCH) was founded in 1855 as the Massachusetts Homeopathic Hospital. In 1910, the Evans Memorial Department of Clinical Research was established by a series of gifts by Mrs. Maria Antoinette Evans to endow a research department of medicine at the Hospital. The Evans Department was one of the few research institutions of its kind when its activities began in 1912. Although technically a separate research institute, the Evans Department has always functioned as an integral part of the clinical care and training programs of Boston Medical Center and of the Department of Medicine at BUSM. This is in accordance with Mrs. Evans' stipulation that research, clinical care, and teaching should be intimately interrelated in the Department that she endowed.

Boston City Hospital (BCH) opened in 1864 and was the first municipal hospital established in the United States. In 1923, the Thorndike Memorial Laboratory was established with support provided by Dr. George L. Thorndike in memory of his brother, William, a long-time BCH staff member. The Thorndike became one of the

nation's most distinguished research facilities under the aegis of the BCH Harvard Medical Services. In 1968, the Finland Laboratory for Infectious Diseases was established at BCH in honor of Dr. Maxwell Finland, a leading clinical investigator in infectious diseases. When academic and clinical responsibility for BCH passed to Boston University in 1973, these laboratories were incorporated into the research programs of the Department of Medicine faculty.

In July 1996, BUMCH and BCH were merged into the Boston Medical Center, a not-for-profit institution that fully retains the missions and commitments of its predecessor institutions.

The Boston Veterans Administration Medical Center was the first Dean's Committee VA hospital, i.e., the first specifically designated as a teaching hospital. It is a major training site for students and residents. In addition, its faculty conduct a varied research program, including active, basic, clinical, and health services research efforts.

**CURRENT STATUS**

Departmental faculty are responsible for major National Institutes of Health- (NIH) sponsored specialized research centers and program projects. These include a Specialized Clinical Center of Research titled, "Vascular Consequences of Insulin Resistance and Obesity"; a Specialized Center of Research in Pulmonary Fibrosis; a National Multipurpose Arthritis Center; a Program for Interdisciplinary Study of Fungal Infections and another for study of Pelvic Inflammatory Disease (each one of only two such nationally designated NIH centers); a participating center in the national AIDS Clinical Trials Group; program projects in pulmonary



immunology and lung development; a federally established healthcare research advisory center; programs with the internationally famous Framingham Heart Study; and a program project titled, “Endothelial Redox State and Phenotype in Health and Disease”.

Training programs are available in internal medicine and in all traditional medical subspecialties, as well as in a number of novel research areas. Clinical training programs currently involve approximately 150 medical residents and more than 100 subspecialty and research trainees, including M.D. fellows and pre- and postdoctoral Ph.D. students.

The Department of Medicine is based at the Boston University School of Medicine and at two principal teaching hospitals: Boston Medical Center (BMC), and the Boston Veterans Administration Healthcare System (BVAHCS). The integrated medical residency and fellowship programs take advantage of training facilities in both hospitals. Important affiliations with the Boston Neighborhood Health Center Network (HealthNet) and with a number of community hospitals contribute importantly to the clinical and teaching activities of the department.

The faculty are organized in a number of Sections, which include not only the usual medical subspecialties but also a number of special research sections such as Molecular Medicine and Preventive Medicine and Epidemiology. Many of the Department’s research programs involve extensive collaboration between Sections and with other departments of the School of Medicine. The Department’s research and research training programs are supported by grants from outside agencies, principally the National Institutes of Health, as well as by endowment income.

## EVANS MEMORIAL DEPARTMENT OF CLINICAL RESEARCH

The Evans Memorial Department of Clinical Research was established on June 19, 1910, when Mrs. Maria Antoinette Evans made the first in a series of gifts to University Hospital (then the Massachusetts Homeopathic Hospital) to endow a research department of medicine. Her purpose was to create a memorial to her husband, Robert Dawson Evans, a very successful businessman, whose estate also provided a wing for Boston’s Museum of Fine Arts. The current Evans Building, which is the third structure to house the ever-growing Department, was dedicated in 1971. It contains more than 100,000 square feet of research laboratories and offices. This building was purchased by Boston University in fiscal year 2000. The majority of Evans Department of Medicine researchers were relocated to the new Evans Biomedical Research Center located at 650 Albany Street.

## DIRECTORS OF THE EVANS MEMORIAL DEPARTMENT OF CLINICAL RESEARCH

Dr. David Coleman	2006 – present
Dr. Thomas Moore, <i>ad interim</i>	2005 – 2006
Dr. Joseph Loscalzo	1997 – 2005
Dr. Norman Levinsky	1972 – 1997
Dr. Robert Wilkins	1960 – 1972
Dr. Chester S. Keefer	1939 – 1960
Dr. Reginald H. Fitz	1935 - 1939
Dr. Allen W. Rowe	1930 – 1935
Dr. Henry M. Pollock	1918 - 1930
Dr. Frank C. Richardson	1912 - 1918



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## **EVANS MEDICAL FOUNDATION**

The Evans Medical Foundation was founded in 1975. The faculty of the Department of Medicine voted to reorganize themselves as a non-profit corporation, the Evans Medical Foundation, to improve medical care for all patients and to provide one-class, first-class care for all. In addition, the reorganization facilitates the use of income from the clinical activities of Department faculty to enhance patient care and to support teaching and clinical research at Boston University Medical Center. The title, Evans Medical Foundation, was chosen to indicate the close relation of the Foundation to the Evans Department of Medicine, the formal name for the research activities of the Department of Medicine at the Boston Medical Center. By supporting research, education, and clinical care, the Foundation has developed a new approach to fulfilling the mandate of Maria Antoinette Evans.

## **BOSTON UNIVERSITY MEDICAL GROUP**

In 1977, the Foundation contracted with the former University Hospital to provide ambulatory services for the Hospital, both in general medicine and in all the subspecialties of internal medicine. The Foundation represented the legal mechanism for reorganizing the clinical practice of the Department of Medicine at the University Hospital. Before that time, the Department's full-time faculty had maintained separate office practices. The offices were scattered around the Hospital, typically in association with the laboratory facilities of each faculty member. The patients were "private" patients of the faculty. At the same time, there were general medical and subspecialty clinics of the Hospital in which "public" patients were seen. These clinics were staffed by residents and fellows, usually with limited faculty supervision. They were old-fashioned, "hard-bench" clinics with few amenities.

At the same time a new Section of the Department of Medicine, General Internal

Medicine, was organized to develop academic and clinical programs in that area. The Hospital outfitted a floor of the Doctors Office Building to house the Evans Medical Group, the ambulatory activities of the Department of Medicine. The Evans Medical Group undertook to provide clinical care in a uniform manner for all patients, ending the traditional separation of private and public patients. At the same time, the new facility and a new support staff enhanced the style and amenities of the practice for all patients receiving ambulatory medical care at University Hospital.

During the first decade of activity, the number of patient visits to the Evans Medical Group more than doubled, from approximately 21,000 visits in 1977-78 to more than 45,000 visits by 1986-87. By 1995, it had reached approximately 55,000. In accordance with its charter as a non-profit academic support corporation, the Foundation has used clinical income to recruit and support faculty, to help pay research costs, and to enhance educational programs within the Department of Medicine. The Foundation also assumed full financial responsibility for the practice expenses of the Evans Medical Group. By virtue of its steady growth, indicating patient satisfaction, and the substantial improvements to inpatient care, the Foundation has fulfilled its original mission.

Following the creation of the Boston Medical Center on July 1, 1996, the Evans Medical Group changed its name to the Boston University Medical Group to reflect its expanding, integrated clinical practice. The Boston University Medical Group represents the clinical arm of the Department of Medicine and all of its ambulatory practices. The number of patient visits in the integrated ambulatory practices in fiscal year 2007 was approximately 218,000.

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## SECTIONS OF THE DEPARTMENT OF MEDICINE

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# CARDIOVASCULAR MEDICINE



## SECTION CHIEF:

*Wilson S. Colucci, M.D.*

*Thomas J. Ryan Professor of Medicine*

## RESEARCH ACTIVITIES

The Section of Cardiovascular Medicine has been highly productive in its research activities. In the past year, the Section was awarded eleven new research grants, for a total of forty ongoing research grants. The net annual direct research support to Section investigators in 2007 was \$10.1 million, with indirect support of \$5.2 million. The major source of funding was the National Institutes of Health at \$9.2 million, with \$877,720 from other sources.

Of the net direct funds, \$7.7 million were attributable to physicians with a clinical appointment in the Section, and \$2.3 million was attributable to non-physician scientists. Section members published 102 journal articles, book chapters, and review articles.

## CLINICAL ACTIVITIES

In Fiscal Year 2006-2007, overall clinical activity within the Section of Cardiovascular Medicine increased by approximately 15%, as reflected by an increase in total work RVU's from 90,118 to 103,593. The number of echocardiograms increased 8% from Fiscal 2006, for a total of 11,099 performed. Section faculty performed more electrocardiograms than they did in Fiscal 2006, with that procedure experiencing a 3% increase to 63,660 tests.

Exercise tests numbered 4,092, an increase of 1% from the previous Fiscal Year.

In addition, the number of clinic visits increased 9% to 11,015. The number of consultations decreased 4% to 1,789, with the number of days of medical care that Section faculty provided in Fiscal 2006 also experiencing a slight decline of 1% to 7,307.

The 1,696 catheterizations and interventional procedures that were performed represented a decline of 4% from 2006. The Electrophysiology Program conducted approximately the same number of procedures as it had the previous year, 941 procedures in 2007 as compared with 943 in 2006. Section faculty in the Peripheral Vascular Interventional Program performed 217 procedures in 2006. Within the newly established Advanced Cardiac Imaging Program, 75 cardiac MRI and 51 CT angiographic studies were conducted.

These overall trends in clinical practice reflect the Section's increased emphasis on ambulatory and diagnostic services, and the development of new programs in Vascular Medicine and Advanced Cardiac Imaging.

## EDUCATION

The Section of Cardiovascular Medicine provides extensive educational activities at all training levels for medical students, residents, clinical fellows, and post-doctoral research fellows. Section faculty teach the cardiovascular block of the "Biology of Disease" course offered to Boston University School of Medicine (BUSM) students, as well as conduct clinical electives in clinical cardiology for third- and fourth-year BUSM students. Medical residents rotate through the cardiology inpatient services and the consult service.

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In 2006-2007, the Section trained eighteen general cardiology fellows, two interventional fellows, one electrophysiology fellow, and one cardiomyopathy fellow. Pre-doctoral Ph.D. and post-doctoral M.D.s and Ph.D.s are trained in numerous laboratory and clinical research settings throughout the Section of Cardiovascular Medicine.

### MAJOR ACCOMPLISHMENTS

Eric Awtry, M.D., Director of Education for the Section, and Assistant Professor of Medicine, received the Robert Dawson Evans Special Teaching Award from BUSM. He was also the recipient of the Excellence in Teaching Award presented by Cardiovascular Medicine fellows and he was named a “Top Doctor” by *Boston Magazine*.

Gary Balady, M.D., Director of the Preventive Cardiology Program and Co-Director of the Non-Invasive Cardiac Labs at Boston Medical Center (BMC), and Professor of Medicine, was named one of the Top Doctors in America – 2007 by the Castle Connolly List.

Sheila Bernard, M.D., Director of Ambulatory Cardiovascular Services at BMC, and Clinical Associate Professor of Medicine, was named a “Top Doctor” by *Boston Magazine*.

Ravin Davidoff, M.D., Director of Clinical Cardiology and Director of the Echocardiography Program at BMC, Executive Director of Clinical Affiliations for Boston University Medical Center, and Professor of Medicine, was named a “Top Doctor” by *Boston Magazine*.

Alice Jacobs, M.D., Director of the Cardiac Catheterization Laboratory and Interventional Cardiology at BMC, and Professor of Medicine, was named a “Top Doctor” by *Boston Magazine*.

George Philippides, M.D., Director of the Coronary Care Unit at BMC, and Assistant Professor of Medicine, was elected president of the American Heart Association, Greater Boston Division. He was also named a “Top Doctor” by *Boston Magazine*.

Thomas J. Ryan, M.D., Senior Consultant and Emeritus Chief, Section of Cardiovascular Medicine, and Professor of Medicine, was presented with the Distinguished Fellow Award by the Council on Clinical Cardiology at the American Heart Association’s Annual Dinner.

Joseph Vita, M.D., Director of Clinical Research, and Professor of Medicine, was elected a member of the Association of University Cardiologists.

In addition, several Section faculty members were promoted, including Jane Freedman, M.D., to the rank of Professor of Medicine, and Robert Eberhardt, M.D., Director of Vascular Medical Services and Co-Director of the Non-Invasive Vascular Laboratory at BMC, and Flora Sam, M.D., to Associate Professor of Medicine.

Hans Meier-Ewert, M.D., was appointed Assistant Professor of Medicine, and Ravi Lala, M.D., was named Instructor in Medicine.

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## FACULTY

### Professors

Gary J. Balady, M.D.  
Emelia J. Benjamin, M.D., Sc.D.  
Jay D. Coffman, M.D.  
Wilson S. Colucci, M.D.  
Ravin Davidoff, M.D.  
Rodney H. Falk, M.D. (adjunct)  
Alice K. Jacobs, M.D.  
John F. Keaney, Jr., M.D.  
Michael D. Klein, M.D.  
Daniel Levy, M.D.  
Joseph Loscalzo, M.D., Ph.D. (adjunct)  
Farouk A. Pirzada, M.D.  
Philip J. Podrid, M.D.  
Vasan Ramachandran, M.D.  
Thomas J. Ryan, M.D.  
Joseph A. Vita, M.D.  
Donald A. Weiner, M.D.

### Associate Professors

Sheilah A. Bernard, M.D.  
Jane E. Freedman, M.D.  
Noyan Gokce, M.D.  
Jacob Joseph, M.D.  
Ronglih Liao, Ph.D.  
Flora Sam, M.D.  
Shiow-Shih Tang, Ph.D.

### Assistant Professors

Lisa Antonelli, M.D.  
Barry Arkin, M.D.  
Eric H. Awtry, M.D.  
Clifford J. Berger, M.D.  
John B. Cadigan, M.D.  
Kai Chen, M.D., Ph.D.

Chester Conrad, M.D., Ph.D.  
Joseph L. DiCola, M.D.  
Mandeep Dhadly, M.D.  
Robert T. Eberhardt, M.D.  
Carl M. Fier, M.D.  
Alan E. Garstka, M.D.  
Andrew L. Kriegel, M.D.  
Bruce J. Kriegel, M.D.  
Robert M. Lavery, M.D.  
Paul A. LeLorier, M.D.  
Hans Meier-Ewert, M.D.  
Kevin M. Monahan, M.D.  
Zoran Nedeljkovic, M.D.  
Henry H. L. Ooi, M.D.  
George J. Philippides, M.D.  
David Pimentel, M.D.  
Khether E. Raby, M.D.  
Richard R. Ress, M.D.  
Frederick L. Ruberg, M.D.  
Nicholas Ruocco, Jr., M.D.  
Ichiro Shiojima, M.D., Ph.D. (adjunct)  
Sushil Singh, M.D.  
Deborah A. Siwik, Ph.D.  
Barbara Voetsch-Forgione, M.D., Ph.D.  
George A. Waters, M.D.  
Ying Yi Zhang, Ph.D.  
Benoy Zachariah, M.D.  
Adriana Zuccollo, Ph.D.

### Instructors

Jill Downing, M.D.  
Ravi Lala, M.D.

### Clinical Associates

Arlene Dermovsesian, N.P.  
Densie Eckstrom, N.P.  
Diane F. Gauthier, N.P.  
Tracey Lavey, N.P.  
Mary A. Morabito, N.P.  
Amanda Woodruff, N.P.

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# VASCULAR BIOLOGY UNIT



## UNIT CHIEF

Richard Cohen, M.D.,  
*Jay and Louis Coffman Chair in Vascular Medicine*

## Research Activities

The Vascular Biology Unit was established in 1990 as an independent research unit within the Department of Medicine. It is under the direction of Richard Cohen, M.D., the Jay and Louise Coffman Chair in Vascular Medicine, and Professor of Medicine, Physiology and Pharmacology. The Unit's mission is to maintain a diverse research program in vascular biology; it places a special emphasis on understanding the basic mechanisms of vascular dysfunction and disease. The Unit currently comprises five faculty members who have expertise in various aspects of the role that oxidant stress plays in the vascular diseases associated with atherosclerosis, diabetes mellitus, and hypertension. The Unit's staff, including its faculty, fellows, students, and technicians, represents a talented group with varied backgrounds and experience.

Dr. Cohen's current research is focused on understanding the effects of endogenous oxidant/antioxidant systems in diabetic, hypertensive, and atherosclerotic vascular disease, including the involvement of hypercholesterolemia, angiotensin II, thromboxane A<sub>2</sub>, NADPH oxidase, p21ras, and AMP-activated protein kinase. Dr. Cohen is Co-principal Investigator of Boston University Medical Center's Cardiovascular Proteomics Center, funded by the National Institutes of Health (NIH), which focuses on

oxidant-induced post-translational protein modifications in cardiovascular disease.

Bingbing Jiang, M.D., Ph.D., Assistant Professor of Medicine, is an expert in inflammatory cytokine signaling. A Scientist Development Grant from the American Heart Association funds his independent research on smooth muscle cells, which has elucidated the role of the MAP kinase signaling pathway in promoting the prolonged activation and expression of NF- $\kappa$ B dependent genes in the vasculature. Dr. Jiang also maintains an important role in the ten-year Strategic Alliance with the Institut de Recherche Servier.

Reiko Matsui, M.D., Assistant Professor of Medicine, studies oxidant-signaling and redox mechanisms in the context of aging and cardiovascular disease. During the last year, she has studied the role of glutaredoxin-1 in modulating the cellular and *in vivo* response to angiotensin II-induced hypertension.

Mengwei Zang, Ph.D. Assistant Professor of Medicine, focuses her research on the regulation of hepatic lipid metabolism by AMP-dependent protein kinase in the context of a Program Project on AMP kinase directed by Neil Ruderman, M.D., D.Phil., a member of the Section of Endocrinology, Diabetes, Nutrition and Weight Management, Director of the Diabetes Research Unit, and Professor of Medicine, Physiology and Biophysics. This work is also a focus of the Strategic Alliance with Servier. Last year, Dr. Zang published a paper demonstrating that polyphenols, including those in red wine, activate AMP-dependent protein kinase that, in turn, prevents the increases in hepatic and serum lipids associated with diabetes. Her most recent work addresses the role of the histone deacetylase, SIRT1, in the regulation of lipid metabolism.

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Two new faculty members were appointed this year. Markus Bachschmid, Ph.D., Assistant Professor of Medicine, studies the effects of oxidants in the response to aging in the vasculature. During the last year, he discovered that acetaminophen is a potent peroxynitrite scavenger. Xiao Yong Tong, Ph.D., an Assistant Professor of Medicine, is experienced in transgenic mice and electrophysiology. She is studying the physiological dysfunction caused by protein oxidation in diabetes, particularly in the calcium regulatory protein, SERCA2.

### MAJOR ACCOMPLISHMENTS

As an independent research unit in the Department of Medicine, the Vascular Biology Unit's major activities are made up of the individual and group research programs for which its members receive funding. This year has been very successful in terms of both research accomplishments and funding. Unit papers have been published in the *Arteriosclerosis, Thrombosis and Vascular Biology*, *Diabetes*, and *Free Radical Biology and Medicine*.

Discoveries by Unit researchers highlighted the fact that vascular function is modulated by oxidant modification of vascular endothelial and smooth muscle proteins that participate in cell signaling. Unit investigators found that oxidant-induced S-glutathiolation of a reactive cysteine thiol on p21ras mediates novel signaling pathways in vascular endothelial cells that may contribute to insulin resistance. Researchers also found oxidants that arise in

diabetes prevent the regulation by nitric oxide of a smooth muscle calcium transporter that normally controls calcium and cell migration.

The Unit's research funding currently comprises four NIH Program Project grants, including component projects on an NIH Program Project studying endothelial oxidants that is under the direction of Kenneth Walsh, Ph.D., Professor of Medicine, and an NIH-funded program project in diabetic complications led by Dr. Ruderman. Dr. Cohen is also Principal Investigator of two R01 grants from the National Heart, Lung, and Blood Institute, as well as the Institute on Aging. In addition, grants from the American Heart Association and a Strategic Alliance with Institut de Recherche Servier provide funds for the Unit. The Unit also receives support and is actively involved in studies within the Cardiovascular Proteomics Center. Total annual funding to the Unit currently exceeds \$1.3 million in direct costs.

### Faculty

#### Professor

Richard A. Cohen, M.D.

#### Assistant Professors

Markus Bachschmid, Ph.D.

Bingbing Jian, M.D., Ph.D.

Reiko Matsui, M.D.

Xiao Yong Tong, Ph.D.

Mengwei Zang, Ph.D.



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# CLINICAL EPIDEMIOLOGY RESEARCH AND TRAINING UNIT



## UNIT CHIEF

*David Felson, M.D., M.P.H.*

## RESEARCH ACTIVITIES

The Clinical Epidemiology Research and Training (CERT) Unit's mission is to perform and promote high-quality research using clinical epidemiologic methods to answer questions about the causes of, and therapy for, disease and disability. The Unit focuses primarily on musculoskeletal diseases, but its mission extends to other diseases as well. The Unit's goals are to train students at various levels and from various disciplines who wish to enter academically based careers in clinical research. The Unit also seeks to advance the statistical, epidemiological, and clinical epidemiological methods used to address clinical research questions. In addition, Unit faculty members strive to develop the Internet as a tool to perform clinical research. The Unit's work also looks to foster scientific collaborations both within and outside Boston University.

The Unit's research activities are centered geographically and intellectually around weekly staff meetings, at which all major research projects are both developed and critically evaluated. Called Research Evaluation Support Core Unit (RESCU), this meeting doubles as the methodology core for the Center Grant from the National Institutes of Health (NIH).

The CERT Unit has grants and contracts supporting research in the amount of \$3.6

million in annual direct costs. Although a few grants are from the Arthritis Foundation, most of the Unit's funding is from the NIH, specifically, a Multidisciplinary Clinical Research Center (MCRC) grant (formerly a Multipurpose Arthritis and Musculoskeletal Diseases Center Grant) from NIH's National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). This funding allows the Unit to be constituted as a multidisciplinary team and include doctoral, non-physician-level investigators who bring methodological expertise to clinical research questions.

The Unit received the MCRC grant for the first time in October 2001, when the Unit was formed, and it was renewed in 2006. This recently renewed Center Grant funds the performance of four specific projects, all of which could have significant impact in the field of arthritis clinical research.

A novel clinical trial is evaluating realignment of the patellofemoral joint of the knee with a knee brace. Most pain in those with knee osteoarthritis (OA) is thought to emanate from the patellofemoral joint; with disease, the patella moves out of its track, the femoral trochlear sulcus. Biomechanical interventions could be inexpensive and effective for treating osteoarthritis, and it is unlikely that industry will study them. David Hunter, M.D., Ph.D., Assistant Professor of Medicine, is a rheumatologist/epidemiologist directing the project.

A second MCRC project evaluates risk factors for gout using a novel, Internet-based epidemiologic method called a case-crossover study. The goal is to evaluate factors that cause flares of gout by identifying the risk factors present in persons with gout just before a flare and comparing these with risk factor status at times when the same person is

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not experiencing a flare in gout. Yuqing Zhang, Ph.D., Professor of Medicine, is the Principal Investigator on this project.

The third MCRC project evaluates biomarkers for vasculitis, including markers that tie the inflammation seen in active vasculitis with measures of thrombosis. Peter Merkel, M.D., M.P.H., Director of the Boston University Vasculitis Center, Associate Director of Clinical Trials for the Section of Rheumatology, and Associate Professor of Medicine, has recently found a high rate of venous thrombosis in persons with active vasculitis. This grant proposes to investigate broadly the elements of micro- and macro-thrombosis and see how they relate to disease activity in vasculitis. Preventing activation of thrombosis pathways may constitute a promising treatment approach for active vasculitis.

A fourth MCRC project has also been funded as a R01 from the NIH and focuses on structural correlates of knee pain. The project, under the direction of David Felson, M.D., M.P.H., Chief of the Clinical Epidemiology Research and Training Unit, Director of the Health Services and Epidemiology Research Program, and Professor of Medicine and Public Health, uses a cohort of 3,000 subjects he and his colleagues have recruited from the community as part of the Multicenter Osteoarthritis Study (MOST). Subjects with knee OA or risk factors for disease are being followed with serial MRIs and X-rays, and Dr. Felson will add to these a gadolinium-enhanced MRI to quantify knee synovium and test if this structural feature or others correlate with the presence or severity of knee pain.

Collaborating with researchers from around the United States, Dr. Felson has successfully sought funding to evaluate risk factors for incident and progressive knee osteoarthritis. Funding for this evaluation was obtained through three different studies. The first, which started in early 2001, is the Framingham Osteoarthritis Study. With the

recruitment of new participants from Framingham, Dr. Felson and his group are expanding the Framingham Heart Study subject group; researchers will use a variety of new osteoarthritis assessments, including MRIs, to evaluate knees. This research will longitudinally evaluate subjects who were previously studied to look at risk factors for the development and progression of disease, focusing on physical activities and vitamin D status, as well as other factors. In addition, the new MRI information will provide among the first population-based data concerning what MRIs look like in knees, with and without disease, that are drawn from the community.

Coupled with the restarting of the Framingham Osteoarthritis Study, Dr. Felson and his colleagues from the University of California, San Francisco; University of Alabama at Birmingham; and University of Iowa obtained funding for MOST. The MOST study has recruited 3,000 subjects from among either those who already have the disease or those at high risk for developing knee osteoarthritis. Researchers are following them longitudinally for clinical outcomes. A large range of potential risk factors will be studied at baseline, including biomechanical factors, bone factors, structural factors, and activity-related factors, to see which predispose individuals either to disease progression or to incidence.

The MOST study will afford the best opportunity yet to identify factors that might prevent disease progression in those who have early disease and to identify risk factors that cause the disease in the first place. The study's expansive scale is necessary because previous studies have been inconsistent and generally underpowered in evaluating important risk factors.

The third study in which Dr. Felson is an active investigator is a large-scale NIH osteoarthritis study, the Osteoarthritis Initiative (OAI). This multi-site investigation will focus on biomarkers for osteoarthritis by looking at MRI-based cartilage loss and

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serological markers that most efficiently identify those at risk of cartilage loss. Research results should permit more rapid drug development in osteoarthritis. Dr. Felson also recently was awarded an R01 to examine the consequences of mal-alignment across the knee in subjects in the OAI. The project's overall goals are to measure long limb alignment in the 4,200 subjects being followed and evaluate whether the effects of knee risk factors for OA, such as obesity, differ if alignment is different. This would suggest that both treatments and preventive measures for OA might vary depending on the alignment status of the knee.

The multitude of observational studies focusing on osteoarthritis promise to be productive intellectually for several years and will serve as rich sources of information about the onset and natural history of the most common form of arthritis.

The Unit pursued several other projects over the past year. Saralynn Allaire, Sc.D., M.S.N, Associate Director of the CERT Unit, and Research Professor of Medicine, continues with other funded studies of osteoarthritis-related work disability. She recently reported positive results from a clinical trial that paired vocational rehabilitation counselors and persons with arthritis in an effort to prevent work disability. This intervention has the potential for widespread use among persons with chronic diseases at risk for work loss. Dr. Allaire has been awarded a grant from the National Institute on Disability and Rehabilitation Research (NIDRR), an agency of the U.S. Department of Education, to help disseminate this intervention.

On June 1, 2007, Dr. Hunter moved to New England Baptist Hospital to become the head of research there. He continues to serve as the Principal Investigator of Project 1 in the MCRC grant (Dr. Felson is Principal Investigator of the Center grant funding this project), and the project will remain at Boston University Medical Center (BUMC). Dr. Hunter spends one day per week at BUMC

finishing up projects and overseeing this funded project.

Kristin Baker, Ph.D., Instructor of Medicine, is an exercise physiologist interested in exercise and nutritional interventions for the treatment of arthritis and other chronic diseases. She has received funding to perform a home-based exercise trial in knee osteoarthritis using TLC, a telephone-based intervention developed by Robert Friedman, M.D., Director of the Medical Information Systems Unit for the Section of General Internal Medicine, and Professor of Medicine and Public Health. Dr. Baker also recently received a K23 to investigate the ratio of omega3/omega6 fatty acids in blood and their relation to knee pain and synovitis. Any relation would provide evidence that pain or synovitis in knee osteoarthritis might be treatable with dietary modification.

Tuhina Neogi, M.D., Assistant Professor of Medicine, an epidemiologist focusing on the association of vitamin K deficiency and arthritis, received the Abbott Scholar Award for her studies of the relationship between low vitamin K status and osteoarthritis, the results of which were recently published in *Arthritis and Rheumatism*. She also recently garnered funding from the Arthritis Foundation to examine the effect of vitamin K supplements on hand osteoarthritis in a randomized, placebo-controlled trial. Lastly, she received a K23 to investigate bone attrition in knee osteoarthritis and its relation to dietary factors, mechanical factors, and bone density.

Faculty members who have primary appointments in other departments collaborate closely with the Unit. Dr. Merkel is working with Unit concerning investigations of outcome measures in vasculitis and scleroderma. Using data from the Framingham Study, Julie Keysor, Ph.D., P.T., Assistant Professor of Physical Therapy at Boston University's Sargent College of Health and Rehabilitation Sciences and a former recipient of K12 funding, is a

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behavioral scientist working with the Unit to perform a multi-center study concerning the causes of disablement in elders, including measures of environmental barriers and emotional state.

### CLINICAL ACTIVITIES

The CERT Unit's primary missions are in research and training, with clinical activity constituting a secondary activity. Nonetheless, Drs. Neogi and Felson are actively involved in clinical medicine. In the last academic year, Dr. Felson attended two months on the Rheumatology Consult Service and had one clinic session per week.

### EDUCATION

The CERT Unit continues to direct the Boston University K30 Program, the Clinical Research Training Program (CREST). In June 2005, CREST's funding was renewed. CREST is offered to postdoctoral fellows or entering faculty throughout BUMC. Its components include matriculating in a master's degree program, at either the School of Public Health or the School of Medicine, that focuses on training and clinical research methodology; completing a thesis that doubles as a scientific paper; and attending a bi-weekly CREST seminar that covers topics in clinical research. Fellows participating in the program present their own research projects, which are critiqued.

Under the direction of Dr. Felson, CREST has become a very popular program, increasing in size from three students during the first year, to six students entering in the second year, to fourteen students per year in 2005 and 2006. The CREST program attracts students from many different disciplines, including psychiatry, pediatrics, ob/gyn, and various medicine subspecialties. It was successfully renewed in 2005 and is funded through 2010.

In addition to administering the CREST program, the CERT Unit has undertaken

direct, onsite training of fellows whose research interests parallel those of CERT investigators. Currently, this includes one geriatrics fellow, two rheumatology fellows, and one epidemiology doctoral student.

As part of morning report, Drs. Felson and Neogi have taught evidence-based medicine to residents on a biweekly basis. Residents select an article to review, conduct an evidenced-based review, and then attend morning report where the evidence-based review is presented. Drs. Felson or Neogi often offers comments concerning the study methodology used.

### MAJOR ACCOMPLISHMENTS

Despite the fact that NIH/NIAMS cut the number of Center Grants from twelve to seven, the CERT Unit was able to renew its grant this year, a significant achievement. In addition, the MOST study – with its six-and-a-half-year, large-scale, multi-center, longitudinal observational study of osteoarthritis – promises to be a major source of activity for this investigative group for the next several years. CERT Unit involvement in the Osteoarthritis Initiative holds promise for future studies. As noted earlier, the CREST program was recently renewed.

Unit faculty members have a number of recent scientific accomplishments to their credit, including Drs. Felson and Baker's demonstration in a large, randomized trial that wedged shoe inserts, commonly used to treat knee osteoarthritis and thought to work by realigning a knee out of proper alignment, do not work to lessen knee pain.

Dr. Neogi has discovered that deficiency of vitamin K, which is present in many vegetables, may increase the risk of osteoarthritis. Vitamin K is a needed cofactor for some enzymes in cartilage and deficient intake is common. In addition, Dr. Felson, working with Steven Vlad, M.D., Rheumatology Fellow, and Bin Zhang, D.Sc., Research Assistant Professor of Medicine,

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have done a reanalysis of glucosamine trials and found that glucosamine, widely used to treat osteoarthritis, is not effective. The results of large-scale, publicly funded trials were all negative, whereas the only positive results emanated from a trial conducted by one company and may represent biased publication.

Until now, epidemiologic studies have focused on the causes of new onset disease, but many chronic diseases disable people by causing acute episodes of pain and suffering. Dr. Y. Zhang has refined an existing methodology, the case-crossover study, and developed a method to perform these studies over the Internet, thereby facilitating their dissemination.

Finally, Dr. Felson wrote an editorial for *Arthritis and Rheumatism* that was covered by the press and summarized in the *Annals of Internal Medicine*. In it, he discussed that current approaches to developing disease modifying treatments for osteoarthritis are futile and that new approaches acknowledging the centrality of pathomechanics to disease are needed.

## **FACULTY**

### **Professors**

Saralynn Allaire, Sc.D., M.S.N.  
David T. Felson, M.D., M.P.H.  
Yuqing Zhang, Ph.D.

### **Assistant Professors**

David J. Hunter, M.D., Ph.D.  
Tuhina Neogi, M.D., FRCPC

### **Research Assistant Professors**

Jingbo Niu, D.Sc.  
Bin Zhang, D.Sc.

### **Instructor**

Kristin Baker, Ph.D.



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# ENDOCRINOLOGY, DIABETES, NUTRITION, AND WEIGHT MANAGEMENT



**SECTION CHIEF**  
*Shalender Bhasin, M.D.*

## RESEARCH ACTIVITIES

The past year witnessed substantial growth and transition in the Section of Endocrinology, Diabetes, Nutrition and Weight Management as Shalender Bhasin, M.D., Professor of Medicine, assumed the position of Section Chief from Lewis Braverman, M.D., Professor of Medicine, who had provided outstanding leadership to the Section for the preceding eight years.

During this period, the level of federal funding to the Section increased, despite a difficult climate at the National Institutes of Health (NIH). In addition to a pre-existing strong base of federal funding, Section faculty received ten new federal grants from NIH, the Department of Defense, and other federal agencies. Currently the Section has more than \$36 million in total project dollars.

Several new research initiatives were implemented, including the establishment of the Androgen Clinical Research Unit, the Muscle and Aging Research Unit, the Steroid Hormone Assay Laboratory, and the Laboratory of Exercise Physiology and Physical Performance. A new clinical program, the Inpatient Diabetes Management Program, under the direction of Marie McDonnell, M.D., Assistant Professor of Medicine, has already yielded substantial standardization and

improvement in the inpatient diabetes management at Boston Medical Center (BMC).

Over the past year, the Androgen Clinical Research Unit (ACRU) staff grew to a total of fourteen and has currently six NIH-funded clinical research studies underway related to androgen biology in men and women. Studies being conducted within ACRU include the “Testosterone Dose Response in Surgically Menopausal Women” (TDSM Study); the “Role of 5 Alpha Reductase in Mediating Testosterone Actions” (5 AR Study); “Effects of Testosterone Replacement on Muscle Performance and Physical Function in Older Men” (TOM Study); “Testosterone and Physical Function in Men on Hemodialysis” (ESRD Study); “Effects of Testosterone Replacement on Atherosclerosis Progression in Older Men with Low Testosterone Levels” (TEAAM Study); and “Testosterone Modulation of Response to Selective Phosphodiesterase Inhibitors.” These studies are being conducted in the General Clinical Research Center (GCRC), with physical evaluations performed in Laboratory of Exercise Physiology and Physical Performance, under the direction of Nathan LeBrasseur, P.T., Ph.D., Assistant Professor of Medicine. Drug supplies for the studies are dispensed by the Investigational Drug Service, under the direction of Hyeseon Hong, Pharm.D.

The Muscle and Aging Research Unit (MARU) was established to spearhead interdisciplinary translational research to foster the development of anabolic therapies for functional limitations associated with aging and chronic diseases. MARU’s current research focuses on investigating the

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mechanisms by which androgens regulate mesenchymal stem cell differentiation. These investigations are being led by Section faculty members Wen Guo, Ph.D., Assistant Professor of Medicine; Ravi Jasuja, Ph.D., Assistant Professor of Medicine; Carl Morris, Ph.D., Assistant Professor of Medicine; and Dr. LeBrasseur, Ph.D.

Dr. LeBrasseur's translational research is also investigating the mechanisms by which function-promoting anabolic therapies increase skeletal muscle mass. Supported by an NIH Career Development Award, Dr. LeBrasseur's research has provided insights into the role of the Akt/mTOR pathway in regulating ribosomal protein translation.

Dr. Guo is also pursuing investigations, supported by an R01 grant, that focus on the role of free fatty acids in inducing insulin resistance. Dr. Guo's research has provided novel insights into the mechanisms by which myostatin regulates adipogenic differentiation. This research has implicated Wnt signaling pathway as an important player in regulation of fat mass by myostatin.

Under Dr. Bhasin's direction, the Steroid Hormone Assay Laboratory specializes in the measurements of sex steroid hormones and vitamin D analogs using liquid chromatography tandem mass spectrometry (LC-MS/MS). Anqi Zhang, Ph.D., has established new methods for the measurement of testosterone and estradiol. Dr. Zhang is also working under the direction of Michael Holick, M.D., Ph.D., Program Director of the GCRC, Director of the Bone Healthcare Clinic, Director of the Vitamin D, Skin and Bone Research Laboratory, and Professor of Medicine and Physiology. Dr. Zhang established procedures for measuring 25-hydroxy vitamin D2 and 25-hydroxy vitamin D3. In the coming year, the laboratory plans to add assays for dihydrotestosterone and perchlorate, and enhance the estradiol assay's sensitivity.

Under Dr. Jasuja's direction, the Biophotonics

Laboratory uses a variety of biophysical techniques to investigate the kinetics and thermodynamics of the conformational changes associated with androgen binding to the androgen receptor. Dr. Jasuja is developing optical spectroscopy instrumentation to study the molecular fingerprints of ligand-receptor interactions in the androgen receptor-signaling pathway. The instrumentation has an integrated millisecond mixer and utilizes components from photoacoustics, photothermal beam deflection, and time-resolved emission spectroscopies. Combined with the fluorescence lifetime imaging capabilities, these measurements will elucidate the residue-specific perturbations in the ligand binding pocket that modulate functional activation of androgen receptors in cellular milieu.

A better understanding of agonist- and antagonist-induced structural changes will allow for rational design of selective androgen receptor modulators for anabolic therapies. The research is currently being conducted in collaboration with James Dalton, Ph.D., Professor of Pharmaceutics at Ohio State University; James Head, Ph.D., Professor of Physiology at Boston University; and Chris Yengo, Ph.D., Assistant Professor in the Department of Biology at the University of North Carolina at Charlotte. These investigations should help determine the mechanisms of tissue selective actions of selective androgen receptor modulators.

The Laboratory of Exercise Physiology and Physical Performance (LEP<sup>3</sup>) is a state-of-the-art exercise laboratory within the Section under the direction of Dr. LeBrasseur and Thomas Storer, M.D., Ph.D. Renee Miciek, M.S., is the laboratory's research technician. The LEP<sup>3</sup>'s global mission is to assess muscle performance and physical function in states of health and disease. The LEP<sup>3</sup> continues to design and conduct testing protocols for primary and secondary outcomes in several federally-funded research programs investigating the effects of anabolic therapies on muscle mass and function in states of



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health and disease.

Dr. Bhasin is the Principal Investigator for the protocols being tested. The research protocols include “The Role of 5-Alpha Reductase in Mediating Testosterone Actions” (NIH/National Institute of Child Health and Human Development, 1R01HD43348-02); “Testosterone Dose Response in Surgically Menopausal Women” (NIH/National Institute of Diabetes and Digestive and Kidney Diseases, R01); “Effects of Testosterone Replacement on Muscle Performance and Physical Function in Older Men” (NIH/National Institute on Aging, 2R01AG014369-06); and “Testosterone Effects on Atherosclerosis Progression in Older Men.” In addition to forging collaborations with other Sections within the Department of Medicine, the LEP<sup>3</sup> has been working with investigators at Massachusetts General Hospital on Strategies for the “Treatment of HIV-associated Metabolic Syndrome” (NIH/NIDDK 2R01DK0493-02).

Under the direction of Neil Ruderman, M.D., D. Phil., Professor of Medicine, Physiology and Biophysics, the Diabetes Research Unit continues to focus on the AMPK/malonyl CoA fuel sensing and signaling mechanism and its role in regulating cell metabolism and disease prevention. Over the past year, Unit researchers have shown that downregulation of AMPK by genetic or chemical means increases oxidative stress in cultured endothelial cells and makes them more susceptible to the inflammatory effect of TNF $\alpha$ .

Likewise, Dr. Ruderman’s group found that sustained exposure of these cells to a high glucose medium or to the fatty acid palmitate causes similar effects on both AMPK and oxidative stress and inflammation. Jose Cacicedo, a pre-doctoral student, and Yasuo Ido, M.D., Ph.D., Assistant Professor of Medicine, collaborated on this work. Unit researchers have also found that AMPK activation prevents these effects from

occurring. Thus, it appears that AMPK dysregulation by fuel excesses could make the endothelial cell more susceptible to events thought to initiate atherogenesis.

Dr. Ido, collaborating with Fan Lan, Ph.D., and Mr. Cacicedo have also discovered that activation of the sirtuins, histone/protein deacetylases that have been linked to delayed aging, also leads to activation of AMPK. They have shown that this is likely due to their ability to deacetylate and activate the AMPK-kinase, LKB1.

In other Unit studies, Marie-Soleil Gauthier, a post-doctoral fellow working, in part, with. Asish Saha, Ph.D., Assistant Professor of Medicine, has demonstrated that AMPK is activated in the adipocyte by lipolysis, which, in turn, acts by causing an increase in the AMP/ATP ratio. As in the endothelial cell, she found that failure to activate AMPK in this situation causes a substantial increase in oxidative stress. Other Unit projects include Dr. Saha’s examination of the mechanism for glucose-induced downregulation of AMPK and the induction of insulin resistance in skeletal muscle and cultured HepG2 cells, research he is conducting with the assistance of Gabriela Suchankova, Ph.D., a post-doctoral fellow. The Diabetes Research Unit and Dr. Holick’s team is studying the inhibition of keratinocyte growth by AMPK and Vitamin D. Finally, Meghan Kelly, a post-doctoral fellow, is studying the characterization of the IL6 deficient mouse in which a decrease in muscle and adipose tissue AMPK precedes the development of obesity, glucose intolerance, and dyslipidemia. All of these studies are supported by NIH grants, and many have been done in collaboration with other U.S. laboratories, as well as those overseas.

The Iodine and Perchlorate Research Laboratory, under the direction of Dr. Braverman, Xue Mei He, M.D., and Sam Pino, provides iodine analyses for outside investigators and commercial laboratories and continues to be a resource for thyroidologists.

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A mass spectroscopy assay for perchlorate has recently been established at BMC.

Dr. Braverman, Elizabeth Pearce, M.D., Assistant Professor of Medicine, and Angela Leung, M.D., are conducting an ongoing international study of the effects of environmental perchlorate exposure on thyroid function in pregnant women. They are also studying the iodine and perchlorate content of human breast milk, human colostrum, and infant formula to establish the iodine nutrition of breast and formula-fed infants. In addition, with support of an NIH K23 award, Dr. Pearce is examining the effects of thyroid function on lipid subparticle size and cardiovascular risk using BMC clinical studies, as well as data from the Framingham Heart Study cohort.

Physicians and researchers in the Vitamin D, Skin and Bone Research Laboratory, which is under Dr. Holick's direction, continue to be leaders in the field of vitamin D, osteoporosis, metabolic bone disease, psoriasis, and hair research. Dr. Holick and his colleagues have been investigating the important role of sunlight and artificial ultraviolet B radiation devices in providing elders and patients who suffer from fat malabsorption with their daily vitamin D requirement. Studies are underway to understand the mechanism by which 1,25-dihydroxyvitamin D is able to reduce risk of colorectal cancer. Several active vitamin D analogues are being tested in animal models for both prostate and colon cancer, with the goal being to identify one for clinical trials. Progress has been made in formulating a parathyroid hormone-related peptide receptor antagonist for the mitigation of chemotherapy-induced alopecia.

In the Center for Nutrition and Weight Management, which is under the direction of Caroline Apovian, M.D., Associate Professor of Medicine, researchers are collaborating with Noyan Gokce, M.D., Associate Director of Echocardiography at BMC, Associate Professor of Medicine, and a member of the Section of Cardiology, on several trials to

study obesity and its effects on endothelial cell function; vascular consequences of lipid deposition; alterations in fat cell-derived adipocytokine expression before and after weight loss; and between subcutaneous, omental and mesenteric depots. Results have established that weight loss, both medically and surgically induced, can bring about significant improvements in endothelial cell function, which lowers the risk for cardiovascular disease. Two NIH R01 grants are funding this project; Dr. Gokce is the Principal Investigator and Dr. Apovian is the Co-investigator.

Other studies conducted by Nutrition and Weight Management researchers include fingerstick versus alternate site testing for Type 2 diabetes. Funded by the Department of Health and Human Services, this study is complete and a manuscript has been sent to *Diabetes Care*, a publication of the American Diabetes Association. In addition, enter faculty members investigated the use of meal replacement therapy for weight loss in adolescents. Funded by the food industry, this study is also complete and a manuscript is in review by *The Journal of the American Dietetics Association*.

A pilot project investigating the use of medium-chain triglycerides as a novel therapy for weight loss in patients with Type 2 diabetes is also underway. It is funded by the Boston Obesity Nutrition Research Center, which receives funding from the National Institute of Diabetes and Digestive and Kidney Diseases.

Industry-related research within the Center has expanded to include several new projects. Orexigen and Sanofi-Aventis are funding two appetite suppressant studies that are nearing completion with additional studies to follow. Eli Lilly and Company is supporting an investigational drug study that will evaluate weight loss when exenatide is used to treat Type 2 diabetes; participants are currently being recruited. Pfizer is funding a 14-month weight maintenance following a low-calorie

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diet study. It is a crucial time for obesity research because very little research in effective means for weight maintenance currently exists.

### CLINICAL ACTIVITIES

The consolidated clinic at BMC that integrates Endocrinology, Diabetes, Nutrition and Weight Management was established in September 2001 and is a state-of-the-art, 4,500-square-foot facility permitting complete endocrine, nutrition, and weight management evaluation. The clinic includes spacious examining rooms, three thyroid ultrasound instruments, two procedure rooms, two bone densitometry instruments, a patient education and conference room, a phlebotomy room, and rooms for dietitians and nurses who educate patients about diabetes and diet. The clinic's census has increased steadily at an annualized rate of 10% over the past five years; the past year witnessed an impressive 20% increase in patient visits. The wait time for a patient's first appointment decreased by 50% during the past year and is expected to decline further with the recruitment of additional faculty and the streamlining of clinic procedures.

The clinic provides medical consultation in the areas of thyroid disease, obesity, malnutrition and other nutritional disorders, gastric bypass surgery, lipid disorders, Type 1 and 2 diabetes mellitus, androgen-deficiency syndromes, sexual dysfunction in men and women, infertility, and polycystic ovary syndrome. The Center recently added three new physicians: Sonia Ananthakrishnan, M.D., a general endocrinology specialist; Alan Farwell, M.D., a general endocrinology and thyroid specialist; and Lalita Khaodhiar, M.D., Assistant Professor of Medicine, a nutrition specialist who will enhance patient access to the clinic. The clinic houses the Center for Weight Management and Nutrition, which includes three physician nutrition specialists, two bariatric surgeons, four registered dietitians, a behaviorist, and an exercise specialist. Drs. Apovian and Khaodhiar, as well as Nawfal

Istfan, M.D., Ph.D., Associate Professor of Medicine, provide medical consultation in the area of obesity and nutritional disorders. Donald Hess, M.D., Director of the Bariatric Surgery Program at BMC, and Assistant Professor of Surgery, consults on gastric bypass surgery. Drs. Ruderman and McDonnell, as well as Elliot Sternthal, M.D., Clinical Director of Diabetes Services at BMC, and Assistant Professor of Medicine, provide expertise on the management of diabetes mellitus. The clinic takes a comprehensive, multidisciplinary approach to diabetes with a patient management coordinated by a physician, three nurse practitioners, two certified Diabetes Nurse Educators (CDE), and dietitians.

Also housed within the clinic is the Thyroid Diagnostic and Treatment Center. Drs. Braverman and Pearce, as well as Stephanie Lee, M.D., Ph.D., Director of Endocrine Clinics at BMC, and Associate Professor of Medicine, and Joshua Safer, M.D., Assistant Professor of Medicine, offer nationally and internationally recognized expertise in diseases of the thyroid. The Thyroid Center offers comprehensive medical evaluation, as well as medical and surgical therapies, of diseases of the thyroid. In the Thyroid Clinic, thyroid ultrasounds are available to further assess thyroid size, nodularity, and adenopathy. Ultrasound is also utilized to assist in fine needle aspiration biopsies of thyroid nodules and cervical adenopathy.

With seventy-five years of combined experience with radioactive iodine therapies, Drs. Braverman and Lee offer special expertise in the treatment of hyperthyroidism and thyroid cancer. Drs. Braverman and Lee are two of a select number of endocrinologists who directly administer radioactive iodine to patients. Dr. Lee has developed a radioactive iodine dosimetry program for maximal dose I-131 therapy for the treatment of advanced thyroid carcinoma. BMC's program is one of only a dozen in the country to provide extremely high-dose radioactive iodine therapy for life-threatening thyroid malignancies.

Drs. Braverman and Lee's expertise in thyroid disease has made BMC a national and international referral center for patients with complicated thyroid disease. Drs. Lee, Safer, Pearce, and Farwell are certified and experts in thyroid ultrasonography for diagnostic imaging and ultrasound guided biopsies of thyroid nodules and cervical neck adenopathy. The Thyroid Center's endocrinologists and surgeons – the Section of Surgical Oncology and Surgical Endocrinology's David McAneny, M.D., Associate Professor of Surgery; Jennifer Rosen, M.D., Assistant Professor of Surgery; and Michael Stone, M.D., Vice Chair of Administrative Affairs, Division of Surgery, Chief of the Section of Surgical Oncology, and Professor of Surgery, as well as the Department of Otolaryngology – Head and Neck Surgery's Gregory Grillone, M.D., Chief Medical Officer, *ad interim*, and Assistant Professor of Otolaryngology – Head and Neck Surgery; Scharukh Jalisi, M.D., Assistant Professor of Neurosurgery and Otolaryngology – Head and Neck Surgery; and J. Pieter Noordzij, M.D., Associate Professor of Otolaryngology – Head and Neck Surgery – work closely to ensure excellent, coordinated care of patients who require surgical treatment of their thyroid disease.

Robert Levin, M.D., Professor of Medicine, continues to provide superb endocrine care in general endocrinology and Paget's disease. Thomas Moore, M.D., Professor of Medicine, provides special expertise in endocrine hypertension and general endocrinology.

At BMC, Dr. Bhasin has initiated a men's health program that specializes in sexual dysfunction and androgen deficiency in men and women. When fully developed, this program will provide a multidisciplinary team approach to the management of reproductive disorders in men. Working with Dr. Bhasin is Andrea Coviello, M.D., M.Sc., Assistant Professor of Medicine, a nationally-recognized expert in polycystic ovary disease and other androgen-related disorders in women. BMC's Diabetes Clinical Service has greatly expanded under Dr. Sternthal's direction.

Under the leadership of Barbara Jarvis, R.N., C.D.E., the service's Clinical Diabetes Education Program, which is accredited by the American Diabetes Association, successfully completed a re-evaluation and was recertified. The service has expanded to accommodate an increase in both outpatient and inpatient referrals for diabetes care. In the past year, the service has welcomed one registered nurse who is a certified diabetes educator, Mary Rushton, into the outpatient clinic, and two nurse practitioners who are C.D.E.s, Marina Donahue and Lynn White, to provide care in both the clinic and the inpatient diabetes service. In 2006, Patricia Hanrahan, N.P., C.D.E., expanded the outpatient diabetes program by establishing an insulin pump and continuous glucose monitoring service at BMC.

In 2005, Dr. McDonnell and Ms. Hanrahan successfully initiated a comprehensive Inpatient Diabetes Management Service and guidelines for intensive management of diabetes in BMC's surgical and medical intensive care units. Ms. Donahue and Ms. White joined the service in 2006. The Adult Inpatient Diabetes Service is designed to meet current national standards for glycemic control in hospitalized patients. The program recognizes that, with the rising prevalence of insulin resistance due to conditions such as obesity and the metabolic syndrome, the number of inpatients with known diabetes, as well as unknown diabetes, is expected to rise. Moreover, expert opinion and clinical research have identified hyperglycemia as a factor that increases length of stay, hospital complications, and inpatient mortality. Dr. McDonnell and the three nurse practitioners work together as a physician-nurse practitioner team to optimize the care of this large patient population, both in the hospital and following discharge to the outpatient clinics.

An important component of the Inpatient Diabetes Management Service is the education of nurses, physicians, and patients. A multidisciplinary endocrine subcommittee, with representatives from Pharmacy, Nursing,

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Information Technology, Internal Medicine, and the Section of Endocrinology, provides this resource. The committee's goal is safe and effective insulin therapy for all inpatients with hyperglycemia.

In collaboration with BMC's Pharmacy and Information Technology departments, the Section has put a plan in place to continuously evaluate the diabetes-related clinical outcomes in the patient population. The data from this ongoing project will be invaluable for both internal and general knowledge about the management of patients with diabetes and hyperglycemia at BMC. This team will provide daily consultation to all patients with hyperglycemia in all BMC's intensive care units (medical and surgical) and will assist the transition to the floors to improve medical outcomes.

Finally, because of the substantial increase in the volume of consultations, the Section added a third fellow to manage the growing load of inpatient diabetes-related consultations. Through the Endocrine fellowship, the diabetes service has been working with the high-risk prenatal obstetrics group at BMC to manage pregnant women with diabetes mellitus both in and out of the hospital.

## EDUCATION

The Accreditation Council for Graduate Medical Education (ACGME) has accredited the Section's fellowship training program for five years, with the next site visit planned for late 2009. Dr. Safer is now the fellowship training program director.

The fellowship program remains highly competitive and received more than 200 applications for three positions. Endocrinology fellowship graduates continue to do well, with recent graduates obtaining academic and clinical positions at Emory University in Atlanta; Caritas St. Elizabeth's Medical Center in Boston; Reading Hospital and Medical Center in Pennsylvania; Beverly Hospital in Massachusetts; Penn State College

of Medicine in Pennsylvania; and Boston University Medical Center.

The Section's training program in Diabetes and Nutrition has been supported by an NIH T32 Training grant, which is in its 48<sup>th</sup> year of continuous funding. The Training Grant has had only two Principal Investigators during this period: James Melby, M.D., from inception to 1985 and Dr. Ruderman since 1986.

The Section's weekly Endocrine Grand Rounds series – which features national leaders presenting seminars and discussing cases, faculty-led research seminars, and fellows' case reports – continues to be well-attended. Fellows participate in breakfast conferences once or twice a week. The conferences include core topics, case discussion, pathology review, and a journal club. In addition, the fellows run a weekly board review luncheon. The Androgen Research Group also has a journal club and guest lecturer series.

Section members are active in the education of medical residents. Residents from BMC and other institutions participate in Endocrine electives. Section faculty members attend on the general medicine wards, attend on the endocrine inpatient consult service, attend on the diabetes consult service, participate in morning report, and participate in Wednesday firm conferences for medical residents. Dr. Levin coordinates the Department of Medicine's weekly Medical Grand Rounds series.

The Section participates in the "Biology of Disease" (BOD) course offered to second-year Boston University School of Medicine (BUSM) students. Dr. Safer oversees the Section's participation, which continues to garner excellent reviews from students. Section members are involved with the "Introduction to Clinical Medicine" that is offered to first- and second-year BUSM students. Section members participate in the ambulatory portion of the Medicine clinical



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clerkship for third-year students. Fourth-year students, from BUSM and outside institutions, participate in Endocrinology electives that are under the direction of Section members.

As part of the BOD course, faculty members in the Center for Nutrition and Weight Management conduct lectures on nutrition. In addition, Center staff members teach twice a year in the cancer skills lab also offered to second-year BUSM students. In response to requests for increased nutrition education for BUSM students, Dr. Apovian and Carine Lenders, M.D., Assistant Professor of Pediatrics, are collaborating with BUSM faculty directors to meet this need.

### MAJOR ACCOMPLISHMENTS

Dr. Bhasin serves as the Associate Editor of *The Journal of Clinical Endocrinology and Metabolism*, and as Chair of the Endocrine Society's Expert Panel for the development of guidelines for androgen deficiency syndromes in men.

Dr. Apovian co-directs the Harvard Obesity Course on a yearly basis with lecture contributions from Diana Cullum-Dugan, R.D., L.D.

Dr. Braverman received the Endocrine Society's Robert Williams Distinguished Service Award. He was also appointed Editor-in-Chief of the *Endocrine Practice*, the flagship journal of the American Association of Clinical Endocrinologists.

Dr. Holick received the NIH's Annual General Clinical Research Centers Program Award for Excellence in Clinical Research.

Drs. Holick and Ruderman received national awards for excellence in basic and clinical investigation.

Dr. Ruderman was the recipient of the Albert Reynold Award. The award is given to an individual whose career is distinguished by outstanding achievements in the training of diabetes research scientists or the facilitation of diabetes research by diabetes investigators.

Norman Mazer, M.D., Ph.D., Associate Professor Medicine, was the recipient of the Young Andrologist Award of the North American Menopausal Society.

### FACULTY

#### Professors

Shalender Bhasin, M.D.  
Lewis E. Braverman, M.D.  
Tai C. Chen, Ph.D.  
Michael Holick, M.D., Ph.D.  
Robert M. Levin, M.D.  
Thomas J. Moore, M.D.  
Neil Ruderman, M.D., D.Phil.

#### Associate Professors

Caroline M. Apovian, M.D.  
Alan Farwell, M.D.  
Nawfal Istfan, M.D., Ph.D.  
Stephanie L. Lee, M.D.  
Norman Mazer, M.D.  
Rahual Ray, Ph.D.  
Sayon Roy, Ph.D.  
Joshua Safer, M.D.

#### Assistant Professors

Andrea Coviello, M.D.  
Yasuo Ido, M.D., Ph.D.  
Phillip Knapp, M.D.  
Lalita Khaothiar, M.D.  
Nathan LeBrasseur, P.T., Ph.D.  
Alan Malabanan, M.D.  
Marie McDonnell, M.D.  
Elizabeth Pearce, M.D.  
Asish K. Saha, Ph.D.  
Elliot Sternthal, M.D.

#### Instructor

Sonia Ananthakrishnan, M.D.

#### Clinical Associate

Marina Donahue, N.P.  
Patricia Hanrahan, N.P.  
Lynn White, N.P.

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# GASTROENTEROLOGY



**SECTION CHIEF**  
*M. Michael Wolfe, M.D.*

## RESEARCH ACTIVITIES

Under the leadership of M. Michael Wolfe, M.D., Professor of Medicine and Research Professor of Physiology and Biophysics, the Section of Gastroenterology continues to gain widespread prominence for its clinical activities, its basic and clinical research arenas, and its commitment to the education of trainees at all levels.

The Section's clinical research effort has been very successful in terms of its productivity and visibility. Paul Schroy, M.D., M.P.H., Director of Clinical Research for the Section of Gastroenterology, and Professor of Medicine, has achieved national and international recognition as a leading investigator in developing colorectal cancer screening strategies. His work focuses on defining the role of shared decision-making as a strategy for increasing patient adherence to colorectal cancer screening recommendations; developing a prediction model for advanced colorectal neoplasia based on epidemiologic risk factors alone; and quality improvement issues related to screening colonoscopy. In addition, Dr. Schroy collaborates with members of the Department of Radiology and faculty within the Boston University School of Public Health (BUSPH) to explore the clinical feasibility and validity of novel screening tests, such as CT colography and stool-based DNA

testings.

During the next academic year, Dr. Schroy plans to re-submit his R01 risk stratification proposal and begin preparation of a second R01 proposal to continue ongoing investigation related to his current "Shared Decision-Making for Colorectal Cancer Screening" project. He will also assist in the preparation and submission of RFA proposals from BUSPH's "Population Sciences Cancer Working Group" to support collaborative cancer control activities. Finally, Dr. Schroy has continued ongoing activities related to his role as Director of Clinical Research and those of the Section's Clinical Research Working Group. These include negotiations with Ambergen, Inc., to support at least one new translation project and assisting other Section members in their negotiations with other potential sponsors.

David Nunes, M.D., Director of Hepatology at Boston Medical Center (BMC), and Associate Professor of Medicine, continues his active collaboration with the Section of Infectious Diseases at Boston Medical Center (BMC) as a Co-Investigator of a grant from the National Institutes of Health (NIH) that evaluates interactions in individuals co-infected with hepatitis C and HIV. Known as "HALO," this grant was funded for an additional five years by the NIH in 2006. Dr. Nunes has also obtained industry funding to evaluate various treatment modalities for hepatitis C and other hepatitides. Dr. Nunes' studies constitute a very important component of the clinical research being performed in the Section. His plans for next year include ongoing participation in clinical research that will hopefully lead to increased supplemental funding, as well as the successful renewal of the CHARM grant in which he actively participates.



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Brian Jacobson, M.D., M.P.H., Director of Endoscopic Ultrasonography and Associate Director of Endoscopy at BMC, and Assistant Professor of Medicine, is a leading investigator in the area of the natural history of Barrett's esophagus. His May 2006 publication in *The New England Journal of Medicine*, which focused on the impact of obesity on the development of gastroesophageal reflux disease (GERD) in women in the Nurse's Health Study, is widely quoted as the defining study in this important area. Along with Dr. Schroy, Dr. Jacobson comprises the nucleus for the future development of health services research within the Section. Dr. Jacobson plans to continue his attainment of independent status by applying for R03 and R01 grants during the coming academic year.

In addition to his expertise in the area of inflammatory bowel disease (IBD), Francis Farraye, M.D., M.Sc., Clinical Director for the Section of Gastroenterology, Co-Director of the Center for Digestive Disorders at BMC, and Professor of Medicine, is a renowned authority in the area of dysplasia, colonic polyps, and colorectal cancer in IBD. He recently submitted a grant application to the Crohn's & Colitis Foundation of America (CCFA) Senior Investigator Award to develop an IBD dysplasia and cancer registry. Although not funded, Dr. Farraye received an excellent evaluation that will form the basis for his resubmission during the coming academic year. He also plans to apply for extramural funding using data generated by his Department of Medicine pilot grant on Vitamin D malabsorption in IBD patients and to collaborate with other faculty members within the Section and in the Department of Medicine on IBD-related research studies.

David Lichtenstein, M.D., Director of the Endoscopy Program at BMC, and Associate Professor of Medicine, is researching the development and application of endoscopic approaches for the diagnosis and management of pancreaticobiliary tract disorders, gastrointestinal hemorrhage, and gastrointestinal malignancies. Dr. Lichtenstein

is evaluating new "coated" metal stent technology for the treatment of malignant biliary tract obstruction. He is also examining secondary modifications of human trypsinogens in pancreatic disease and modifiable factors influencing polyp detection during colonoscopy screening for colorectal cancer.

In addition, Dr. Lichtenstein intends to evaluate endoluminal antireflux procedures for the treatment of GERD; develop endoscopic techniques to treat post-gastric bypass complications; and assess parameters contributing to compliance and efficiency in an open access endoscopy system. Finally, Dr. Lichtenstein plans to collaborate with members of the Department of General Surgery to explore the feasibility of natural orifice transluminal endoscopic surgery (NOTES) in further attempts to advance minimally invasive surgery.

Christopher Huang, M.D., Instructor of Medicine, is emerging as an expert in the BMC community in the performance of "special" endoscopic procedures. He is collaborating with Michael O'Brien, M.D., M.P.H., Chief of Anatomic Pathology at BMC, and Professor of Pathology and Laboratory Medicine, and Dr. Farraye to examine the significance of hyperplastic polyps as an alternative pathway in the development of colorectal cancer. He is also working with Richard I. Rothstein, M.D., Section Chief of Gastroenterology and Hepatology at Dartmouth-Hitchcock Medical Center, and Professor of Medicine at Dartmouth Medical School, to develop and evaluate new endoscopic modalities for the treatment of GERD.

Daniel Mishkin, M.D., Instructor of Medicine, is developing a reputation as an expert in video capsule endoscopy, and he is working closely with its manufacturer to develop new applications for this technology. Dr. Mishkin's expertise in small intestinal imaging resulted in his selection as the first investigator in New England region to explore the use of the double balloon enteroscope, which will enable

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endoscopists to traverse significant portions of the small intestine previously inaccessible with standard endoscopes.

Albena Halpert, M.D., Instructor of Medicine, received a career development grant from the American College of Gastroenterology (ACG) to support her research evaluating various strategies for the management of functional bowel disorders. She has also received pharmaceutical support to investigate the efficacy of various agents to treat constipation-dominant irritable bowel syndrome and other functional disorders. Owing to personal considerations, Dr. Halpert will be departing BMC during the coming academic year but will continue her present research activities on a part-time basis.

Other Section faculty members engaged in clinical research include Marcos Pedrosa, M.D., M.P.H., Director of Endoscopy at the VA Boston Healthcare System (VABHS), and Associate Professor of Medicine, who is investigating surveillance strategies for and treatment of Barrett's esophagus. He is engaged in trials evaluating hepatitis C treatment protocols, utilizing various agents to treat this very common disorder. Dr. Pedrosa was actively involved in studies that include other investigators throughout the United States in the use of photodynamic therapy (PDT) for the ablation of high-grade dysplasia in Barrett's esophagus. Finally, he has been an active participant in VA cooperative studies evaluating the use of colchicine and other agents in the treatment of alcoholic liver disease.

The Section's basic biomedical research effort includes epithelial cell and oral biology, gastrointestinal carcinogenesis, and obesity and other metabolic disorders. Despite the death of Chi-Chuan Tseng, M.D., Ph.D., Acting Chief of the Section of Gastroenterology at the VABHS, and Associate Professor of Medicine, in September 2006, the Section continued its record of productivity and achieved success in its efforts to procure funding from the NIH and other

medical societies and industry. Dr. Tseng's lab had been investigating role of the transcription factor gut-enriched Krüppel-like factor (GKLF) in colon cell growth and differentiation. The roles of various transcription factors and gastrointestinal regulatory peptides in the pathophysiology of colorectal cancer and other gastrointestinal neoplasms remain the focus of two existing laboratories within the Section.

Research activities in Dr. Wolfe's laboratory include studies examining the contribution of gastrointestinal regulatory peptides to the pathogenesis of obesity, and, specifically, the role of glucose-dependent insulinotropic polypeptide (GIP) on lipid homeostasis and the development of obesity. He utilizes various animal models that simulate the Roux-en-Y gastric bypass procedure and has determined that much of the operation's benefit is derived from bypassing the upper small intestine, the site in which GIP is both synthesized and released in the circulation.

Dr. Wolfe continues to utilize the GIP-specific receptor antagonist developed in his laboratory to perform these important physiological studies. He collaborates on an ongoing basis with Barbara Corkey, Ph.D., Vice Chair for Research, Director of the Obesity Research Center and the Boston Obesity and Nutrition Research Center (BONRC), Professor of Medicine and Biochemistry, and a member of the Section of Molecular Medicine. This GIP-receptor antagonist is also being evaluated for potential commercial use in the treatment and prevention of obesity and obesity-related disorders, such as Type 2 diabetes mellitus and nonalcoholic fatty liver disease (NAFLD).

Dr. Wolfe continues to work closely with Ms. Lisa Jepeal to examine the functional relationship between adipocytes and intestinal (GIP-producing) K-cells. They are also examining the regulation of the GIP gene and its specific relationship to insulin expression, as well as the ontogeny of GIP-producing cells in the intestine. These studies will form the

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basis for eventual attempts at gene therapy to direct insulin expression in GIP-producing K-cells of the upper small intestine. They have recently embarked on new strategies involving the creation of various transgenic models, including conditional GIP-receptor and GIP (ligand) knockout mice.

Another close collaborator of Dr. Wolfe is Diane Song, Ph.D., Instructor of Medicine, who continues to play an instrumental role in the performance of studies involving the role of GIP in adipocyte differentiation and fat cell function. Dr. Song is utilizing her F32 grant from the NIH to examine GIP fat cell signaling, thereby fostering her development as an independent investigator. Drs. Wolfe and Song have initiated a collaborative effort with Konstantin Kandror, Ph.D., Associate Professor of Biochemistry, to investigate the role of GIP in nutrient storage in skeletal muscle. Finally, Dr. Song is playing an instrumental role in formulating animal studies to examine the contribution of GIP to the benefit derived by gastric bypass surgery in the treatment of obesity.

T. Carlton Moore, M.D., Assistant Professor of Medicine, receives funding from a supplemental R01 from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to support his collaboration with Dr. Wolfe. He is seeking to develop a bioassay to measure GIP that will enable this laboratory and other investigators to accurately determine the concentration of bioactive GIP in plasma and tissue samples in both humans and other animals.

In collaboration with Michael Boylan, Ph.D., Research Assistant Professor of Medicine, Dr. Wolfe has been examining the proposed use of engineered stem cells implanted in the small intestinal mucosa and programmed to synthesize and release therapeutic peptides into the systemic circulation. Once implanted in patients, these stem cells will assume many of the characteristics of neighboring cells of the small intestinal lining in which they now reside. After a sufficient number of cells

expressing the therapeutic peptide have been prepared, Dr. Wolfe plans to use minimally invasive endoscopic techniques to implant them into the proximal small intestinal lining. Dr. Wolfe was one of only three recipients of Boston University's Ignition Award to conduct these studies.

In addition to examining the role of GIP on lipid homeostasis and in the development of obesity, Dr. Wolfe's laboratory is also performing research to determine the role of the regulatory peptide gastrin in the pathogenesis of both colorectal cancer (CRC) and esophageal adenocarcinoma, supported by extramural funding from the National Cancer Institute (NCI) and AstraZeneca. In collaboration with Daniel Prabakaran, Ph.D., Dr. Wolfe has expanded his investigation to examine the mechanisms by which cyclooxygenase (COX) isoenzymes play a role in the development and natural history of CRC. Specifically, he is studying the contribution of T-cell immunologic mechanisms in mediating the beneficial effects of COX inhibition in CRC.

Dr. Wolfe continues to collaborate with Satish Singh, M.D., Assistant Professor of Medicine, on studies aimed at determining the mechanisms by which GIP stimulates glucose absorption in the small intestine. Their initial studies were presented at the Obesity and Nutrition Plenary Research Session at Digestive Disease Week in May 2006, and they are currently preparing a manuscript to report these findings. These studies will have important implications with regard to the pathogenesis of obesity and to potential treatment modalities in the future.

In addition to this collaborative effort, Dr. Singh is investigating the barrier and transport processes that participate in maintaining the intracellular pH of epithelial cells within the intestinal mucosa. An R01 from the NIH supports his collaboration with Irving Bigio, Ph.D., a professor in the Department of Biomedical Engineering and the Department of Electrical and Computer Engineering at

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Boston University's College of Engineering, to develop methods for using endoscopic spectrophotometry to detect neoplastic and metaplastic lesions in the esophagus and other areas of the gastrointestinal tract, including the use of elastic scattering spectroscopy for cancer detection.

During the past academic year, Gwynneth Offner, Ph.D., Associate Professor of Medicine, consolidated her laboratories, which involved relocating and transferring the administration of research funds from Boston University School of Medicine (BUSM) to BMC. She and her colleagues have continued their NIH-funded research to examine the expression of mucin glycoproteins in the oral cavity and gastrointestinal tract. Dr. Offner has also continued her investigation of mucin gene expression in inflammatory bowel disease, and she has obtained some promising results using gene-silencing technology. She hopes to expand this portion of her research program and apply to the Broad Foundation for funding during the next academic year. Working with Dr. Wolfe, Dr. Offner played a central role in submitting the Section's T32 grant application to the NIH. Although it received an excellent score (180), the priority was not sufficient to secure funding. Drs. Wolfe and Offner plan to re-submit this application only after additional new research faculty members are successfully recruited to the Section.

H. Christian Weber, M.D., Assistant Professor of Medicine, has expanded his studies examining the role of the bombesin receptor subtype-3 (BRS-3) in obesity and diabetes. Current experiments focus on its role in glucose metabolism in human and rodent fat cells, and he is collaborating with investigators at the Joslin Clinic in Boston and members of BONRC. Dr. Weber will be submitting an R01 application to the NIH to support these research activities. He and his colleagues are also examining the role of receptors to bombesin-like peptides, including gastrin-releasing peptide (GRP), and their cell surface receptors in epithelial neoplasms derived from

the gastrointestinal tract, specifically in the colon. His research includes the regulation of GRP-receptor gene expression and the role of agonist stimulation in colorectal and pancreatic cancer cells and in CRC tumorigenesis.

David Waxman, Ph.D., Professor of Cell and Molecular Biology and Medicine in the Department of Biochemistry/Department of Pharmacology and Experimental Therapeutics and Adjunct Professor of Medicine in the Section of Gastroenterology, continues his research examining the regulation of liver gene expression and the anti-cancer agent cyclophosphamide. He is a recognized leader in the area of liver cytochrome P450 regulation, gene expression, and biochemistry. Dr. Waxman is examining the use of P450 isoenzymes and related drug-metabolizing enzymes as drug susceptibility genes for cancer gene therapy.

The Section's goals for the coming academic year include continued excellence and program expansion, as well as the successful procurement of additional funding from the NIH and other extramural sources and a (T32) GI Fellowship Training Program grant from the NIDDK. Plans are currently underway to recruit a mucosal (T-cell) immunologist to complement the strong clinical program in inflammatory bowel disease at BUSM. In addition, Dr. Wolfe has also begun a concerted effort to recruit a hepatologist with an interest in inflammatory diseases of the liver, such as viral hepatitis and nonalcoholic steatohepatitis (NASH).

### CLINICAL ACTIVITIES

The Section's clinical service continues to be highly regarded in terms of quality and quantity, and new, contemporary, and innovative services have been added during the past academic year.

During the nearly eleven years since Dr. Wolfe assumed the position of Section Chief, the number of patient visits and endoscopic procedures increased significantly, as shown in

Figure 1. In 1996, the former University Hospital and Boston City Hospital performed 3,000 procedures. During the 2006 academic year, the Section exceeded an annual total of 10,000 procedures for the first time.

Although a small decrease in the total number of cases was evident during the past year, Section faculty continue to perform well above (~12.5%) the national mean for other academic Sections of Gastroenterology (Figure 2).

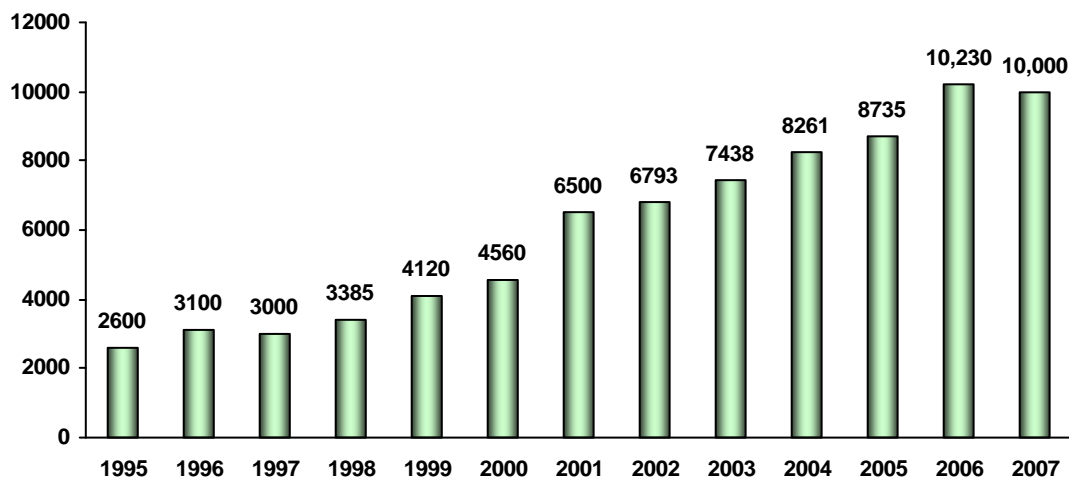


Figure 1. Total endoscopic procedures by GI Section during fiscal years 1995-2007.

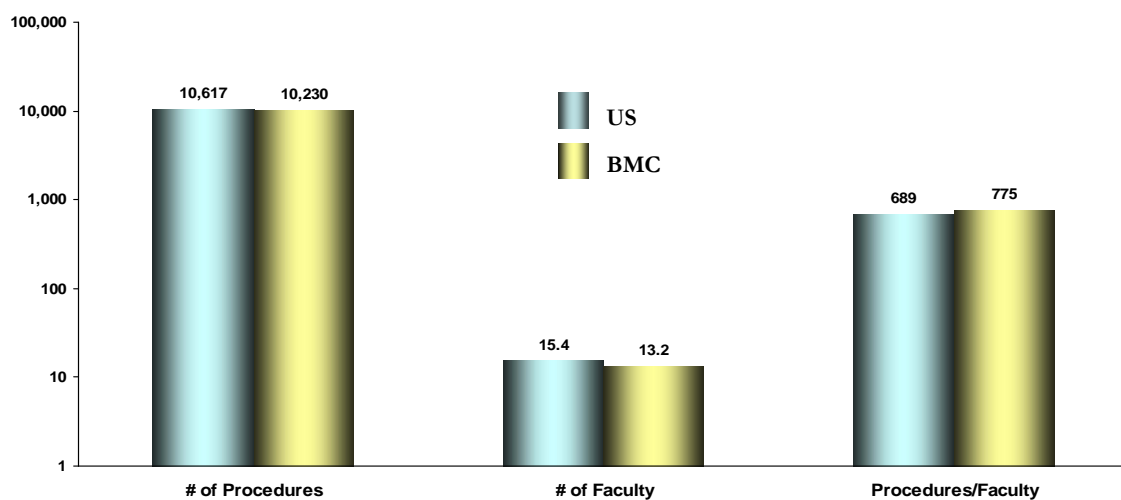


Figure 2. Total endoscopic procedures by GI Section faculty compared to U.S. mean during 2006.



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The Endoscopy Center of Brookline, an independent ambulatory endoscopy center located at 930 Commonwealth Avenue, which the Section established during the 2004-2005 academic year, continues to provide endoscopic services in a conveniently located facility. This ambulatory center is the only center of its kind in Brookline, and it provides the additional resources necessary to meet the growing demand for screening colonoscopy. The Center offers patients the option of receiving necessary endoscopic services in an urban, non-hospital-based setting, and it affords the Department of Medicine and BMC the potential for a significant, new patient population base.

In addition to directing The Endoscopy Center at BMC and leading an active screening colonoscopy program, Dr. Lichtenstein leads an active biliary endoscopy program. The number of pancreaticobiliary cases continued to increase during the past year. To assist Dr. Lichtenstein in accommodating this increase in demand, Drs. Jacobson and Huang actively participate in the performance of ERCP. Dr. Jacobson has also steadily increased BMC's endoscopic ultrasonography (EUS) services, and he is now performing more than 250 cases per year. Because of Dr. Jacobson's significant research commitments, Dr. Huang has received extensive training in the performance of EUS, and he will now assume a lead role in this ever-increasing modality. Finally, Dr. Pedrosa will continue to perform EUS on a limited basis at BMC.

The Section continues to keep pace with the rapidly expanding technologies offered in the field of gastroenterology. In addition to utilizing capsule video endoscopy, which permits the visual examination of the small intestine, Dr. Mishkin has been using this new tool to screen patients with GERD for Barrett's metaplasia. Capsule video endoscopy, the use of which is growing at a rapid pace, enables gastroenterologists to evaluate areas of the gastrointestinal tract previously

inaccessible to standard endoscopes. Similarly, the demand for the performance of ambulatory esophageal pH monitoring led to the replacement of a cumbersome tube-based system with the Bravo® capsule system, which enables the monitoring of pH using wireless technology for up to forty-eight hours. Improved patient receptiveness to this new system has led to the more accurate diagnosis of GERD and its extraesophageal manifestations, as well as other diseases characterized by abnormal esophageal pH.

In addition to these endoscopic services, the Section offers a wide variety of other diagnostic tests. Under Dr. Halpert's direction, esophageal and anorectal manometry are done on a regular basis. Drs. Wolfe, Jacobson, and Halpert are continuing to assess the role of impedance testing of patients with suspected esophageal motor disorders and plan to purchase this equipment during the upcoming academic year. The Section also offers a variety of breath tests, including *H. pylori* and hydrogen, the latter for intestinal malabsorption. The Section continues to perform percutaneous liver biopsies, albeit at a lower rate than in previous years. Because of the uncompromising need for improved specificity and safety, this procedure has been performed increasingly by members of the Department of Radiology, who carry out the procedure using ultrasound and CT guidance.

Dr. Farraye and Steven Sentovich, M.D., Chief of the Section of Colon and Rectal Surgery at BMC, and Assistant Professor of Surgery, co-direct the daily activities of the Center for Digestive Disorders. Patients' ability to utilize this center, which offers multidisciplinary care for digestive diseases, was enhanced significantly during the past academic year by its relocation to the J. Joseph Moakley Medical Services Building. The Center continues to make impressive strides in improving the efficiency and quality of care of patients with various digestive disorders. The Center continues to grow, and it is anticipated that the services offered will continue to expand.

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The Section's "GUTS" beeper system offers healthcare providers within the BMC, Quincy Medical Center, and the affiliated neighborhood health center network the opportunity to receive expeditious phone consultation and the scheduling of patients for urgent consultative and endoscopic evaluation. All physicians participate fully in clinical activities offered by the Section. In addition, the Section operates an efficient and well-respected inpatient consult service. During the past academic year, Dr. Wolfe instituted the GUTS Clinic, an extra clinical session that was held on Friday afternoons and developed to further improve patient access.

## EDUCATION

The Section of Gastroenterology has an established reputation for outstanding educational efforts. Faculty members within the Section serve as mentors and educators residents, students, and fellows. Dr. Lowe serves as a Robert Dawson Evans Educator, Director of the GI Fellowship Program Director, and Director of the entire "Biology of Disease" (BOD) course taught at BUSM. Under Dr. Lowe's guidance, the Section plays a leadership role in the education offered by the Department of Medicine and BUSM.

In addition to providing mentorship, all Section faculty members participate in the lecture series delivered to fellows, residents, and students rotating through the Gastroenterology consult service. These lectures are delivered on a bi-weekly basis during the summer and on a weekly basis during the remainder of the academic year. They provide trainees with a broad array of topics for discussion and instruction, and they enable residents and students to gain considerable expertise during their short rotation on the clinical service. Trainees are exposed to thought leaders in their respective fields and receive state-of-the-art information regarding various topics of interest.

In addition to the Section's formal didactic sessions, fellows and other trainees rotating

through the Gastroenterology consult service have access to the substantial education provided by faculty members in the Departments of Radiology and Pathology. Several Radiology faculty members continue to offer their expertise and participate in didactic sessions in Radiology on a semi-weekly basis. Radiology and Pathology conferences are held on alternating Tuesday mornings and enable the Gastroenterology fellow to obtain proficiency in important ancillary services that are integral to the care of patients with various digestive disorders.

Two additional weekly conferences provide important components to the education of medical students, residents, and Section fellows. The Tuesday afternoon Gastroenterology/Surgery conference is a multidisciplinary meeting of surgeons, gastroenterologists, medical and surgical oncologists, and radiation oncologists. It serves as a forum to discuss patients with gastrointestinal malignancies and other digestive disorders that cross the borders of medical and surgical care required for their optimal management. Members of the Department of Radiology also participate on a regular and ongoing basis by reviewing specimens from patients presented and discussed at this series. This important conference enables Gastroenterology fellows and surgical residents to gain the viewpoint of those faculty members outside their own specific training discipline.

Dr. O'Brien, a recognized expert in gastrointestinal pathology, also contributes to the education of Section fellows. In addition, Department of Surgery faculty members participate in training fellows, as well as students and residents rotating through the GI consult service. Section of Gastroenterology Grand Rounds are held weekly on Thursday afternoons. Under the guidance of Drs. Wolfe and Lowe, junior and senior fellows direct what constitutes the most important didactic venue the Section offers. During these sessions, fellows present cases to other Section fellows and faculty; an intense debate and



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discussion of the case under review follows. The presenting fellow follows the discussion of patient management with a thorough review of the literature pertaining to the specific GI disorder under consideration.

In addition to fellow presentations at Gastroenterology Grand Rounds, which account for approximately 75% of all such sessions, speakers outside BUMC's scientific community are invited once a month to deliver lectures related to their own areas of expertise. The lectures delivered by these guest speakers cover a wide array of both basic and clinical sciences related to digestive disorders, gastrointestinal physiology and pathophysiology, and diseases of the liver. These sessions provide a forum for fellows to present their research in progress, to review presentations for various national meetings, and for BUSM faculty to familiarize others with their own areas of investigation.

In addition to the educational services offered at BMC, the VABHS constitutes a major venue for the education of Section fellows, medical students, and residents. Working with colleagues from Harvard Medical School, Drs. Pedrosa, and Singh, as well as Elihu Schimmel, M.D., Professor of Medicine, accomplish the important task of providing educational services at the VA.

Section faculty are committed to educating the Department of Medicine, as well as the entire BUSM community. The educational services offered constitute a significant effort on the part of the faculty and is considered by all faculty members as one of the Section's principal academic responsibilities. Applicants vying for fellowship positions in the Section are medical residents from outstanding programs throughout the nation, including all Harvard-affiliated institutions, as well as the University of Pennsylvania; The Johns Hopkins University; the University of California, San Francisco; Stanford University; Washington University; Yale University; Columbia University; the University of Michigan; the University of Texas

Southwestern; and the University of Chicago.

## MAJOR ACCOMPLISHMENTS

Section faculty continue to deliver medical grand rounds at BMC and other hospitals throughout New England and the United States. Faculty members engaged in basic biomedical research are invited to deliver lectures in various research venues throughout Boston and New England, as well as across the United States and internationally.

In addition, numerous manuscripts resulting from Section members' research have been published in *Gastroenterology*, *The New England Journal of Medicine*, *Journal of Infectious Diseases*, *The American Journal of Gastroenterology*, *Gastrointestinal Endoscopy*, *Clinical Gastroenterology and Hepatology*, *The Journal of Clinical Gastroenterology*, *The Journal of Biological Chemistry*, *American Journal of Physiology*, *The American Journal of Surgical Pathology*, *Regulatory Peptides*, and *Obesity Research*. Faculty members continue to publish review articles, and several members of the faculty wrote chapters in the Gastrointestinal Diseases section, edited by Dr. Wolfe, in the latest edition of *Cecil's Essentials of Medicine*, published in early 2007.

Dr. Wolfe received an "Ignition Award" from Boston University in 2006 to examine the proposed use of engineered stem cells to treat various systemic disorders. He was one of two representatives from the American Gastroenterological Association (AGA) who authored the national core curriculum for fellowship training to be adopted by all accredited fellowship programs in the United States and linked to the Accreditation Council for Graduate Medical Education (ACGME) Outcome Project's General Competencies. The curriculum was published in *Gastroenterology* in May 2007. Dr. Wolfe also served as co-chair the AGA's annual Division Chief Workshop in November 2006 in Orlando, Florida, and he was inducted as an alumnus member of the Gamma Chapter of *Alpha Omega Alpha* at The Ohio State University. Dr. Wolfe was included in the

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Castle Connolly list of “Best Doctors in America” for the third consecutive year. He was invited to deliver keynote lectures at Digestive Disease Week in May 2007 in Washington, D.C.; was an invited speaker at the Annual GI Fellowship Directors’ Workshop held in San Antonio, Texas, in March 2007; and delivered an invited lecture on “Obesity and the GI Tract” at the International Symposium on GI Regulatory Peptides in Hakone, Japan, in September 2006. Finally, Dr. Wolfe was named to the Steering Committee of the International Regulatory Peptide Society and was elected as a member of the first group of Fellows of the AGA.

Dr. Farraye continues to serve as Chair of the Board of Governors and a member of the Board of Trustees of the American College of Gastroenterology (ACG). He was the senior author of the AGA guideline on the “Diagnosis and Management of Dysplasia in IBD.” In addition to numerous invitations to deliver medical grand rounds, Dr. Farraye was invited to deliver keynote lectures at Digestive Disease Week in May 2007 in Washington, D.C., as well as at the ACG’s annual meeting in October 2006 in Las Vegas, Nevada. Finally, he became a Fellow of the American Society of Gastrointestinal Endoscopy (ASGE).

Dr. Halpert received a career development grant from the ACG to support her research evaluating various strategies for the management of functional bowel disorders.

Dr. Jacobson received a REGAL award and an ASGE TAP endoscopic research award. He served as the ASGE’s representative to the National Quality Forum and as a member of the five-member panel of the Nation Quality Forum GI technical advisory panel. He continued to serve on the ASGE Health and Public Policy Committee and the ASGE Task Force on Quality in Endoscopy. He delivered a state-of-the-art lecture on quality in EUS at Digestive Disease Week in May 2007 in Washington, D.C., and he lectured at the Harvard International Conference on Obesity

in Cambridge, MA, in June 2007. Finally, Dr. Jacobson accepted the position of co-chair for a symposium on obesity and GERD to take place at the 9<sup>th</sup> World Congress of the World Organization for Specialized Studies on Diseases of the Esophagus (OESO) in April 2008 in France.

Dr. Lichtenstein was included in the Castle Connolly list of “Best Doctors in America” for the third consecutive year, and he was named to *Boston Magazine*’s list of Top Doctors in the area. In addition, Dr. Lichtenstein has assumed leadership positions in both the ASGE and the New England Endoscopy Society and is a member of the ASGE’s Research Committee. Dr. Lichtenstein served as Co-Director of the Annual Boston International Live Endoscopy (BILE) Course, and he serves on the American Society for Gastrointestinal Endoscopy Annual Scientific Program Committee as a Subchair of the ERCP Section. Finally, Dr. Lichtenstein was elected to membership in the first group of Fellows of the AGA.

Dr. Lowe was named a Robert Dawson Evans Educator in the Department of Medicine, and he was inducted as an alumnus member of *Alpha Omega Alpha* at Boston University School of Medicine.

Dr. Nunes was included in the list of Top Doctors by *Boston Magazine*.

Dr. Schroy received an Excellence in Teaching Award from BUSPH in 2007. He also assumed several new leadership roles, including membership on Leadership Team of the Massachusetts Comprehensive Cancer Control Coalition; Chair of the Massachusetts Comprehensive Cancer Control Coalition’s Steering Committee of the Colorectal Cancer Working Group; and Chair of the American Cancer Society/Centers for Disease Control and Prevention’s Nominating Committee of the National Colorectal Cancer Roundtable.

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Dr. Singh received a Translation Research Award from the Coulter Foundation to investigate the use of elastic scattering spectroscopy for cancer detection.

Dr. Song received a New Investigator Award from the North America Association for the Study of Obesity (NAASO).

## **FACULTY**

### **Professors**

Francis A. Farraye, M.D.  
Elihu M. Schimmel, M.D.  
Paul C. Schroy, M.D., M.P.H.  
David J. Waxman, Ph.D.  
M. Michael Wolfe, M.D.

### **Associate Professors**

David R. Lichtenstein, M.D.  
David Nunes, M.D.  
Gwynneth D. Offner, Ph.D.  
Marcos C. Pedrosa, M.D.  
Chi-Chuan Tseng, M.D.

### **Assistant Professors**

Charles Bliss, Jr., M.D.  
Michael O. Boylan, Ph.D.  
Zhi-Yi Chen, Ph.D.  
Brian C. Jacobson, M.D.  
Robert C. Lowe, M.D.  
T. Carlton Moore, M.D.  
Jaime A. Oviedo, M.D.  
Satish K. Singh, M.D.  
H. Christian Weber, M.D.

### **Instructors**

Albena Halpert, M.D.  
Christopher Huang, M.D.  
Daniel Mishkin, M.D.  
Diane H. Song, Ph.D.

### **Clinical Associate**

Lizabeth M. Cline, N.P.  
Angela C. Reffel, P.A.



**Section of Gastroenterology  
Boston University School of Medicine  
2006-2007**

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# GENERAL INTERNAL MEDICINE



## **SECTION CHIEF, VICE CHAIR, PUBLIC HEALTH**

*Jeffrey Samet, M.D., M.A., M.P.H.*

The Section of General Internal Medicine (GIM) has had an active year under the leadership of Jeffrey Samet, M.D., M.A., M.P.H., Vice Chairman of Medicine for Public Health, and Professor of Medicine and Public Health. With its more than 100 faculty members, the Section continues to be highly productive in clinical, educational, and research realms.

## **RESEARCH ACTIVITIES**

Over the past year, GIM's research activities have grown. Direct research support to GIM faculty during the 2006-2007 academic year increased by 14% and exceeded \$10.7 million, with the vast majority of funding coming from the National Institutes of Health (NIH). The Section's active research and training grants account for direct costs totaling more than \$47.5 million. In addition, faculty members have submitted research proposals with total direct costs of \$22.6 million. GIM faculty co-authored fifty-four medical articles in peer-reviewed journals in 2006, an increase from forty-six and thirty-one in 2005 and 2004, respectively.

The Women's Health Unit (WHU) is under the direction of Karen Freund, M.D., M.P.H., Associate Director of Boston University

School of Medicine's (BUSM) Women's Health Interdisciplinary Research Center, and Professor of Medicine. The WHU's research activities continue to provide new insight through interventions to address health outcomes disparities in minority and underserved women.

The WHU is one of nine sites nationwide funded through the National Cancer Institute's Patient Navigation Research Program, which studies the potential benefit of patient navigators as an intervention to address health disparities. Co-Principal Investigator Tracy Battaglia, M.D., M.P.H., Assistant Professor of Medicine, has secured two additional research grants through the Avon Foundation to investigate work design, social network, and outcome effectiveness of patient navigation. WHU researchers Frank Perna, Ed.D., Ph.D., Associate Professor of Medicine, and Bonnie Sherman, Ph.D., Instructor of Medicine, have focused on exercise and physical activity interventions within the primary care setting, including the benefit of exercise during active breast cancer treatment and exercise for rural women.

The WHU continues to expand its focus on research training. During the past year, the WHU supported the training of four women's health fellows as part of the combined General Internal Medicine/Family Medicine fellowship program. The WHU was successful in its competitive renewal of the K-12 institutional junior faculty scholar award, Building Interdisciplinary Research Careers in Women's Health (BIRCWH), which provides resources to four junior faculty members yearly in a mentored career development program.

The WHU has increased its role in influencing health policy within as it affects women's health. Michele David, M.D., M.P.H., M.B.A., Assistant Professor of Medicine, secured a

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Health Policy Fellowship through the Soros Foundation. Dr. David collaborates with Massachusetts Health Care for All in policy initiatives focusing on the health of minority women. The WHU sponsors a Health Policy Grand Rounds series to increase interest, awareness of, and participation in health policy on campus.

Another GIM unit, the Health Care Research Unit (HCRU), is under the direction of Arlene Ash, Ph.D., Research Professor of Medicine. The HCRU is involved in a variety of projects and frequently uses large, claims-based databases, especially from Medicare, to understand differences in healthcare utilization and outcomes by gender and race or ethnicity. A key tool in these studies is the Diagnostic Cost Group (DCG) method for summarizing the illness burden of individual patients and facilitating risk-adjusted comparisons of healthcare outcomes. Developed by Dr. Ash and her colleagues, these methods are used to facilitate equitable payments to HMOs in the Medicare program.

Major HCRU projects include a multi-year NIH study focusing on racial differences in healthcare utilization and costs for Medicare beneficiaries at the end of life. HCRU investigators have worked on several contracts with the Department of Defense (DoD) to examine the power of models to predict future healthcare costs in the TRICARE health system, which is the DoD's health system for members of the armed services, their families and survivors; to explore the implications of a prospective payment system; and to assist the DoD in understanding and addressing small-area variations in its healthcare delivery. The HCRU also provides support to the BIRCWH Program, an NIH-funded K-12 faculty program that supports an interdisciplinary group of junior faculty and provides mentorship to departmental fellows and assistance to the Graduate Program in Molecular Medicine.

Dr. Ash and Amresh Hanchate, Ph.D., Research Associate, work with multiple

Boston University Medical Center (BUMC) researchers on projects funded by a number of different agencies, including the Centers for Disease Control and Prevention's (CDC) "Examining Quality of Epilepsy Care"; the Food and Drug Administration's glucose-monitoring study; the National Cancer Institute's "Impact of Breast Cancer on Older Survivors" and "Patient Navigation in the SafetyNet"; and the National Institute on Aging's "Exceptional Survival and Longevity in New England" and the "Long Life Family Study."

Dr. Hanchate is also pursuing the following projects: "Surgery Volume and Mortality," which is funded by the Agency for Healthcare Research and Quality (AHRQ); "Examining the Validity of Community Based Screening Questions for Assessing Epilepsy," funded by the CDC; the Veterans Administration-funded "The Demographic Assessment of Health Literacy, A New Independent Covariate of Health Status in the Elderly"; and "Patient Safety Indicators in the VA," funded by AHRQ.

Andrea Kronman, M.D., M.Sc., is a BIRCWH faculty scholar researching "The Role of Primary Care at the End of Life" and "Improving Risk Adjustment Methods for Illness Burden."

A third unit within the Section is the Clinical Addiction Research and Education (CARE) Unit, an academic unit addressing the clinical, educational, and research aspects of alcohol and other drug use. CARE is under the direction of Richard Saitz, M.D., M.P.H., Associate Director of the BUMC Office of Clinical Research, and Professor of Medicine and Epidemiology. Faculty members include Dr. Samet; Daniel Alford, M.D., M.P.H., Associate Professor of Medicine; Sheila Chapman, M.D., Medical Director of the Pregnant Women's Program, the Methadone Maintenance Treatment Program at the Boston Public Health Commission (BPHC), and Assistant Professor of Medicine; Debbie Cheng, Sc.D., Associate Professor of



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Biostatistics at the Boston University School of Public Health and Medicine; Theresa Kim, M.D., Medical Director of CAB Detoxification Unit, and Assistant Professor of Medicine;; Colleen LaBelle, R.N.; Jane Liebschutz, M.D., M.P.H., Director of the Preventive Medicine Residency Program, Associate Director of the General Internal Medicine Fellowship Program, and Associate Professor of Medicine; and Christopher Shanahan, M.D., M.P.H., Director of the Community Medicine Unit at Boston Medical Center (BMC), and Assistant Professor of Medicine. During the 2007-2008 academic year, the Unit will add a new research faculty member, Alexander Walley, M.D., former BU General Internal Medicine and CARE research fellow. CARE Unit projects directly employ approximately fifteen staff members as well as several college and medical students, and they provide research experiences for medical students, residents, and fellows.

The CARE Unit collaborates with a number of other Boston University departments, other universities, and outside agencies. Dr. Saitz is Associate Director of a P60 NIH Center grant, awarded to the BU School of Public Health, to address alcohol problems among young people. In addition, the CARE Unit is collaborating with faculty in Boston University's Departments of Psychology, Gastroenterology, and Psychiatry; the Schools of Social Work and Public Health; eight other American universities; and the Pavlov State Medical University in St. Petersburg, Russia.

In 2006-2007, the NIH, the Health Resources and Services Administration (HRSA), and the Robert Wood Johnson Foundation provided support for nine randomized controlled trials and observational studies conducted by CARE Unit faculty. These studies address hazardous drinking among college freshmen via a Web intervention; unhealthy alcohol use in hospitalized medical patients; the role of alcohol in hepatitis C and HIV outcomes; post-traumatic stress disorder (PTSD) and substance use in a primary care setting; a study of the interaction between PTSD and

substance use in people with chronic pain; drinking and health across the lifespan (in collaboration with the Framingham Heart Study); a Russian study of HIV prevention in drinkers with HIV who pursue risky behavior and in uninfected narcology hospital patients; and the quality of care for people with addictions. The Unit also addressed studies of screening tests for alcohol and other drug use disorders.

During the past year, the National Institute on Drug Abuse (NIDA) awarded the Unit a \$3.4 million award for which Dr. Samet is the Principal Investigator; this is a complementary study to the National Institute on Alcohol Abuse and Alcoholism (NIAAA) grant that the CARE Unit received in 2005, a \$4.4 million award for which Dr. Saitz is the Principal Investigator. Both of these grants fund the test of a disease management/chronic care model for people with alcohol and/or drug dependence in the primary care setting. Three additional NIH proposals, (K24, R25, and R01) for which Dr. Samet is the Principal Investigator, were funded this past year, and a \$14 million proposal was funded by Substance Abuse and Mental Health Services Administration (SAMHSA). This proposal to disseminate screening and brief intervention was spearheaded by former Massachusetts Governor Mitt Romney's office, and the CARE Unit was the lead agency, with BMC receiving the majority of the funds as a subcontract to the state. Dr. Alford is the Principal Investigator for this proposal, and most CARE Unit faculty are working on this project in some capacity.

To support its research dissemination and educational activities, the CARE Unit has two NIH R-25 grants for drug abuse and alcoholism training for physicians and other health providers, including a well-established and popular Chief Resident Immersion Training (CRIT) Program. Generalist chief residents from around the United States are trained at this annual four-day immersion course on addictions. These projects have visible Web sites and produce a highly



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regarded electronic alcohol and health research summary newsletter. This year, the newsletter was expanded to address alcohol and other drugs. A Web-based curriculum for physicians is being disseminated in collaboration with the American College of Physicians. These R-25 awards support an Addiction Medicine research track in the GIM fellowship program.

Drs. Alford and Saitz contribute to a national mentoring program for physicians prescribing buprenorphine for the American Society of Addiction Medicine. Dr. Alford has led national efforts to train physicians in the use of buprenorphine in collaboration with the American Society of Addiction Medicine. Dr. Samet was a member of the Institute of Medicine committee that released the 2005 report *Improving the Quality of Health Care for Mental and Substance Use Conditions*. Dr. Saitz has served on a SAMHSA advisory committee and on the Washington Circle Group to implement the report's recommendations.

Dr. Liebschutz continued her work on an NIH K23 career development award to study the intersection between drug abuse, PTSD, and primary care. BUSM residents have access to addiction clinical experiences with Unit faculty during primary care block time, and the CARE Unit has a longstanding Summer Medical Student Research Program. Two Unit members play active roles in a Center for Substance Abuse Treatment-supported residential facility for homeless adults with addictions.

CARE Unit faculty members provide the major physician leadership of the BPHC Substance Abuse Prevention and Treatment Services (SAPTS). Dr. Samet serves as SAPTS Medical Director. Dr. Alford has been Medical Director of the Methadone Clinic and is turning this position over to Dr. Walley in the coming year. Ms. LaBelle provides clinical leadership for the Office Based Opioid Treatment (OBOT) Program, which was recently funded by the Massachusetts Department of Public Health to expand its efforts to include statewide training for the

delivery of buprenorphine for opioid dependence in primary care settings. Drs. Shanahan and Sheila Chapman also provide clinical services to SAPTS. Dr. Shanahan oversees the Transitional Opioid Program (TOP), which helps hospitalized, opioid-dependent patients engage in substance abuse treatment, and Dr. Chapman works with pregnant methadone-treated patients.

Robert Friedman, M.D., Director of the Medical Information Systems Unit (MISU) for the Section, and Professor of Medicine and Public Health, leads research and education in medical informatics (computer applications in biology and medicine). The MISU has a staff of forty-three, including five full-time faculty members and four post-doctoral fellows. During 2006-2007, the MISU had sixteen federally funded research projects and one foundation funded research project, including one new NIH K07 training award.

The MISU is internationally known as the first research laboratory to demonstrate that a totally automated, computer-controlled telephonic intervention program helps patients and consumers modify lifestyle behaviors that significantly contribute to the prevalence of chronic disease, morbidity, and premature mortality. These programs also promote self-care in patients with chronic disease and facilitate disease monitoring and the alerting of responsible health professionals for patients with chronic disease. The MISU is a leader in integrating these automated systems into traditional healthcare delivery systems to improve control of important chronic health conditions such as hypertension.

Currently, the MISU research laboratory is focusing on developing and evaluating totally automated primary prevention programs directed to people who have multiple health behavior risks: smoking, unhealthy eating habits, and sedentary lifestyles. In the area of disease management, Dr. Friedman directs a research project that is developing an innovative, multi-component, computer-assisted chronic disease management system.

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MISU is evaluating this system, which utilizes both automated telephone communications and automated home measurement devices in patients' residences.

Dr. Friedman is completing a research project that compares automated telephone calls with the traditional approach of mailed reminders to motivate women to have a routine screening mammogram. In addition, he is completing a study in which an automated telephonic intervention for patients with hypertension has been culturally adapted for African-Americans. Finally, Dr. Friedman leads research teams that are applying computer technology to the management of patients with spinal cord injury and disease and that are facilitating the transition between hospital inpatient care and post-discharge primary care.

Julie Wright, Ph.D., Assistant Professor of Medicine, is a co-investigator on five studies related to computer-assisted interventions that target cancer prevention behaviors (e.g., healthy diet, regular physical activity, weight management). Three of these studies are delivered in primary care settings. Two of her projects involve the development and evaluation of behavioral informatics systems that use electronic health records (EHR) and telephony systems to increase healthy behaviors in pediatric patient populations. Dr. Wright is also a recipient of a Cancer Career Development Award (NCI K07).

Ramesh Farzanfar, Ph.D., Assistant Professor of Medicine, has designed and developed two automated mental health systems. One, which is funded by the National Institute of Mental Health (NIMH), is a disease management system intervention for patients with unipolar depression. The second, funded by the CDC, is designed to detect mental health problems, particularly those that affect productivity, in the workplace. Dr. Farzanfar is also the site Principal Investigator of a multi-institutional research project to improve the management of depression in medical illness through the use of computer-assisted programs. This year,

she completed a Robert Wood Johnson Foundation-funded research project in which she developed new research methods to measure factors that affect the utilization of computer-based behavioral change programs.

Julien Dedier, M.D., M.P.H., Assistant Professor of Medicine, is conducting an NIH-funded study on the relationship between ethnic identity and the prevalence of behavior-related risk factors for cancer in African-Americans. He is also evaluating the influence of ethnic identity on the use and effectiveness of culturally-adapted behavior change interventions in this population. Dr. Dedier recently obtained a career development award from the American Cancer Society to develop and evaluate culturally-tailored messages to promote physical activity among urban African-Americans.

Amy Rubin, Ph.D., Research Associate, is a psychologist whose interests include early intervention and treatment research for alcohol problems and investigating technology-based treatment intervention and dissemination. Dr. Rubin has joined her interest in substance abuse research and technology-based treatment dissemination in a number of studies evaluating computer telephony. She has collaborating roles in the NIAAA-funded (R01 AA014258) study titled "Telecom & Bibliotherapy Programs for Problem Drinkers," as well as the SAMHSA-funded project to bring screening, brief intervention, and referral to treatment to medical care. Dr. Rubin is also collaborating with colleagues at the Boston VA Healthcare System on a Web-based treatment program for veterans returning from Iraq and Afghanistan who have alcohol problems and PTSD symptoms.

The MISU leads the Boston University Biomedical Informatics Training Program, which provides two to three years of post-doctoral training in biomedical informatics to physicians, psychologists, and other scientists. During 2006 – 2007, the program combined existing programs at BUMC and the Boston

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VA Healthcare System.

Other active GIM researchers include Elaine Hylek, M.D., M.P.H., Associate Professor of Medicine, and Michael Paasche-Orlow M.D., M.P.H., Assistant Professor of Medicine. Dr. Hylek's research has focused on cardiovascular epidemiology issues, specifically the risks and benefits of anticoagulation for atrial fibrillation and other clinical conditions. Dr. Paasche-Orlow is a national leader in health literacy. His publications include a special issue of the *Journal of General Internal Medicine* for which he was a Co-Editor.

### CLINICAL ACTIVITIES

Clinical activities within the Section of General Internal Medicine have been active. Guided by Peter Davidson, M.D., Associate Chief of Clinical Affairs, and Associate Professor of Medicine, Section faculty handled more than 73,000 ambulatory visits, and GIM faculty were the attendings on 69% of all medicine inpatient blocks on non-subspecialty services. Total outpatient visits have decreased over the past year by 13% from 2006, largely because of the attrition of GIM outpatient faculty in BMC's Yawkey Ambulatory Care Clinic (YACC) and the Doctors Office Building (DOB).

A clinical incentive program has evolved in its fourth year of existence and measures work-RVUs (relative value units). Outpatient clinical activity in primary care practices in the YACC is under the direction of Jason Worcester, M.D., Assistant Professor of Medicine. The leadership of the DOB's primary care practice was assumed by a newly recruited physician, Peggy Chou, M.D., Assistant Professor of Medicine. The Women's Health Group (WHG) primary care practice and the Boston University Medical Group at Quincy Medical Center is under the direction of Elizabeth Dupuis, M.D., Assistant Professor of Medicine. The WHG provides primary care and mental health services to address women's health comprehensively. During this time of a primary care physician shortage nationwide,

the WHG has continued to increase its panel, with 16% of all visits in the past year from new patients. The WHG is part of the multidisciplinary Breast Health Group, which moved into the new Moakley Building this year. The Breast Health Group provides consultation to patients with breast problems, abnormal screening results, or increased cancer risk.

The Commonwealth Medical Group practice continues under the leadership of Steven Abreu, M.D., Clinical Assistant Professor of Medicine. The Medicine Consult Service at BMC, under the direction of David Halle, M.D., Assistant Professor of Medicine, has undergone extensive transformation and growth during the past year, with the development of a newly constituted pre-operative evaluation center in collaboration with other hospital departments.

The Section's Hospital Medicine Unit (HMU) has been transformed with the addition of six new faculty members this year. Under the direction of Jeffrey Greenwald, M.D., Associate Professor of Medicine, the HMU will increase its provision of inpatient care for the Department of Medicine from 15% in 2006 to nearly 50% in 2008. HMU faculty members have been consistently ranked highly for their teaching skills by both residents and medical students. They made substantive contributions to BMC's quality improvement efforts, including medication reconciliation and inpatient influenza vaccinations.

Under Dr. Shanahan's direction, the Community Medicine Unit (CMU) pursues its mission is to support the development and management of community-focused clinical, educational, and research programs. The Joint Hire Program (JHP), overseen by the CMU, is a collaboration between BMC and the Department of Medicine to support physician efforts to integrate general internists at BMC and the neighborhood health centers. This year, fifteen physicians provided thirty clinical sessions each week with JHP support. The JHP attracts highly qualified primary care

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clinicians into academic clinical positions with creative teaching arrangements. Elizabeth Rourke, M.D., a physician at the South Boston Community Health Center, and Alexandra Molnar, M.D., a physician at the Upham's Corner Health Center, were recruited into the JHP.

CMU faculty members also provide inpatient attending supervision. This year, the CMU worked actively with the East Boston Neighborhood Health Center, the South Boston Neighborhood Health Center, and the Upham's Corner Health Center to coordinate recruitment efforts and facilitate JHP arrangements for highly qualified, community-based clinician educators. Dr. Shanahan maintains an ongoing dialogue with the leadership of the Boston HealthNet, medical directors, key staff physicians, and administrators at more than fifteen community-based sites.

The Section contributes to BMC Information Technology (IT) activities, and Dr. Shanahan serves as the IT Medical Director. This BMC department supports two other general internists to develop a clinically user-friendly electronic medical record and utilize the electronic health record to assess and improve the quality of medical care delivery.

The clinical practice recruited new faculty members in 2006-2007. Leila Obeid, M.D., joined the YACC primary care practice. Carol Bravo, M.D., joined the Latino Health Clinic practice located on YACC, as did Dr. Chou. Nicolette Fontaine, M.D., joined the Quincy Medical Center practice.

Several Section units also perform clinical functions. The Women's Health Unit plays an active role in patient outreach and policy advocacy in addressing health disparities for minority women. The Women's Health Network, under the direction of Chava Chapman, M.D., M.P.H., Associate Professor of Medicine, provides uninsured women with comprehensive cancer screening. Michele David, M.D., M.P.H., M.B.A., Assistant

Professor of Medicine, leads the Unit's public policy and advocacy activities.

## Education

All program directors at BMC within the Department of Medicine continue to be Section faculty. Leadership was provided by David Battinelli, M.D., Vice Chairman of Medicine for Education, and Professor of Medicine, until his departure at the end of the academic year. Angela Jackson, M.D., Associate Program Director for the Boston University Residency Training Program in Medicine, and Associate Professor of Medicine, continues in the role of Director of the Primary Care Training Program. Medical student education within the Department of Medicine is under the direction of Warren Hershman, M.D., M.P.H., Associate Professor of Medicine. Robert Dawson Evans Educators were appointed this year, and Drs. Davidson and Hylek will serve in these roles.

Medical students receive extensive clinical exposure in the primary care clinics, with Section faculty providing one-on-one precepting in 399 clinic sessions this past academic year. GIM faculty and fellows provide a substantial portion of the Department's teaching contribution to the "Introductory to Clinical Medicine" course offered to BUSM students. Twelve Section faculty members attend at the Department's traditional resident morning report, and nine attend at the ambulatory morning report.

Section faculty members play a leading role in resident and student education on diversity through the activities of the BUSM Diversity Curriculum Task Force. In addition to the Department's Grand Rounds, GIM faculty continue their medical education at the weekly General Internal Medicine Grand Rounds lecture series organized by Bernard Kreger, M.D., M.P.H., Professor of Medicine. The latter conferences included lectures by William Ghali, M.D., M.P.H., Assistant Professor of Medicine at the University of Calgary, who was the 2007 Mark Moskowitz Memorial

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Visiting Professor.

Under the direction of Drs. Friedman and Liebschutz, the General Internal Medicine Fellowship Program and Preventive Medicine Residency Program provide a collaborative two- or three-year fellowship experience with the Department of Family Medicine. Assistant Program Directors Drs. Paasche-Orlow and Battaglia make significant contributions to this program. These fellowship experiences include concentrations in women's health, substance abuse, cancer prevention, and informatics. Five fellows completed the program in 2007. This fellowship program continues to enjoy broad support from HRSA, National Research Service Awards, Department of Veterans Affairs, National Institute on Drug Abuse, and the American Cancer Society.

The Core Curriculum in Adult Primary Care Medicine, a Continuing Medical Education course sponsored by the Section, transitioned its leadership this year to Beth Manning, M.D., M.P.H., Assistant Professor of Medicine. It reviews the spectrum of general internal medicine in half-day monthly presentations attended by more than 180 generalist clinicians in suburban Boston. Dr. Manning is also Assistant Program Director for BUSM's Residency Program in Medicine and Director of the Preliminary Program in Medicine.

In addition, individual units with the Section contribute to the Section's educational activities. The WHU serves as a training resource for BUSM students and internal medicine and family medicine residents; Renee McKinney, M.D., Instructor of Medicine, directs training activities. The Unit supports a nationally recognized women's health fellowship, which is embedded in the Section's fellowship program and provides training for future leaders in academic women's health across the nation. The Unit also administers BIRCWH.

CMU faculty Julie Crosson, M.D., leads the Medical Interviewing Course for Internal Medicine residents. The CMU also continues

to support the efforts of the Residency Training Program, specifically the Primary Care Training Program, to recruit excellent residents after graduation from the program.

### MAJOR ACCOMPLISHMENTS

Dr. Samet received an NIAAA career development award (K-24) to examine HIV and alcohol in the United States and Russia.

Dr. Alford was selected for the national Nyswander Dole Award given by the American Association for the Treatment of Opioid Dependence.

Drs. Battinelli, Dedier, Jackson, Liebschutz, as well as Sondra Crosby, M.D.; James O'Connell, M.D., and were inducted to the BUSM Humanism Honor Society.

Dr. Davidson has been awarded a quality grant award from Harvard Pilgrim Health Care. This project focuses on improving the health care of Latinos with diabetes using the Internet.

Dr. Halle was appointed Director of the Internal Medicine Pre-Operative Assessment Center. In addition, he received the 2007 Section of General Internal Medicine's Most Valuable Player Award.

Nancy Kressin, Ph.D., Associate Professor of Medicine, received a VA Research Career Scientist award.

Geoffrey Modest, M.D., Medical Director of the Upham's Corner Neighborhood Health Center, and Clinical Associate Professor of Medicine, was honored with the inaugural 2007 Robert Witzburg Outpatient Teaching Award from the Section of General Internal Medicine.

Jay Orlander, M.D., M.P.H., was appointed Associate Chief of General Internal Medicine for the VA Boston Healthcare System. He is also Assistant Chief of the Medical Service for Clinical Affairs and Associate Director for Education for the GIM Fellowship Training



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program.

Dr. Perna received the Walter Peach Award from the Association of Applied Sport Psychology.

Christine Phillips, M.D., Assistant Professor of Medicine, received the Dean's Recognition Award for Teaching.

## **FACULTY**

### **Professors**

David L. Battinelli, M.D.  
Daniel Berlowitz, M.D.  
Joel G. Caslowitz, M.D.  
Karen M. Freund, M.D.  
Robert H. Friedman, M.D.  
Bernard E. Kreger, M.D.  
John Noble, M.D.  
Richard Saitz, M.D.  
Jeffrey H. Samet, M.D., M.P.H.  
Robert A. Witzburg, M.D.

### **Adjunct Professor**

Brian Hoffman, M.D.

### **Clinical Professors**

Geoffrey A. Modest, M.D.  
James O. Taylor, M.D.

### **Research Professor**

Arlene S. Ash, Ph.D.

### **Associate Professors**

Daniel P. Alford, M.D.  
Thomas W. Barber, M.D.  
Dan R. Berlowitz, M.D.  
Phyllis L. Carr, M.D.  
Peter Killip Davidson, M.D.  
Benjamin Graeme Fincke, M.D.  
Jeffrey L. Greenwald, M.D.  
Warren Y. Hershman, M.D.  
Elaine Hylek, M.D.  
Angela Jackson, M.D.  
Nancy Kressin, M.D.  
Jane Liebschutz, M.D.  
Joanne M. Murabito, M.D.  
Jay D. Orlander, M.D.  
Janice Quan, M.D.  
Subha Ramani, M.D.  
Charles P. Tift, M.D.  
Brant Viner, M.D.

### **Clinical Associate Professors**

Chava E. Chapman, M.D.  
H. Emerson Thomas, M.D.

### **Assistant Professors**

Tracy A. Battaglia, M.D.  
Kathleen M. Bennett, M.D.  
Sheila E. Chapman, M.D.  
Sondra S. Crosby, M.D.  
Kathleen A. Crowley, M.D.  
Michele M.A. David, M.D.  
Julien J. Dedier, M.D.  
Leyda D. Delgado, M.D.  
Elizabeth Dupuis, M.D.  
Ramesh Farzanfar, Ph.D.  
Stephan A. Gachde, M.D.

David A. Halle, M.D.  
Anand Kartha, M.D.  
Theresa Kim, M.D.  
Jeong M. Lee, M.D.  
Mary E. Manning, M.D.  
Jeffrey Migneault, Ph.D.  
James J. O'Connell, M.D.  
Michael Paasche-Orlow, M.D.  
Christine Phillips, M.D.  
Nila Radhakrishnan, M.D.  
Margaret Seaver, M.D., M.P.H.  
Alfredo J. Selim, M.D.  
Christopher Shanahan, M.D.  
Jerome E. Sobieraj, M.D.  
Robert Sokolove, Ph.D.  
Lorraine Stanfield, M.D.  
Jason Worcester, M.D.  
Julie Wright, Ph.D.

### **Adjunct Assistant Professor**

Matthew W. Gillman, M.D.

### **Clinical Assistant Professors**

Steven P. Abreu, M.D.  
Monica Bharel, M.D.  
Julie M. Crosson, M.D.  
Richard L. Kalish, M.D.  
Julie Kaufmann, M.D.  
Vasken Kroshian, M.D.  
Sandra Looby-Gordon, M.D.  
Sandra L. Marwill, M.D.  
Unique Michaud, M.D.  
Julita Mir, M.D.  
Susan L. Phillips, M.D.  
Phillip E. Pulaski, M.D.  
Madhusudan Thakur, M.D.

### **Instructors**

Aisling M. Bastible, M.D.  
Leyda D. Delgado, M.D.  
Alison G. May, M.D.  
Renee McKinney, M.D.  
Catherine Rich, M.D.  
Bonnie Sherman, Ph.D.  
Laura Wung, M.D.



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**Clinical Instructors**

Susan Cabot, M.D.

Mark Drews, M.D.

Jessie M. Gaeta, M.D.

**Clinical Instructors**

Roger Jean-Charles, M.D.

Frances Kuebler, M.D.

Andrea C. Kronman, M.D.

Teresa Lim, M.D.

Judith Lytle, M.D.

Jonathan M. Pincus, M.D.

Daniel S. Simpson, M.D.

Puneet Sud, M.D.

Carol A. Waldmann, M.D.

Keith N. Williams, M.D.

**Clinical Associates**

Eunice J. MacAllister, N.P.

Susan Morrissey, N.P.

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# GERIATRICS



## SECTION CHIEF

*Rebecca A. Silliman, M.D., Ph.D.*

## RESEARCH ACTIVITIES

The Section of Geriatrics occupies 9,300 square feet on the second floor of the Robinson building, a location that affords almost all Section members the opportunity to work in contiguous space. The central location allows for considerable efficiencies for research, clinical, educational, and administrative activities, and facilitates collaboration and communication with other disciplines.

The Section has three major research groups, in addition to collaborating with many other Sections and Departments.

Rebecca Silliman M.D., Ph.D., Chief of the Section, Director of the Gerontology Center, and Professor of Medicine and Public Health, leads a research group that studies breast cancer etiology, disparities in breast cancer therapy, and the consequences of those disparities. Current funding from the National Cancer Institute (NCI) includes two R01s and a K05 (the K05 was renewed for five years beginning July 1, 2006) that support mentoring and research collaborations both at Boston University and across the nation. During this academic year, three senior doctoral students in Dr. Silliman's group completed their

degrees. The group also published research that highlighted the consequences of under treating breast cancer in older women.

Dr. Silliman is also Principal Investigator of the BU Building Interdisciplinary Research Careers in Women's Health program (K-12). Karen Freund, M.D., M.P.H., Director of the Boston University Center of Excellence in Women's Health, Chief of Women's Health at Boston Medical Center, and Professor of Medicine, is the Program Director.

The Section's second research group is under the direction of Thomas Perls, M.D., M.P.H., Director of the New England Centenarian Study, and Associate Professor of Medicine. Current projects focus on the heritability of exceptional longevity; the compression of disability vs. morbidity with exceptional longevity; and genetic association studies. Funding from the National Institute on Aging (NIA) is supporting the "Long Life Family Study," a collaboration involving Boston University, Columbia University, the University of Pittsburgh, and the University of Southern Denmark. Through the identification and enrollment of 1,000 families, investigators will determine the familial aggregation and modes of transmission of exceptional survival within families, as well as characterize the phenotypes associated with exceptional survival for eventual genetic linkage analysis.

In addition to working with Dr. Perls on this project, a member of his team, Dellara Terry, M.D., M.P.H., Assistant Professor of Medicine, is investigating the offspring of centenarians, in particular, the delayed development and expression of age-related diseases. Initially supported by a K08 grant, Dr. Terry's work is being funded by a Paul Beeson Career Development Award from the NIA.

A second member of the Section, Angela Jefferson, Ph.D., a second-year scholar, was also awarded a Paul Beeson Career Development Award. Dr. Jefferson's award

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increases the number of Beeson Scholars at Boston University Medical Center to two.

James Kirkland, M.D., M.Sc., Ph.D., Associate Professor of Medicine and Research Associate Professor of Biochemistry, is Director of Basic Science Research for the Section. Dr. Kirkland is studying the effects of age and fat depot origin on adipose tissue function. He is particularly interested in how changes in the function of fat cell progenitors, known as preadipocytes, contribute to effects of aging and fat depot origin on fat tissue function and metabolic disease. Dr. Kirkland and his colleagues are seeking to understand the mechanisms underlying age-related changes in preadipocyte transcription factor expression and stress response system activity, as well as the mechanisms and effects of preadipocyte cellular senescence. These studies will contribute to understanding the mechanisms of age-related changes in fat tissue function, cell differentiation, diabetes, and atherosclerosis.

With regard to fat depot origin, Dr. Kirkland's group has found that preadipocytes from different human and rat fat depots are distinct cell types with unique morphology and distinct patterns of developmental gene expression. They are studying how regional variation in preadipocyte developmental regulators contribute to differences in preadipocyte capacities for replication, adipogenesis, and apoptosis, as well as fat tissue inflammatory cytokine, chemokine, and hemostatic factor release. This work is important for developing methods to treat diabetes, atherosclerosis, hypertension, and dyslipidemia in the elderly, including strategies to target particular fat depots.

Dr. Kirkland serves as a mentor for Erica Bernstein, M.D., Ph.D., Assistant Professor of Medicine, who joined the Section's basic research group in July 2005. Dr. Bernstein is investigating the intersection of aging, oxidative stress, and diastolic dysfunction.

Efforts to create linkages between the Section

and other research groups at Boston University continue. Shalender Bhasin, M.D., Chief of the Section of Endocrinology, Diabetes, Nutrition and Weight Management, and Professor of Medicine, has become an important collaborator for Section researchers. Under Dr. Bhasin's leadership, investigators in the Section of Geriatrics, in conjunction with researchers from Tufts University and the Joslin Clinic, submitted a Claude D. Pepper Older American Independence Center grant application to the NIA this spring.

### CLINICAL ACTIVITIES

BU Geriatric Services at Boston Medical Center, the Section's clinical program, provides ongoing primary care and case management to older residents of Boston. The program also provides geriatric consultative services to primary care physicians and specialists at Boston Medical Center (BMC) and promotes geriatric education through comprehensive training programs. A collaborative practice model is used, and care is provided by geriatricians, clinical nurse specialists, nurse practitioners, registered nurses, and a social worker. BU Geriatric Services cares for approximately 2,000 patients in a range of settings, including the Geriatric Ambulatory Practice, the Home Care Program, the Nursing Home Program, and the Geriatric Inpatient Service (Firm C).

The Geriatric Ambulatory Practice (GAP) cares for older adults who are able to use available transportation to BMC. The number of patients served has increased significantly over the past five years, thus requiring a concomitant increase in physician sessions. Currently, approximately 1,000 patients are cared for during nine geriatrician sessions per week; one Geriatric Medicine fellow session per week; and one registered nurse session/week. Additionally, the GAP holds two geriatric assessment sessions per month.

The Home Care Program cares for approximately 570 homebound frail elders living in Boston. Many are eligible for nursing

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home placement, but are able to remain at home because of an extensive network of formal and informal nursing and personal care services. BU Geriatric Services clinicians work in close collaboration with a patient's other caregivers, including the certified home health agency, community agencies, and family and friends.

Section faculty have gained considerable experience with a special capitated program for patients who have both Medicaid and Medicare. Faculty members have also expanded the use of Logician, a computerized medical record program, that they access via a wireless connection while in patients' homes. During a 2007 accreditation visit by The Joint Commission (formerly known as the Joint Commission on the Accreditation of Healthcare Organizations), the site visitor noted that Section's Home Care Program was a "national model" and did not issue any Requirements for Improvement (RFIs).

Using a nurse practitioner-physician collaborative model, the Nursing Home Program cares for approximately 450 patients in ten Boston nursing homes. Patients enrolled in the program typically require long-term care, and many are patients who were initially cared for in GAP or the Home Care Program. The Nursing Home Program also cares for short-stay patients with skilled nursing or rehabilitation needs. Implementation of the Logician medical records program is nearly complete, but technical issues related to remote computer access in a nursing home setting have presented challenges.

BU Geriatric Services is also responsible for the Geriatric Inpatient Service, which is known as Firm C and is under the direction of Eric Hardt, M.D., Medical Director of the Home Care Program, and Associate Professor of Medicine. Most Section physicians annually undertake two, two-week rotations as the Firm's attending physician. The service admits patients twenty-four hours a day, seven days a week. A resident and two interns make up the housestaff team, which is complemented by a

nurse practitioner from the Section. Whenever possible, patients within any of the Section's programs who require inpatient care are admitted to Firm C. In the academic year 2006-2007, there were 853 discharges from Firm C.

The Section continues to use a range of strategies this year to improve clinical operations. Lisa Caruso, M.D., M.P.H., Assistant Professor of Medicine, and Clare Wohlgemuth, M.S., R.N., C.S., Director of Nursing for the Section of Geriatrics, Nurse Case Manager for the Home Care Program, and Clinical Associate in Medicine, are Co-leaders of the Section's Performance Improvement Task Force. Current projects include identification of risk and prevention of falls; emergency room utilization reduction; improvement of medication prescribing; and improvement of advance directives documentation.

Following a retreat in 2005, the Section received a two-year grant from the John A. Hartford Foundation in January 2006 to support practice redesign activities, with the goal of improving the efficiency, effectiveness, and quality of the Section's clinical programs while enhancing staff and patient satisfaction. Dr. Silliman is the grant's Principal Investigator. With the grant, the Section has focused its clinical redesign on integrating the Home Care and Nursing Home programs. Nurse practitioners are now practicing in both programs, creating job diversity and continuity across settings. With completion of the redesign process in spring 2007, Section faculty are fine-tuning the redesign's downstream implications for clinical productivity and the Section's educational programs.

The Section's database manager has developed information technology strategies to improve infrastructure support for the Section's clinical practice, as well as to monitor clinical productivity and quality of care. In addition to supporting the performance improvement activities, the database manager also is revamping the BU Geriatric Services database to better meet the clinical and business needs of the practice; developing an online evaluation mechanism for the Section's clerkship and other

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educational activities; developing strategies to integrate include homes, nursing homes, and a Program of All-Inclusive Care of the Elderly (PACE) site. An additional two to five residents in the Primary Care Training Program elect to follow home care or nursing home patients in a “second clinic” over one to two years. Finally, twenty-six interns and thirteen residents per year form the housestaff team for the Geriatrics Inpatient Service.

The Section of Geriatrics has also served as the “Model Department” for the redesign of Logician templates for use throughout BMC. In addition, Section faculty have worked hard to connect the Section’s entire practice via Logician, which has meant finding technical solutions so that connections can be made reliably in nursing homes and in patients’ homes. This process is almost complete.

## EDUCATION

All Boston University School of Medicine (BUSM) students participate in the Geriatrics curriculum, which has been added to the required third-year Family Medicine Clerkship. The Geriatrics course of study has online, small group discussions, as well as home visit components. The curriculum places emphasis on the development of geriatric assessment skills.

During their mandatory four-week Geriatrics and Home Medical Care Clerkship, fourth-year BUSM students are exposed to interdisciplinary care in a variety of practice settings, including patients’ homes, ambulatory clinics, senior centers, and nursing homes. These precepted clinical experiences allow them to practice their geriatric assessment skills and are complemented by a defined curriculum that is delivered via case-based seminars as well as online directed learning exercises.

Four clinical geriatrics experiences are included in the Section’s residency program. All Primary Care interns participate in a two-week block experience designed to introduce them to community-based services and the Section’s interdisciplinary primary care team model of geriatric care. Each year, twenty-six residents complete a four-week outpatient rotation in geriatrics, the sites for which

Since its inception in 1988, the Geriatric Medicine Fellowship, under the direction of Sharon Levine, M.D., Director of Education for the Section of Geriatrics, and Associate Professor of Medicine, has trained academic geriatricians, the majority of whom are practicing in underserved areas. Both one- and two-year training options are available. In 1991, with the support of a Bureau of Health Professions Faculty Training Grant in Geriatric Medicine and Dentistry, the fellowship expanded to include dental fellows, and in 2000, the program was further expanded to include psychiatry fellows. A renewal grant was funded in July 2005, but defunded by Congress as of July 2006. Congress restored these monies early in 2007, and the Section submitted a new application for funding in June 2007.

The Geriatric Medicine Fellowship includes a strong mentored research component, with all two-year fellows completing a research project that fulfills the thesis requirements for a Master of Science in Epidemiology or a Master of Science in Health Services through the Boston University School of Public Health. Over the past five years, seven fellows have completed the M.Sc. program under the mentorship of faculty members in the Clinical Epidemiology Research and Training Unit (David Felson M.D., M.P.H., Director of the Clinical Epidemiology Research and Training Unit, Chief of the Multidisciplinary Clinical Research Center Grant, and Professor of Medicine and Public Health); the Alzheimer’s Research Center (Robert Green, M.D., M.P.H., Co-Director of the Alzheimer’s Disease Clinical and Research Program, and Professor of Neurology, Genetics and Epidemiology); and the Center for Health

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Quality, Outcomes, and Economic Research at the Bedford Veterans Administration Medical Center (Dan Berlowitz, M.D., Assistant Professor of Medicine), in addition to Section faculty.

The Section also co-sponsors a Geriatric Oncology Fellowship in collaboration with the Section of Hematology/Oncology. This fellowship program continues to grow and serves as a highly regarded national model.

In addition, the Section's John A. Hartford Foundation Center of Excellence in Geriatrics trained another six faculty scholars this year, bringing the total number of trained faculty scholars to fifty. A five-year renewal grant, for which Dr. Silliman is the Principal Investigator, was awarded to the Section in April 2007. Four faculty scholars, representing General Internal Medicine (including Hospital Medicine) and Family Medicine, have been accepted for the coming academic year.

Finally, the Summer Institute in Geriatric Medicine, funded by the NIA and designed to provide a week-long intensive research experience, drew a class of seventeen medical students (from a pool of thirty-seven applicants) from across the United States to Boston University Medical Center in June. As of May 1, 2006, a competitive renewal application for the institute was funded for five years. Dr. Silliman serves as the Principal Investigator.

## MAJOR ACCOMPLISHMENTS

Dr. Silliman serves as Vice-chair of the Research Committee of the American Geriatrics Society, serving also as the Chair of the Abstract Selection Committee for the annual national meeting. She is an associate editor of the *Journal of Gerontology: Medical Sciences*.

Adam Burrows, M.D., Assistant Clinical Professor of Medicine, was elected to the board of the National PACE Association and received its Volunteer Leadership Award for

work on rural PACE expansion.

Serena Chao, M.D., M.Sc., Associate Director of the Geriatric Medicine Program, and Assistant Professor of Medicine, received "best poster" honors at the second annual John McCahan Medical Education Day at BUSM for her poster "Comparison of Online Curriculum to Lecture Format in Teaching Delirium to 4<sup>th</sup>-year Medical Students."

Dr. Hardt was appointed a Robert Dawson Evans Educator.

Dr. Levine was appointed Associate Dean for Academic Affairs at BUSM.

## FACULTY

### Professors

Rebecca A. Silliman, M.D., Ph.D.  
Gabriel H. Brandeis, M.D.  
Eric J. Hardt, M.D.  
James L. Kirkland, M.D., Ph.D.

### Associate Professors

Timothy Lash, D.Sc., M.P.H.  
Sharon A. Levine, M.D.  
Thomas T. Perls, M.D., M.P.H.

### Clinical Associate Professor

George Rosenthal, M.D.

### Assistant Professors

Heidi P. Auerbach, M.D.  
Erica Bernstein, M.D., Ph.D.  
Karen M. Bryant, M.D.  
Lisa B. Caruso, M.D., M.P.H.  
Serena H. Chao, M.D., M.Sc.  
Daniel Oates, M.D., M.Sc.  
Matthew L. Russell, M.D., M.Sc.  
Dellara Terry, M.D., M.P.H.

### Clinical Assistant Professors

Adam B. Burrows, M.D.  
Maha M.I. Khodeir, M.D., M.P.H.  
Lisa E. Norton, M.D.

### Instructor

Tamara Tchkonja, Ph.D.

### Clinical Associates

Kathleen A. Byrne, M.S.  
Kimberly R. Claude, A.P.R.N., B.C.  
Katherine Concilio, A.P.R.N., B.C.  
Katie A. Creedon, A.P.R.N., B.C.



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**Clinical Associates**

Catherine Fabrizi, A.P.R.N., B.C.

Ellen B. Harrington, LICSW

Monica L. Hogan, A.P.R.N., B.C.

Patricia Kimball, M.S., R.N., C.S.

Brenda B. McKeon, A.P.R.N., B.C.

Debra Sylvester, A.P.R.N., B.C.

Maureen Q. Russell, M.P.H., R.N., B.C.

Julie L. Wentworth, M.S., R.N.P.-C

Clare M. Wohlgemuth, A.P.R.N., B.C.

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# HEMATOLOGY AND MEDICAL ONCOLOGY



## SECTION CHIEF

*Jack Ansell, M.D., ad interim*

## RESEARCH ACTIVITIES

The Section of Hematology/Oncology continues to experience significant growth in its clinical, research, and teaching missions. Jack Ansell, M.D., Vice Chairman of Medicine for Clinical Affairs, and Professor of Medicine, is currently serving as interim chief of Hematology/Oncology. A search for a permanent chief is in progress.

The Section of Hematology/Oncology currently has sixteen full-time M.D. or M.D./Ph.D. faculty members; nine Ph.D. faculty members; two nurse practitioners; and six part-time faculty members. In addition, five Boston University School of Medicine faculty members provide care through the Veterans Administration Boston Healthcare System (VABHS).

The development of unique research programs and Centers of Excellence has been a priority for the Section, and during the past ten years, a number of specialized clinical and basic research programs have emerged. These initiatives include a Sickle Cell Disease Center of Excellence, a Geriatric Oncology Fellowship Program, and a Stem Cell Transplant Program that is focused on the treatment of plasma cell dyscrasias and AL amyloidosis.

Extramural grant funding (both direct and indirect) for the Section's research was approximately \$7 million in Fiscal Year 2007. The areas of interest in the Section's basic research programs include breast cancer and other solid tumors; leukemia and lymphoma; the plasma cell disorders multiple myeloma and AL amyloidosis; sickle cell disease and other hemoglobinopathies; and basic cancer genetics, signal transduction, host defenses, and pharmacologic and immunotherapy.

Research on hemoglobinopathies and thalassemia has included studies of mechanisms underlying abnormal endothelial cell function in the sickle syndromes; studies of genetic modifiers of sickle cell disease severity; and studies of butyrate compounds, which induce fetal hemoglobin, as candidate therapeutic agents for these diseases. Martin Steinberg, M.D., Director of the Sickle Cell Disease Center of Excellence, and Professor of Medicine, has led research in these areas in collaboration with Henry Adewoye, M.D., Assistant Professor of Medicine; Douglas Faller, M.D., Ph.D., Vice Chairman of the Department of Medicine and Director of the Cancer Research Center at Boston Medical Center, and Professor of Medicine; and Susan Perrine, M.D., M.S., Professor of Medicine, Pediatrics and Pharmacology and Experimental Therapeutics. As Principal Investigator of the Sickle Cell Disease Center of Excellence, Dr. Steinberg has also initiated new clinical research, under the Center's aegis, to examine both the pathogenesis and treatment of sickle cell disease. He is collaborating with Lillian McMahon, M.D., Associate Professor of Medicine and Pediatrics, and with faculty members in other Sections of the Department of Medicine.

David Chui, M.D., Director of the Hemoglobin Diagnostic Reference Library, and Professor of Medicine and Pathology, is pursuing new research on the genetic

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epidemiology and genetic variants of thalassemia and sickle cell syndromes. In addition, Dr. Chui has established a hemoglobin genomic reference laboratory serving the region.

Molecular oncogenesis research focuses on interactions between cancer genetics and the environment, with emphases on cellular oncogenes and growth factor signal transduction pathways in neoplastic cells. Researchers are also working to detect genetic instability in pre-malignant breast lesions and are using transgenic mice as models for understanding multi-step oncogenesis pathways leading to leukemia, lymphomas, and breast cancer.

Adam Lerner, M.D., Assistant Professor of Medicine and Pathology; Carol Rosenberg, M.D., Associate Professor of Medicine and Pathology; and David Seldin, M.D., Ph.D., Associate Director of the Graduate Program in Molecular Medicine for the Section of Hematology/Oncology, and Professor of Medicine and Microbiology, have funded breast cancer research projects. Drs. Faller, Lerner, Seldin, as well as Gerald Denis, Ph.D., Assistant Professor of Medicine, and colleagues study various aspects of lymphocyte and plasma cell biology and transformation. Affiliated members of the Cancer Research Center have additional projects in prostate and other solid tumors.

In the sphere of patient-based clinical research, Hematology/Oncology faculty members participate actively in clinical cancer trials sponsored by the Southwest Oncology Group (SWOG), the National Surgical Adjuvant Breast and Bowel Project (NSABP), the American College of Surgeons Oncology Group (ACOSOG), and the Radiation Therapy Oncology Group (RTOG). Faculty members developing and pursuing institutionally unique clinical research initiatives and partner with industry to conduct a number of industry-sponsored studies.

Vaishali Sanchowala, M.D., Clinical Director

of the Autologous Stem Cell Transplant Program at Boston Medical Center, and Associate Professor of Medicine, and her colleagues continue to develop clinical studies of dose-intensive chemotherapy and autologous peripheral blood stem cell transplantation for the treatment of AL amyloidosis and related diseases, as well as non-transplant innovative therapeutics for these diseases.

In addition, Dr. Lerner has designed and is conducting studies of novel phosphodiesterase inhibitors in the treatment of chronic lymphocytic leukemia. He is working with Jianlin Gong, M.D., Associate Professor of Medicine autologous cancer vaccines. Drs. Faller, Perrine, and Steinberg are studying the efficacy of butyrate analogs, as well as hydroxyurea with erythropoietin, to treat sickle cell disease and thalassemia syndromes by inducing the expression of fetal hemoglobin.

## CLINICAL ACTIVITIES

The Section's clinical activity has grown considerably every year over the past several years. Current outpatient activity is approximately 22,000 visits per year, and approximately 700 Hematology/Oncology inpatient admissions take place per year at Boston Medical Center (BMC).

Approximately 40% of patients who receive care at Boston University Medical Center (BUMC) come from inner-city Boston and represent ethnically diverse and economically disadvantaged populations who have limited means to cope with serious illnesses. The incidence of cancer in these populations is unusually high, and disease is typically advanced at the time of diagnosis. Hence, the understanding, design, and development of more effective cancer screening and treatment strategies for such patients represent important programmatic and academic goals, as well as creative opportunities for academic program development, for the Section.

While the Section is committed to building

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excellence in medical oncology and cancer care generally, its goal has also been to develop focused, multi-disciplinary clinical and research programs of excellence that are relevant to the particular potential strengths of BUMC and VABHS, including gastrointestinal malignancies, prostate cancer, breast cancer, and lung cancer. The Section co-sponsors a geriatric oncology program with the Section of Geriatrics. Fellows spend time in each of the clinical programs.

In addition, BMC's Center for Thoracic Oncology is under the direction of Benedict Daly, M.D., Chief, ad interim, of the Department of Cardiothoracic Surgery, Clinical Director of General Thoracic Surgery, and Professor of Cardiothoracic Surgery. Ken Zaner, M.D., Ph.D., Clinical Director of the Center for Cancer and Blood Disorders, and Associate Professor of Medicine, serves as Associate Director. The Center represents a collaborative effort between Radiation Oncology, Medical Oncology, Thoracic Surgery, Pulmonary Medicine, Pathology, and Clinical Trials to improve the efficiency and effectiveness of the care of patients with thoracic malignancies.

Section faculty members have continued full-time supervision of a dedicated subspecialty inpatient service. This service has a daily census of about twenty patients. All ambulatory Hematology/Oncology evaluation, management, and treatment visits at BMC are conducted at the Center for Cancer and Blood Disorders.

The Sickle Cell Service, including a Sickle Cell "Day Hospital" that is unique in New England, continues to expand and improve the care provided to sickle cell patients (from late teenage years through adulthood) in the Greater Boston area. Approximately 8% of patients seen in the Day Hospital are admitted to BMC, while 92% are sent home at the end of the day, preventing a large number of potential admissions.

BMC's Autologous Stem Cell Transplant

Program is internationally recognized as a leader in the treatment of AL amyloidosis. In collaboration with the Amyloid Treatment and Research Program, which is under the direction of Martha Skinner, M.D, a member of the Section of Rheumatology, and Assistant Professor of Medicine, and co-directed by Dr. Seldin, the Transplant Program provides a multidisciplinary team approach for patients undergoing high-dose chemotherapy followed by autologous peripheral blood stem cell rescue. The transplant program is accredited by the Foundation for the Accreditation of Cellular Therapy (FACT) and Massachusetts State Licensure. BMC's Autologous Stem Cell Transplant Program has been an approved SWOG transplant facility since 1996. Patients with AL amyloidosis account for approximately 85% of the transplants performed at BUMC. Seven percent have multiple myeloma (MM) or both MM and amyloidosis. Non-Hodgkin's lymphoma patients make up 5% of transplants.

Major changes in the conduct of Hematology/Oncology clinical activities by VABHS-based Hematology/Oncology faculty resulted from the merger of the Jamaica Plain VAHCS and the West Roxbury VAHCS. All VABHS Hematology/Oncology inpatient activities are conducted at the West Roxbury facility, while all ambulatory E&M and treatment visits are at Jamaica Plain. Together with three Harvard Medical School-affiliated hematologist/oncologists, Hematology/Oncology faculty members supervise inpatient and outpatient activities at both VABHS sites. Daniel Jacobson, M.D., Professor of Medicine, assumed the role of Chief of Oncology at VABHS in May 2003.

## EDUCATION

Over the past ten years, an exceptional subspecialty fellowship program has developed from four previously separate and uneven programs. The Section of Hematology/Oncology continues to improve and expand its three-year fellowship program, which prepares fellows for subspecialty

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certification in both medical oncology and hematology. Eleven current fellows are engaged in clinical training based on diverse patient populations at both BMC and VABHS. Fellows participate in clinical and basic research and have access to a broad range of research opportunities. In addition, Hematology/Oncology faculty members supervise pre- and post-doctoral fellows under the aegis of National Institutes of Health training grants in hematology and immunology. Dr. Lerner is Principal Investigator of the Hematology training grant.

In collaboration with the Section of Geriatrics, the Hematology/Oncology Section recently began a Geriatric Oncology Fellowship Program that prepares trainees for certification in both oncology and geriatrics. This program is one of the few in the nation to have been awarded an American Society of Clinical Oncology grant, and it is now in its third year of funding.

Elective rotations also continue to be available to residents and students both on the clinical services and in laboratory-based projects.

## MAJOR ACCOMPLISHMENTS

Dr. Ansell spoke at the International Society of Thrombosis and Haemostasis Presidential Symposium.

Dr. Chui addressed the International Society for Laboratory Hematology.

Isabel Dominguez, Ph.D., Research Associate Professor of Medicine, received Boston University School of Medicine's Karin Grunebaum Faculty Research Award. She also spoke at the Society for Developmental Biology, and offered presentation at Boston University School of Medicine, Massachusetts General Hospital, and the University of Massachusetts.

Kathleen Finn, R.N., A.N.P., A.O.C.N., Clinical Trials and Stem Cell Transplant Program Director for the Cancer Research

Center, was awarded a new grant.

Kevan Hartshorn, M.D., Program Director for the Hematology/Oncology Fellowship Training Program, and Professor of Medicine, received a new grant.

Dr. Rosenberg was the recipient of a new grant.

## FACULTY

### Professors

Jack E. Ansell, M.D.  
David Chui, M.D., Ph.D.  
Douglas V. Faller, M.D., Ph.D.  
Kevan L. Hartshorn, M.D.  
Daniel Jacobson, M.D.  
David C. Seldin, M.D., Ph.D.  
Martin H. Steinberg, M.D.  
Lewis R. Weintraub, M.D.

### Associate Professors

Rita A. Blanchard, M.D.  
Zhiyi Chen, Ph.D.  
Adam Lerner, M.D.  
Lillian E.C. McMahon, M.D.  
Carol Lisa Rosenberg, M.D.  
Vaishali Sanchorawala, M.D.  
Ken S. Zaner, M.D.  
Timothy P. Cooley, M.D.

### Assistant Professors

Nancy Andrea, M.D.  
Henry Adewoye, M.D.  
Valia Boosalis, M.D.  
Mary T. Brophy, M.D.  
Louis Fiore, M.D.  
Michelle Hankins, M.D.  
Jochen Lorch, M.D.  
Hong Yuan Luo, Ph.D.  
Richard I. Near, Ph.D.  
Lauren Jean Oshry, M.D.  
Karen Quillen, M.D.  
Surinder Safaya, Ph.D.

### Instructors

Maria Isabel Dominguez, Ph.D.  
Xuemei Zhong, Ph.D.

### Clinical Instructors

Joan Sully, N.P.  
Mark Yoder, N.P.

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# HYPERTENSION



## SECTION CHIEF

*Haralambos Gavras, M.D.*

## RESEARCH ACTIVITIES

The Section of Hypertension is most heavily research-oriented, with activities ranging from clinical research to experimental animal studies to genetic and genomic basic research. Several research associates work on specific projects under the supervision of the clinical faculty and that of molecular biologist Ekaterina Kintsurashvili, Ph.D., Research Assistant Professor of Medicine.

The National Institutes of Health (NIH) supports the Section's research activities via R01 grants (although currently expired, renewal applications are pending with Haralambos Gavras, M.D., Chief of the Section and Professor of Medicine, as the Principal Investigator). Support is also provided by a PGA grant that represents a consortium agreement with The Jackson Laboratory in Bar Harbor, Maine. In addition, the Section has two small grants from the pharmaceutical industry, namely, Boehringer-Ingelheim and Apotex, Inc..

## CLINICAL ACTIVITIES

The Section's clinical activities consist of three outpatient clinic sessions per week and inpatient consultations as requested, which are conducted by the two senior faculty members, Dr. Haralambos Gavras and Irene Gavras, M.D., Professor of Medicine. The patient load consists of highly selected cases referred

because they present difficult diagnostic or management problems.

## EDUCATION

Dr. Haralambos Gavras lectures extensively (locally, nationally, and internationally), primarily providing updates on the evaluation and treatment of hypertensive patients and on the pathophysiology and mechanisms of hypertension. Over the past year, he has given clinical and research teaching rounds at several universities in the United States, China, Greece, and Malta.

Dr. Irene Gavras is responsible for teaching Boston University Medical School students and housestaff who choose elective rotations in Hypertension. The Hypertension Laboratory trains research fellows in the genetic epidemiology and molecular genetics of hypertension, as well as the production and use of specific experimental animal models suitable for investigation of the pathophysiology and physiopharmacology of hypertensive disorders.

## MAJOR ACCOMPLISHMENTS

An important achievement in the past year for the Section was the development of two genetically engineered mouse models. One is a knockout mouse with deletion of a novel gene, the cardiomyopathy associated 3 (Cmya3) gene, which mediates the angiotensin-induced ischemic cardiomyopathy. The second is a genetically hypertensive mouse model with brain-selective overexpression of the  $\alpha_{2B}$ -adrenergic receptor, which is a unique model of endogenously driven sympathetic overactivity.

Dr. Haralambos Gavras was awarded an Honorary Doctorate in Medicine by the Aristotelian University of Thessaloniki, Greece, in March 2007.



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## **FACULTY**

### **Professors**

Aram V. Chobanian, M.D.

Haralambos P. Gavras, M.D.

Irene M. Gavras, M.D.

### **Research Assistant Professor**

Ekaterina Kintsurashvili, Ph.D.

### **Adjunct Assistant Professor**

Athanasios Manolis, M.D.

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# INFECTIOUS DISEASES



**SECTION CHIEF**  
Paul Skolnik, M.D.

## RESEARCH ACTIVITIES

Faculty in the Section of Infectious Diseases are studying bacteria, chlamydia, and viruses, focusing on how these pathogens alter and/or evade the host immune response and interact with the host. Support for this research comes from federal, state, and industry grants. In academic year 2007, the Section received more than \$7.1 million of annual direct research support. This research resulted in forty-four publications and seventy-five presentations at national and international meetings.

Caroline Genco, Ph.D., Professor of Medicine and Microbiology, and Associate Professor in the Department of Periodontology and Oral Biology at the Boston University Goldman School of Dental Medicine; Frank Gibson, Ph.D., Research Assistant Professor of Medicine, Paola Massari, Ph.D., Assistant Professor of Medicine and Lee Wetzler, M.D., Associate Professor of Medicine and Microbiology, study bacterial pathogenesis through research projects funded by the National Institutes of Health (NIH). Drs. Genco and Gibson are researching the mechanisms by which invasive bacteria accelerate atherosclerosis through the innate immune recognition receptors (toll-like receptors, or TLRs). These studies utilize two principal model systems: the ApoE-knockout mouse model and primary cultures of human aortic endothelial cells (HAEC). Through

independent NIH funding, Dr. Gibson has focused on understanding the immuno-stimulatory effects of *Porphyromonas gingivalis* capsular polysaccharide (CPS) using a murine macrophage-based system. He published several articles describing his work this year. Dr. Genco joined the Section of Molecular Medicine during the academic year.

Drs. Massari and Wetzler continue to work on aspects of *Neisseria* pathogenesis. This NIH-funded research examines TLR2-mediated events as elicited by Neisserial porin proteins. Dr. Wetzler is Principal Investigator for a project to devise vaccines against tularemia. In addition to working on *Neisseria*, Guillermo Madico, M.D., Ph.D., Research Assistant Professor of Medicine, continues to run a core for the *Francisella tularensis* program project, including work on a polymerase chain reaction (PCR) method for the detection and quantification of sub-species of *F. tularensis* and expression of pilin genes as candidate antigens for protective vaccines.

Dr. Madico and Robin Ingalls, M.D., Assistant Professor of Medicine, are studying aspects of pathogenesis concerning *Neisseria meningitidis* and *N. gonorrhoeae*. Dr. Ingalls – in collaboration with other Section faculty, the broader Boston University Medical Center (BUMC) campus, and other national and international investigators – focuses on the role of TLRs and other aspects of innate immunity in defending the female reproductive tract against sexually transmitted infections. Dr. Ingalls' work is supported by two NIH R01 grants, and her laboratory continues to grow. She was the senior author on two publications that appeared in peer-reviewed journals and presented data at two international meetings.

Li Shen, M.D., Ph.D., Research Assistant Professor of Medicine, and You-Xun Zhang, Ph.D., Research Associate Professor of Medicine are investigating *Chlamydia*

*trachomatis*. They have studied the sigma factor 28, and specific disulphide bridge epitopes, of *C. trachomatis*. Dr. Shen presented data concerning mutagenesis of the C-terminal region of Chlamydial sigma factor 28 to study interactions with the promoter and RNA polymerase. She and Dr. Zhang published data concerning the degradation of CD1d by chlamydial and cellular proteasomal activity in the *Journal of Biological Chemistry*. Another active area of investigation for Drs. Shen and Zhang is the dsbG gene of *Escherichia coli*, which enhances chlamydia infectivity in HeLa cells. An NIH R01 award supports this work.

Section faculty Mark Klempner, M.D., Associate Provost for Research, and Professor of Medicine, and Zhihui Zhao, M.D., Ph.D., Research Assistant Professor of Medicine, study the pathogenesis of Lyme disease. Their research examines the delineation of the signaling pathway and regulatory mechanisms affecting the upregulation of MMP-9 by *Borrelia burgdorferi* in U937 cells, fibroblasts, and keratinocytes. The polymorphism of MMP-9 and CD14 in Lyme disease is also a focus of their work, as is the induction of monocyte chemoattractant protein-1 (MCP-1). This NIH-funded research led to several peer-reviewed publications this year. Dr. Klempner continues to direct the planning and construction of the National Emerging Infectious Diseases Laboratory (NEIDL) and is recruiting faculty to work in the NEIDL's various core and operations facilities.

Philip Carling, M.D., M.P.H., Assistant Professor of Medicine, and Carol Sulis, M.D., Associate Professor of Medicine, are researching infection control. Dr. Sulis investigates mechanisms to reduce the incidence of errors in the use of antimicrobial prophylaxis as part of a national group. Dr. Carling uses a unique dye method, visible only by UV light, to detect areas that have been inadequately cleaned on cruise ships, patient care floors, and chemotherapy infusion facilities.

## CLINICAL ACTIVITIES

The Section provides substantial primary and consultative care in the outpatient and

inpatient settings. The outpatient Center for Infectious Diseases (CID) at Boston Medical Center (BMC) continues to expand its services. The CID comprises the clinical activities of the Center for HIV/AIDS Care and Research, the sexually transmitted diseases (STD) program and the international health program, which includes both refugee care and travel medicine. Davidson Hamer, M.D., Director of the Travel Clinic at BMC, has significantly expanded the travel medicine program during this academic year. All of these programs are integrated to provide seamless patient care. The large volume of visits, and the funding of services by hospital, state, and federal sources, necessitates an organized approach and one that also attends to patients' social needs.

Section faculty provided inpatient care on the general medical service and infectious diseases consultation service at BMC and the VA Boston Healthcare System (VABHS). Faculty who provide these clinical services at BMC include Tamar Barlam, M.D., Associate Professor of Medicine; Anita Barry, M.D., M.P.H., Assistant Professor of Medicine; Ioana Bica, M.D., Assistant Professor of Medicine; Deborah Cotton, M.D., M.P.H., Professor of Medicine; Robert Horsburgh, M.D., Chairman of the Department of Epidemiology at Boston University School of Public Health, and Professor of Epidemiology, Biostatistics and Medicine; Paul Skolnik, M.D., Chief of the Section, and Professor of Medicine; Judith Steinberg, M.D., Clinical Assistant Professor of Medicine; Margaret Sullivan, M.D., Assistant Professor of Medicine; Thomas Treadwell, M.D., Assistant Clinical Professor of Medicine; and Catherine Yu, M.D., as well as Drs. Carling, Hamer, Ingalls, Klempner, Sulis, and Wetzler.

David Thornton, M.D., Medical Director of the HIV Clinics for the VABHS, provides services at the VABHS, where he and Richard Serrao, M.D., Assistant Professor of Medicine, support the clinical infectious diseases program. Dr. Yu provides infectious diseases consultative services at Radius Healthcare, and

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Dr. Skolnik provides HIV consultative services at Whittier Street Health Center.

Dr. Barlam provides antibiotic oversight at both BMC and the VABHS. She chaired the Antibiotic Subcommittee of the Pharmacy and Therapeutics (P&T) Committee, sits on the P&T committees at both BMC and VABHS, runs an antibiotic stewardship program at BMC and an antibiotic task force at the VABHS, and works with the Microbiology Laboratory to ensure that diagnostic procedures support the appropriate use of antibiotics. Going forward, she will devote her full energies to providing care and administrative oversight at BMC.

Dr. Sulis runs the infection control program for BMC, BMC's affiliates, and Radius Healthcare. She also sits on many hospital and other agency committees representing the Section and BMC. This included participation on a Pandemic Influenza Task Force convened by Robert Brown, M.S., Ph.D., President of Boston University, to bolster programs throughout the University.

Alan Sugar, M.D., Professor of Medicine, provides clinical care in the HIV/AIDS clinic at Cape Cod Hospital and runs the hospital's Hepatitis C and Hepatitis B programs, which focus on diagnosis and treatment.

## EDUCATION

The Section provides education in multiple venues and at different levels for students. Mentoring occurs in all components of the outpatient CID, on the inpatient services, in the basic and clinical research venues, and during lectures, small classes and seminars for pre- and post-doctoral students, medical, and dental students.

Teaching on the inpatient services was provided by Drs. Barlam, Barry, Bica, Carling, Cotton, Hamer, Horsburgh, Ingalls, Klempner, Skolnik, Steinberg, Sulis, Sullivan, Treadwell, Wetzler, and Yu, as well as by Christopher Gill, M.D., M.S., Assistant

Professor of Medicine, and Barbara Lambl, M.D., M.P.H., Clinical Assistant Professor of Medicine. On the outpatient service, Drs. Bica, Hamer, Lambl, Skolnik, Sullivan, and Yu served as instructors. The Section's ongoing infectious diseases conference series provides educational opportunities for fellows, junior and senior faculty, and outside visitors at all levels of training. All Section faculty share these teaching responsibilities and provide more than 1,000 contact hours of teaching for hundreds of students.

The Infectious Diseases Fellowship Program has been reinvigorated with a new administrative structure and many new educational elements. Drs. Barlam, Hamer, Skolnick and Sullivan have developed new curricula. Drs. Skolnik and Sullivan have taken the lead in these endeavors and have the support of other key faculty, including Drs. Barlam and Thornton. Drs. Cotton and Horsburgh participated in the screening and ranking of fellowship applicants for the 2008-2009 academic year.

The Section also trains pre-doctoral students. Drs. Wetzler and Genco mentored pre-doctoral students in their laboratories and taught courses in the Department of Microbiology and the Goldman School of Dental Medicine. Drs. Genco, Gibson, Ingalls, and Skolnik provide teaching and mentoring for master's degree candidates in the Graduate School of Medical Sciences and post-doctoral students

Section faculty at the VABHS are heavily involved in teaching. Dr. Thornton is an Associate Program Director for the BU Internal Medicine Residency Program in charge of VA rotations. He also teaches and precepts Boston University School of Medicine (BUSM) students rotating through the VA for their third-year clerkships, and precepts Section fellows rotating through the VA on consult service and in the HIV clinic. Dr. Serrao teaches during inpatient rounds and outpatient care in the HIV clinic and directs the "Introduction to Clinical Medicine" course

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at the VABHS.

Dr. Sugar continues to precept BUSM medical students and Section fellows on rotation at Cape Cod Hospital.

### MAJOR ACCOMPLISHMENTS

The Section of Infectious Diseases continues to have strong scientific output as evidenced by the high volume of quality publications and continued significant federal grant support during this time of limited federal funding. Drs. Gibson and Ingalls have been especially successful in maintaining high levels of NIH support.

Three new faculty members were appointed to positions for the coming academic year: Lisa Ganley-Leal, Ph.D., was appointed Assistant Professor of Medicine, and Susan Weir, Ph.D., was appointed Research Assistant Professor of Medicine.

Dr. Ganley-Leal studies B cell function in the context of several different infectious pathogens, including parasites. Dr. Weir studies *F. tularensis* and is particularly skilled in the biosafety aspects of dealing with this select agent. Following completion of her Infectious Diseases fellowship at Boston University, Richa Tandon, M.D., was appointed Instructor of Medicine in the Section of Infectious Diseases. She will have clinical, clinical research, and educational responsibilities.

The reconfiguration of the Infectious Diseases Fellowship Program has significantly enhanced teaching within the Section. Drs. Barlam, Cotton, Horsburgh, Skolnik, and Sullivan interviewed and matched Infectious Diseases fellows for the 2008-2009 academic year. Drs. Barlam, Skolnik, and Sullivan submitted reaccreditation materials to the Resident Review Committee (RRC) and Accreditation Council for Graduate Medical Education (ACGME) for the fellowship program. The recredentialing information documents the program's extensive improvements and

accomplishments.

The Section of Infectious Diseases helped to create the first official Boston University School of Medicine Core Facility, which will include cell sorting and flow cytometry. The Section's administrative and scientific staff were instrumental in formulating Web-based applications, business plans, core committee proposals, and operational aspects for this research core. The Core is now run through BUSM, in conjunction with the Section, the Department of Microbiology, and others.

The volume of patients seen in the CID continues to grow, as new initiatives in travel medicine, administrative organization (under the leadership of Jon Hall, B.A., LADC, Manager of HIV/AIDS Clinical Affairs), and other areas serve to enhance its reputation, quality, and breadth of services.

### CENTER FOR HIV/AIDS CARE AND RESEARCH (CHACR)

#### RESEARCH ACTIVITY

Both basic and clinical research were conducted in the Center for HIV/AIDS Care and Research (CHACR).

Andrew Henderson, Ph.D., joined the CHACR's basic research effort this year. He is interested in transcriptional regulation of HIV replication, and an R01 award from the NIH supports his research. During the past year, the results of Dr. Henderson's work have appeared in the *Journal of Biological Chemistry*, *Genes & Development*, *Experimental Cell Research*, and other peer-reviewed journals.

Monty Montano, Ph.D., Assistant Professor of Medicine, studies genome-wide expression profiling of HIV-1 infection *in vitro* and among isolates (subtypes) from regions, such as southern Africa and southeast Asia, that are experiencing expanding epidemics. He also analyzes human genetic polymorphisms *in loci* that influence viral entry and post-entry expression and that affect transcriptional



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control and evolution of viral gene expression. Dr. Montano was recently awarded another R01 award to study muscle stem cell biology, which has implications for the lipodystrophy that complicates HIV infection in many patients.

Dr. Skolnik and Marlynne Quigg Nicol, Ph.D., focus their research efforts on immune response to HIV-1, especially in the lung. Alterations of cytokines and chemokines during HIV infection are studied to determine why the lung is particularly prone to opportunistic infections in persons with HIV/AIDS. Drs. Skolnik and Nicol are also interested in changes in innate immunity (namely toll-like receptors) during HIV infection, and the effects these changes have on functional aspects of the immune response. Mathematical modeling of these networks, performed in conjunction with James Collins, Ph.D., Professor of Biomedical Engineering at the BU College of Engineering, seeks to understand how perturbation of one component of the cytokine/chemokine network affects other components. These studies may lead to immunotherapeutic interventions that can be used in addition to highly-active antiretroviral therapy. An NIH R01 award supports these efforts.

Federal, state, and industry funding support clinical research activities, including epidemiologic, prevention, and experimental therapeutic trials. Grants from the Centers for Disease Control and Prevention (CDC) and the Massachusetts Department of Public Health support deployment of rapid HIV testing and prompt linkage to care, as well as enhanced medical management and home care for HIV-positive patients. During the academic year, CHACR received a new grant to fund HIV education and prevention for Haitian women, as well as an industry grant to perform rapid HIV testing in the Women's Center.

Dr. Horsburgh has recently handed off Principal Investigator duties to Dr. Cotton for an NIH-funded study of HIV and HCV

coinfection. This study follows a cohort of subjects initially enrolled seven years ago. Conducted in collaboration with Drs. Bica, Skolnik, Thornton, and others in the Department of Medicine and the BU School of Public Health (BUSPH), this study has yielded important insights into predictors of liver pathology, as well as differences between those infected with HCV alone and those with HIV/HCV coinfection.

Drs. Gill and Hamer, working with Donald Thea, M.D., M.Sc., Professor of International Health in the Center for International Health at the BU School of Public Health, carry out important international HIV-related research through studies in Africa, China, India, and Vietnam. These studies include aspects of mother-to-child transmission, adherence, service delivery, and the effects of antiretroviral and prophylactic therapies.

Dr. Skolnik and Dr. Hélène Hardy, who directs [HIV Pharmacotherapy program in the CHACR](#), collaborated on an NIH grant to understand and improve adherence to HIV drug therapy. Grants from the Massachusetts Department of Public Health also address this central problem in HIV care.

Drs. Hardy and Skolnik, working with Anela Stanic, Pharm.D., and Stephen Brady, Ph.D., Director of the Mental Health and Behavioral Medicine Program, and Associate Professor of Psychiatry and Graduate Medical Sciences, initiated a collaborative effort to study HIV prevention, using motivation-skills methodology, in individuals with serious mental illness. Dr. Brady is the recipient of an R34 award from the National Institute of Mental Health for this work.

Dr. Skolnik is site Principal Investigator, and Drs. Bica and Yu are co-investigators, for the Harvard/BMC Adult Therapeutic Clinical Trials Group (ACTG), funded by the NIH, which studies new therapeutic interventions and treatment strategies. This grant was



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refunded this year through the efforts of Dr. Skolnik and others. This national and international network has provided data that have changed the way HIV disease is treated and managed. Industry-sponsored trials of novel therapeutic agents provide cutting-edge treatment opportunities for patients where no other treatments may exist or where better options for adherence and potency may be discovered. This year, trials of integrase inhibitors and chemokine receptor antagonists were completed or continued, along with studies of protease inhibitors and non-nucleoside reverse transcriptase inhibitors that retain activity when HIV-1 has become resistant to currently available treatments. Dr. Skolnik continued as protocol immunologist for an ACTG trial of a chemokine receptor inhibitor (A5211).

CHACR research resulted in several publications and presentations at national and international meetings.

### CLINICAL ACTIVITY

CHACR's clinical care comprises the majority of clinical activity in the CID. The approach is multidisciplinary because the needs of patients often go beyond the medical to include social and behavioral issues. Care is organized into teams, each comprising a case manager, nurse, and physician. This team follows the patient from initial encounter, often after discovery of HIV infection during rapid HIV testing, and longitudinally, to provide comprehensive care by providers with whom the patient has built a trusting relationship from the outset. The patient is walked into care in the CHACR and provided with immediate support and any necessary interventions.

CHACR's pharmacy and clinical studies teams are an integral part of the overall care provided to patients. In addition, specialty care, including nutrition, pulmonology, hepatology, and psychiatry, is available

within the CID. Dr. Lambl provides STD services. Physicians involved in outpatient efforts include Jon Fuller, M.D., attending physician in the Center for Infectious Diseases, and Associate Professor of Medicine and Beth Zeeman, M.D., as well as Drs. Bica, Hamer, Skolnik, Sullivan, and Yu.

Other faculty providing care through CHACR include Sondra Crosby, M.D; Julita Mir, M.D., and Jon Pincus, M.D. from the Section of General Internal Medicine; Harrison Farber, M.D., Professor of Medicine, and a member of the Section of Pulmonary, Critical Care and Allergy; and David Nunes, M.D, Director of Hepatology at BMC, Associate Professor of Medicine, and a member of the Section of Gastroenterology.

Under Dr. Hardy's direction, the HIV pharmacotherapy team provides crucial input to overall patient care. This group of Pharm.D. specialists provides care to enhance adherence, which is central to a consistent response to therapy and prevention of resistance to anti-HIV medications. The HIV pharmacotherapy team also provides information to providers about proper drug dosage and potential interactions between HIV medications or other drugs.

In conjunction with the Departments of Pediatrics and Obstetrics/Gynecology, Dr. Sullivan leads a multidisciplinary team that cares for HIV-positive pregnant women. She provides pre-conception counseling for couples in which one or both partners are HIV positive, in an effort to minimize partner risk. She also spearheaded the initiation of studies and services regarding human papillomavirus infection of HIV-positive men and women in the CID. Dr. Sullivan will lead an industry-sponsored effort to provide HIV counseling and testing for patients in the Women's Center at BMC, and she will continue to expand and initiate

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the pre-conception counseling program to include conception services for sero-discordant couples (intrauterine insemination and “sperm washing”).

The refugee health program, which is under the direction of Elizabeth Barnett, M.D., Assistant Professor of Pediatrics, and a member of the Section of Pediatric Infectious Diseases, and the STD program refer HIV-positive patients directly into CHACR care, thus providing consistency of care that is crucial to patients with multiple health and social difficulties. Dr. Crosby and the case manager who focuses on refugee care are central to efforts to care for refugees, asylum seekers, and victims of torture in culturally appropriate and effective ways.

The CHACR’s consumer advisory board continued to help guide programs and policies in the CID.

## EDUCATION

Teaching about HIV/AIDS occurs in multiple venues for students at different points in their careers. Dr. Skolnik mentors an NIH K08 recipient, Michael Jeong, M.D., Assistant Professor of Medicine, and a member of the Section of Pulmonary, Critical Care and Allergy, in basic research studies concerning redox potential, and its effects on HIV replication, in the lung. Dr. Montano is devoted to teaching undergraduate students and has solidified an interest in basic research in these students. Andrew Henderson, Ph.D., is actively engaged in training pre-doctoral students. Dr. Nicol helped mentor a student in the master’s of medical science program; the CHACR basic research laboratories are sought-after venues for students in this program who are seeking to complete their required thesis.

Drs. Bica, Skolnik, and Yu provide formal lectures for medical and dental students concerning HIV/AIDS in the medical

microbiology and pharmacology courses at BUSM and in graduate and post-graduate courses at the Goldman School of Dental Medicine.

An ambulatory “morning report” format is used to teach primary care residents about HIV/AIDS clinical care. Drs. Bica, Fuller, Pincus, Skolnik, and Sullivan participate in this activity. Dr. Lambl helps to teach a course about STDs to providers from across the Commonwealth through a grant from the Massachusetts Department of Public Health.

As part of their medicine clerkship, third-year BUSM students rotate through the CHACR/CID to learn the principles of outpatient care in general and HIV care in particular. Drs. Fuller and Skolnik serve as mentors for this activity. Because of the program’s size and reputation and its location in an urban medical center, BUSM students and BMC residents, as well as those from other medical schools and hospitals, look to the CHACR as a prime site to train in HIV care. Dr. Fuller coordinates these outpatient training activities.

In conjunction with the Massachusetts College of Pharmacy and Health Sciences, Dr. Hardy leads an accredited residency program for Pharm.D. students who desire specialized training in HIV pharmacy issues.

An NIH T32 training award, the BU-CHART, supports training in clinical HIV research. Dr. Horsburgh was Principal Investigator for the award, but he has transferred this responsibility to Dr. Cotton for the upcoming academic year. Dr. Skolnik is Co-principal Investigator. This training is done in conjunction with the K30 curriculum award to David Felson, M.D., M.P.H., Chief of the Clinical Epidemiology Research and Training Unit, Director of the Health Services and Epidemiology Research Program, and Professor of Medicine and Public Health. Trainees can receive the M.Sc. or Sc.D. from BUSPH at the end of

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this training. Each trainee has an ethics co-mentor, drawn from BUSPH's world-renowned medical ethics department, and can focus on epidemiologic, interventional, substance use, or health policy areas of clinical research. Drs. Gill and Hamer served as mentors for BU-CHART fellows who are interested in international HIV research.

The Section provides multiple conferences and lectures for BMC and Boston University concerning HIV/AIDS. Dr. Fuller presents an annual HIV/AIDS update during medical grand rounds, and he also organizes a bi-weekly, CME-accredited AIDS conference with local, national, and international speakers.

### MAJOR ACCOMPLISHMENTS

Dr. Andrew Henderson, joined the CHAR and the Section of Infectious Diseases. He adds important research and education activities to CHACR. His research concerning transcriptional regulation is cross-cutting, and will inform the research programs of others, while adding opportunities for collaboration.

Dr. Marlynne Quigg Nicol has been appointed an Instructor of Medicine in the Section. She will continue her research endeavors, which are focused on the innate immune response in the lung during HIV infection.

Funding to the CHACR from the Massachusetts Department of Public Health HIV/AIDS Bureau increased substantially again this year, including a new grant to support prevention and education programs for Haitian women. These grants provide service-related activities and help to support research into these areas that are critical to HIV-related health care. The CDC praised CHACR's successful, integrated model of care, which utilizes both public and private funding, and noted it as a national model for this type of care.

The CHACR's STD program continues to

flourish. The number of visits has expanded, and the HIV rapid testing program has identified many additional HIV-positive individuals. The CHACR's counseling and testing programs identify, and link to care, more newly diagnosed HIV-positive patients than any other program in the Commonwealth.

The CHACR's clinical research portfolio is strong and varied. These studies, such as trials of new integrase inhibitors, provide cutting-edge care to patients and yield important insights into the best treatments for HIV-positive patients. Through the intensive efforts of many people on the national, state, and local levels, BMC will continue to be a clinical research site for the AIDS Clinical Trials Group.

The HIV pharmacotherapy residency program continues as one of only two such accredited programs in the country. The pharmacy team conducts important adherence-related research and provides superb clinical services to patients both directly and through the support of other care providers in the CID and the wider BU community. They also provide investigational drug services for the HIV-related clinical trials in the CID.

CHACR educational programs serve to inform clinicians, researchers, and students about cutting-edge discoveries, treatments, and management issues. Outreach activities to the community, in the form of provision of services and research collaborations, further serve to solidify the CHACR's reputation for expertise in testing and counseling, prevention and education, provision and linkage to care, and research activities, especially concerning disadvantaged populations.

### FACULTY

#### Professors

Deborah J. Cotton, M.D.  
C. Robert Horsburgh, M.D.  
Mark S. Klempner, M.D.  
Paul Richard Skolnik, M.D.  
Alan M. Sugar, M.D.  
Lee M. Wetzler, M.D.

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**Associate Professors**

Tamar F. Barlam, M.D.

Jon D. Fuller, M.D.

Robin R. Ingalls, M.D.

David Hamer, M.D.

Andrew J. Henderson, Ph.D.

Carol A. Sulis, M.D.

**Research Associate Professors**

Guillermo E. Madico, M.D.,Ph.D.

You-Xun Zhang, Ph.D.

**Assistant Professors**

M. Anita Barry, M.D.

Ioana Bica, M.D.

Philip C. Carling, M.D.

Richard Serrao, M.D.

Christopher Gill, M.D.

Margaret M. Sullivan, M.D.

David Thornton, M.D.

**Clinical Assistant Professors**

Barbara Lambl, M.D.

Judith Steinberg, M.D.

Beth A Zeeman, M.D.

Frank C. Gibson, Ph.D.

**Clinical Adjunct Assistant Professor**

Thomas L. Treadwell, M.D.

**Research Assistant Professors**

Paola Massari, Ph.D.

Monty A. Montano, Ph.D.

Susan K. Weir, Ph.D.

**Instructors**

Richa Tandon, M.D.

Catherine Yu, M.D.

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# MOLECULAR MEDICINE



**SECTION CHIEF**  
*John Murphy, Ph.D.*

The Section of Molecular Medicine comprises the following units and programs within the Department of Medicine: the Biomolecular Medicine Unit; Genetics Program; Immunotherapy Unit; Molecular Genetics Unit, Obesity Research Center; and Whitaker CVI Digital Imaging Microscopy Center. In the past year, two additional research units have been added to the Section: the Ion Channel and Calcium Signaling Unit and the Chronic Inflammation and Bacterial Pathogenesis Unit.

The Section of Molecular Medicine represents a diverse set of basic science interests that apply state-of-the-art technologies to understand the underlying molecular basis of disease. Accordingly, the Section's research focus ranges from basic genetics to the development of novel biotherapeutics for the targeted elimination of disease-causing cells.

Common to each Unit, Center, or Program is the application of molecular biologic and molecular genetic methods toward the long-term goal of bringing new therapies and approaches to the management of refractory human disease. Section members are actively involved in the training of graduate students enrolled in Boston University School of Medicine's basic science departments, as well as graduate students in the Graduate Program in Molecular Medicine within the Department

of Medicine. The Section also provides opportunities for advanced post-doctoral training.

## BIOMOLECULAR MEDICINE UNIT

Research in the laboratory of John R. Murphy, Ph.D., Chief of the Section of Molecular Medicine, Associate Director of the Graduate Program in Molecular Medicine, and Professor of Medicine and Microbiology, focuses on the development of diphtheria toxin-based fusion protein toxins as experimental probes for cellular biochemistry, as well as the genetic and structural analysis of the diphtheria toxin repressor, DtxR. During the past year, Dr. Murphy's research has continued to investigate the molecular mechanism by which the catalytic domain of DAB389IL-2, a diphtheria toxin-based interleukin-2 receptor-targeted fusion protein toxin, is specifically translocated from the lumen of early endosomes to the cytosol of target eukaryotic cells.

Recent studies have demonstrated that the translocation process is dependent upon a cytosolic translocation factor (CTF) complex. This complex is, in part, made up of Hsp90 and thioredoxin [reductase, which play essential, but not sufficient, roles in the entry process. In addition, recent studies have suggested that those protein toxins that enter the cell from an acidified early endosomal compartment carry a highly conserved "translocation motif," T1. Eukaryotic cell transfectants that express this "translocation motif" become resistant to the action of both DAB389IL-2 and diphtheria toxins. Recent observations from GST-DT140-271 fusion protein pull-down experiments have demonstrated the specific binding of  $\beta$ -COP to the T1 peptide. This observation, coupled



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with the finding that anti- $\beta$ -COP inhibits *in vitro* translocation of the diphtheria toxin catalytic domain from the lumen of purified early endosomes, demonstrates that  $\beta$ -COP is also a member of the CTF complex of proteins. This observation further raises the possibility that interaction between the T1 motif in the transmembrane domain of the toxin and  $\beta$ -COP may be the first interaction in the toxin entry process.

Because this putative translocation motif is also present in the N-terminal portions of catalytic subunits of anthrax toxin, lethal factor (LF) and edema factor (EF), Unit researchers have now asked whether anthrax lethal factor entry into the cell might also be facilitated by target cell cytosolic proteins. In this study, the team has employed an LFn-DTA fusion protein and its associated ADP-ribosyltransferase activity (DTA) to determine the requirements for its translocation from the lumen of endosomal vesicles to the external medium *in vitro*. Although low-level release of LFn-DTA from enriched endosomes occurs in the absence of additional factors, translocation was markedly enhanced by the addition of cytosolic proteins and ATP to the reaction mixture. Unit investigators have shown by GST-LFn pull-down assays that LFn specifically interacts with the COPI coatamer subunits  $\zeta$ -COP and  $\beta$ -COP. Depletion of COPI coatamer complex proteins from cytosolic extracts blocks *in vitro* LFn-DTA translocation, and this block may be reversed by the addition of partially purified bovine COPI to the translocation assay mixture. Further, the addition of a DT peptide containing the T1 motif to the translocation assay mix also blocks *in vitro* LFn-DTA translocation. Taken together, this data suggests that the delivery of LF to the cytosol is facilitated by at least some components of the COPI coatamer complex, and this facilitated delivery appears to use a mechanism that is similar to that of DT catalytic domain entry.

Additional studies in Dr. Murphy's laboratory

focus on elucidation of the molecular mechanism(s) and structural basis by which DtxR undergoes a metal ion-dependent transition from the inactive apo-form to the metal ion-bound active form of the repressor. Unit researchers have recently demonstrated that the C-terminal SH3-like domain of the repressor plays a critical role in stabilizing the apo-repressor in its molten globule state. The activation of apo-DtxR appears to involve at least three sequential steps during which the repressor structure undergoes a dynamic transition to a fully ordered state. These steps lead to homodimerization and a fully functional metal ion-bound form of the repressor. The DtxR system continues to provide the paradigm for understanding metal ion control of virulence gene expression in pathogenic gram-positive bacteria.

Based upon the analysis of hyper-active mutants of DtxR, Unit researchers hypothesized the isolation of metal ion-independent peptides could activate the wild type repressor. Following the screening of a peptide library, researchers have isolated two peptides that have this capacity. One of these peptides has been analyzed for structure activity relationships, and Dr. Murphy's team found that a 12-mer derivative, PAD-1.17, also displays antimicrobial properties *in vivo*. Using the Sterne vaccine strain of *Bacillus anthracis*, researchers have shown that the peptide antibiotic at 20  $\mu$ M is lethal to vegetative cells and prevents the vegetative outgrowth of *B. anthracis* spores. Current studies are examining the molecular mode of action of this novel antimicrobial agent. Recent analysis has shown that this peptide antibiotic enters the prokaryotic cell cytosol and disrupts the 70S structure of ribosomes, resulting in the accumulation of 50S and 35S ribosomal subunits. This disruption is followed by ribosomal degradation and bacterial death. This observation is consistent with metabolic labeling studies that have shown that the interruption of RNA synthesis is the first metabolic lesion that can be observed. These studies are the first to demonstrate that PAD-1.17 displays a unique mechanism of action for



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peptide antibiotic agents. Current studies are focused on the elucidation of the mechanism of PAD-1.17 uptake into the prokaryotic cell cytosol.

#### CHRONIC INFLAMMATION AND BACTERIAL PATHOGENESIS UNIT

Under the direction of Caroline Genco, Ph.D., Professor of Medicine and Microbiology and Associate Professor in the Department of Periodontology and Oral Biology at the Goldman School of Dental Medicine, the Chronic Inflammation and Bacterial Pathogenesis Unit studies the characterization of specific bacterial virulence factors produced by the mucosal pathogens *Neisseria gonorrhoeae*, *N. meningitidis*, and *Porphyromonas gingivalis*, as well as the underlying molecular mechanisms by which these factors enable these organisms to cause disease. Dr. Genco is interested in mechanisms utilized for colonization and, in particular, the ability of environmental factors to modulate bacterial gene expression. Her laboratory has defined the mechanisms of iron transport in both *N. gonorrhoeae* and *P. gingivalis* and characterized several outer membrane receptors required for transport and utilization of iron.

Dr. Genco's laboratory is seeking to understand how virulence genes are expressed *in vivo* and the role of iron in gene regulation *in vivo*. Iron starvation is used as a signal by many pathogens that they are in a host environment; it results in the expression of virulence factors that are transcriptionally regulated by iron through the ferric uptake regulator protein, Fur. Dr. Genco's laboratory has defined the Fur-regulon in *N. gonorrhoeae*, *N. meningitidis*, and *P. gingivalis*. Her studies have established that the transcriptional regulatory protein Fur controls the expression of numerous genes that are required for the virulence of *N. meningitidis* and *N. gonorrhoeae*. In collaboration with Tim Gardner, Ph.D., Assistant Professor of Biomedical Engineering at Boston University's College of Engineering, Dr. Genco and her team are examining regulatory gene networks in the pathogenic *Neisseria*.

Current studies are aimed at examining the regulation and expression of Fur-regulated genes *in vitro*, and *in vivo* directly in clinical specimens.

The Unit recently identified a novel mechanism for Fur-mediated regulation through small regulatory RNAs. In collaboration with Brian Tjaden, Ph.D., Assistant Professor of Computer Science at Wellesley College, Unit researchers have developed an *in silico* approach to identify potential mRNA regulatory targets of a newly identified small RNA (sRNA) of *N. meningitidis*, *nrrF*. This approach utilized a novel algorithm developed by Dr. Tjaden that analyzed potential base pairing interactions between sRNAs and candidate mRNA sequences, taking into account known biases of sRNA interactions, such as interactions near 3' untranslated regions and short discontinuous base pairing interactions. This work helped identify the function of the first regulatory small RNA of *N. meningitidis*.

In conjunction with Bjoern Reinhard, Ph.D., Assistant Professor of Chemistry in the Department of Chemistry at Boston University, and Lynell Skewis, a graduate student under his direction, Unit investigators have been examining the intermolecular interactions of the *N. meningitidis nrrF*, with its mRNA target messages and an RNA chaperone protein name host factor for Q-phage replication (Hfq). These investigations have used fluorescence imaging to examine Hfq binding interactions with these RNA molecules in electrophoretic mobility shift assays, as well as fluorescence resonance energy transfer (FRET) experiments to quantitatively examine the nature of the binding interactions of these molecules.

Several different model systems are used to examine the interactions of bacteria with the host. These include animal models for gonococcal infection and *P. gingivalis* oral infection. Dr. Genco's laboratory also utilizes epithelial and endothelial cells to study the interactions of *N. gonorrhoeae* and *P. gingivalis*

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with host cells, which are permissive for these pathogens. In collaboration with Robin Ingalls, M.D., Assistant Professor of Medicine, and a member of the Section of Infectious Diseases at Boston Medical Center (BMC); Paola Massari, Ph.D.; and Lee Wetzler, M.D., Associate Professor of Medicine and Microbiology, and a member of the Section of Infectious Diseases at BMC, Dr. Genco and her team have conducted studies on the influence of *N. gonorrhoeae* infection on the host cell's apoptotic response. They have utilized human cervical epithelial cells developed by Deborah Anderson, Ph.D., a member of the Division of Reproductive Biology in the Department of Obstetrics and Gynecology. Currently the laboratory is examining the interactions of *N. gonorrhoeae* expressing GFP (green fluorescent protein) with endocervical, ectocervical, and vaginal cell lines. Using these cell lines, they have demonstrated distinct proinflammatory responses in different compartments of the female lower genital tract.

Furthermore, Dr. Genco has utilized these cells to demonstrate that infection with *N. gonorrhoeae* inhibits these cells' apoptotic response. Thus, *N. gonorrhoeae* may establish infection in women by inhibiting the apoptotic response to infection, thereby resisting killing from both the host cell and the innate immune response. Furthermore, prolonged survival of the host cell potentially allows the bacteria to successfully invade cervical tissue, eventually transcending to the upper genital tract. More recently, this work has focused on a new area of collaboration with Greg Viglianti, Ph.D., Associate Professor of Microbiology, with whom they are examining the effects of *N. gonorrhoeae* co-infection with HIV in macrophages and dendritic cells.

Another area of research in Dr. Genco's laboratory is the development of vaccine candidates to prevent *P. gingivalis*-induced periodontal disease. Using several different animal models, researchers in her laboratory have demonstrated that the *P. gingivalis* cysteine proteases (gingipains), major virulence factors

of this organism, function in a protective manner in animal models following *P. gingivalis* challenge. These studies have led to several collaborative studies with biotech companies. A new avenue of research being pursued in Dr. Genco's laboratory is the examination of the specific cellular and molecular mechanisms by which infectious agents contribute to chronic inflammation and, specifically, the role of the innate immune response in atherosclerosis. Dr. Genco has established that the gram-negative pathogen *P. gingivalis* accelerates atherosclerotic plaque accumulation and that it is mediated by innate immune recognition to invasive bacterial infection. Her laboratory has established that *P. gingivalis* infection and inflammation in endothelial cells is mediated through fimbriae signaling through Toll-like receptors. Finally, she and her team have established that TLR2 plays a critical role in the atherosclerotic inflammatory response that is independent of dietary lipids. Current studies are focused on other chronic infections such as that caused by the respiratory pathogen *Chlamydia pneumoniae*. These studies employ *in vitro* model systems for platelet, endothelial cells, and macrophages. The common theme of these studies is to examine the role of infection and the innate immune response in early events associated with atherosclerosis in well-defined *in vitro* and *in vivo* systems.

In collaboration with James Hamilton, Ph.D., Professor of Physiology and Biophysics in the Department of Biomedical Engineering within BU's College of Engineering, Dr. Genco recently conducted studies on live mouse imaging. This work has focused on imaging mice infected with pathogens that induce chronic inflammation. In particular, they are examining lung inflammation and inflammatory atherosclerosis in mouse models. Drs. Genco and Hamilton are also developing contrast agents together with Joyce Wong, Ph.D., Associate Professor of Biomedical Engineering and Associate Chair for Graduate Studies for the Department of Biomedical Engineering at the College of Engineering, to be used in ultrasound imaging

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of infected mice.

#### DIGITAL IMAGING MICROSCOPY CENTER MULTI-PHOTON IMAGING MICROSCOPY CENTER

Usage of the Multi-Photon Imaging Facility has been somewhat uneven during the past year as investigators' awareness of the facility continues to grow. Imaging has included fixed and living cell preparations, as well as living tissue fluorescence imaging. Images from the facility are regularly being published and included in grant proposals. A brief study of an artifact of photobleaching Yellow Fluorescent Protein (YFP), commonly done in fluorescence resonance energy transfer (FRET) experiments, is in press for *Nature Methods*. Included in this submission is an online supplement containing a novel method Center researchers developed for quantitative determination of co-localization of fluorescently tagged molecules.

Center faculty recently made some modifications to allow the use of 3-photon excitation to obtain autofluorescence in the ultraviolet range from serotonin-containing vesicles. Preliminary results were positive.

Data from a novel, multi-focal, experimental, high-speed 2-photon imaging configuration was recently published in *Optics Express*. In the prototype system, Center faculty members were able to obtain fluorescence images in living cells at a frame rate of 640 frames per second, the highest speed 2-photon imaging reported anywhere. This system has been redesigned, and it is anticipated that the newer version will be operational soon. Any delay in getting this version up and running was due, in part, to the necessity of having some custom software developed to normalize the gains of the camera's 16 data ports.

The Center was selected to send one of three institutional Major Research Instrumentation Grants to NSF. This was

done in collaboration with the Advanced Imaging Technology Group at Massachusetts Institute of Technology's Lincoln Laboratory. NSF did not fund the proposal but did make a number of positive comments. The proposed system adapts a LADAR hybrid-imaging device developed at Lincoln Laboratory for defense applications. It comprises an array of Geiger-mode avalanche photodiodes bonded to CMOS counters, which record the arrival times of photons emitted by fluorescent molecules in response to a flash of laser light. The proposed system should provide fluorescence lifetime images at a rate close to two orders of magnitude faster than current lifetime imaging systems. This would permit the study of key intracellular signaling events, such as protein phosphorylation, in real time.

Presently, funding to support the facility running is coming from the Department of Medicine, the BUSM Dean's office, several grants, and hourly charges. More grants, with funds earmarked for the facility, are pending. Center faculty will continue to seek to increase visibility and obtain funding.

#### GENETICS PROGRAM

The Genetics Program is a multidisciplinary, cross-sectional unit the missions of which are to foment and provide leadership in human and medical genetics research, as well as to extend and develop new genetics curricula for graduate and medical students and M.D. fellows seeking academic research careers. Research programs represent a broad range of both clinical and basic research. Under the direction of Lindsay Farrer, Ph.D., Chief of the Genetics Program and Professor of Medicine, the Genetic Epidemiology Center designs and directs National Institutes of Health (NIH)- and industry-sponsored multi-center projects aimed at identifying genes and gene-environment interactions for complex diseases. The program houses the Molecular Genetics Core facility and an Informational Technology Unit.

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The Genetics Program's funded research and grant support increased nearly 30% compared with the prior year, with total annual direct research grant in the amount of approximately \$10.2 million, despite a progressively bleaker federal funding situation.

The Genetics Program recruited a new faculty member this year. Mark Logue, Ph.D., is a genetic epidemiologist who brings to the Program research skills in psychiatric diseases and statistical genetics, as well as a newly funded five-year Career Development Award from the National Institute of Mental Health, the research component of which is focused on identifying genes for panic disorder.

The Program's Information Technology (IT) Unit greatly expanded its secure and flexible local area network and standardized protocols on personal and workstation computers. In addition, the IT Unit expanded its capabilities for scanning and storing data from questionnaire forms, conducting questionnaire interviews via laptop computer, and acquiring primary epidemiological and genetic data over the Internet. The IT Unit also manages multi-user workstation systems for computational genetics projects, bioinformatics, and the Laboratory Information Management System that underpins all the Core facility's activities. These systems include a 24-node (48-processor) IBM Linux cluster capable of handling CPU-intensive analytic projects (including those that can exploit parallel processing). This system, which has already facilitated data analysis for several genome scan projects, was the model for a much larger system that the NIH awarded to Boston University School of Medicine (BUSM) through a shared instrumentation grant known as LinGA (Linux Cluster for Genetic Analysis) that has 134 nodes (= 268 processors). Dr. Farrer is the Co-Principal Investigator.

The Molecular Genetics Core facility continues to have a major role in research activities at Boston University, providing DNA extraction, sequencing, and genotyping services to laboratories on both University

campuses and non-University laboratories. The Core performs DNA extractions from various tissues and provides tissue culture services, including the establishment and maintenance of lymphoblastoid cell lines, for several large projects in BUSM and the Slone Epidemiology Unit. The Core participated in the design of several large research projects that are now funded by NIH. A full-time laboratory manager who supervises three to four technicians directs the Core's daily activities. The Core facility continues to be self-sustaining and fiscally distinct from the Genetics Program's administration and research projects.

The Genetics Program's research programs in Alzheimer's disease (AD) continue to expand and gain profile locally, nationally, and internationally. Funded by grants from the NIH and the Alzheimer Association, Dr. Farrer and Clinton Baldwin, Ph.D., Professor of Pediatrics—working with scientists at the University of Toronto, Columbia University, Case Western Reserve University and in Israel -- have marshaled one of the world's largest collections of AD families as a resource to identify AD genes. Dr. Farrer's MIRAGE (Multi Institutional Research on Alzheimer Genetic Epidemiology) Study compares variations in genes related to vascular functioning with disease and pre-clinical changes evident on MRI scans done of the brains of 1,000 white, African-American and Asian-American AD families. Robert Green, M.D., M.P.H., Co-Director of the Alzheimer's Disease Clinical and Research Program, Professor of Neurology, Genetics, and Epidemiology, and a member of the Department of Neurology at BMC, serves as the Clinical Core Director for Boston University's NIH-funded Alzheimer's Disease Center (ADC) and is Principal Investigator of several large, funded clinical genetic studies of AD. Several new grant awards were received this year: renewal of the federally funded ADC; Dr. Green's REVEAL (Risk Evaluation and Education for Alzheimer's disease) Study; a multi-million dollar genome-wide association study of AD in the MIRAGE cohort jointly

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sponsored by the NIH and a Boston-based non-profit foundation; and a large, industry-sponsored project to evaluate differences in brain MRI scans between AD and vascular dementia patients.

Last year, an international effort by researchers led by Dr. Farrer and his colleagues at the University of Toronto and Columbia University uncovered a major new gene – SORL1 – for late-onset AD. Replicated in four distinct ethnic groups, SORL1 is only the second gene discovered for late-onset Alzheimer's. APOE, the first gene, was identified in 1993. In an article published in *Nature Genetics*, the research team described how variants in the SORL1 gene were found to be more common in people with late-onset Alzheimer's than in healthy people of the same age. This work, which is based on analysis of DNA specimens from more than 6,800 individuals, has already been replicated in several independent studies. Results of additional *in vitro* experiments in the original report suggested that these genetic variants alter the normal function of SORL1, sending the amyloid precursor protein (APP) down a pathway that increases the production of the toxic amyloid beta (A $\beta$ ) peptides in the brain, resulting in AD. When the SORL1 gene works properly, it sends APP along recycling pathways, thus preventing it from being cut into toxic A $\beta$  forms.

The Genetics Program has an integral role in expanding existing and developing new cross-sectional research programs. Section faculty are working together with members of the Section of Pulmonary, Allergy, Critical Care and Sleep Medicine to study the genetics of severe asthma and lung cancer; with the Section of Hematology/Oncology on three NIH-funded projects aimed at identifying genes influencing the severity and expression sickle cell anemia and beta thalassemia; and with the Section of Geriatrics on a federally funded project (with Dr. Baldwin as the Principal Investigator) exploring the genetic basis of exceptional longevity. The centenarian cohort assembled for the exceptional longevity

studies is a unique comparison group for tracking the genetic determinant of many adult-onset conditions including cardiovascular disease, metabolic disorders, arthritis, and dementia. Drs. Baldwin and Farrer are co-investigators of a multi-million dollar project, funded by the National Heart, Lung, and Blood Institute, to conduct a genome-wide association study in the sickle cell and centenarian study cohorts.

Genetics Program faculty have established highly productive NIH-funded research projects with scientists at other institutions. In collaboration with scientists at Yale and the University of Connecticut, Dr. Farrer and Caroline Panhuysen, M.D., Ph.D., identified a specific haplotype (a genetic variant in the population covering a small portion of a chromosome) in the ANKK1/TTC12 gene region that strongly influences smoking behavior in both whites and African-Americans. They also completed a genome scan for tobacco dependence resulting in the identification of several novel loci. Dr. T. Cuenca directs the analysis of candidate gene and genome scan data for a project on uterine fibroids based at Harvard Medical School. She also coordinates the genetic analyses for an infectious disease genetics project involving researchers at the Influenza Branch of the Centers for Disease Control and Prevention and the National Institute of Allergy and Infectious Diseases.

The laboratory of Sam Thiagalingam, Ph.D., Associate Professor of Medicine and Pathology and Laboratory Medicine and Genetics and Genomics, employs breast and lung cancer model systems to shed light on genomic instability, genetic and epigenetic aberrations, and metastasis of cancer. A goal of this research strategy is to invent new tools for the diagnosis, prognosis, management, and therapy of cancer. His laboratory continues to study the epigenetic alterations in schizophrenia and bipolar disease. This past year, he published a second pioneering report demonstrating that hypo-methylation-associated over-expression of the M-COMT



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isoform is likely to cause hypodopaminism in schizophrenic and bipolar patients. Dr. Thiagalingam received an Independent Investigator Award from the **National Alliance for Research on Schizophrenia and Depression (NARSAD)** and was named the 2006/2007 NARSAD Dr. Walter F. Nichols Investigator.

In her laboratory, Faina Schwartz, Ph.D., Associate Professor of Medicine, studies the influence of variation in the mitochondrial genome to the pathogenesis of essential hypertension. Recently, she directed a study that demonstrated an association between mtDNA single nucleotide polymorphisms (SNPs) and hypertension in 1,800 participants in the Framingham Heart Study (FHS). Currently, her laboratory is examining sequences of the entire mtDNA genome from 33 FHS participants with extreme blood pressure phenotypes.

In his laboratory, Kenneth Albrecht, Ph.D., Assistant Professor of Medicine, Genetics and Genomics, conducts genetic crosses in mouse models to identify and characterize sex determination genes, many of which have been implicated in pathological processes in humans and have essential roles in the normal development of organs other than the gonads. This past year, his laboratory published findings of a study demonstrating direct regulation of adult brain function by the male-specific factor SRY.

The Genetics Program attracts outstanding postdoctoral fellows and graduate students from doctoral programs across Boston University, including the Graduate Program in Molecular Medicine, Genetics and Genomics, Cell and Molecular Biology, Epidemiology, and Bioinformatics. Drs. Albrecht, Baldwin, Farrer, Thiagalingam and Richard Myers, Ph.D., Professor of Neurology, serve on qualifying examination and thesis committees of many students in various graduate programs. Despite the diverse background in interests and matriculation through different graduate programs, all pre- and postdoctoral trainees in the Genetics Program participate in

sanctioned trainee-lead meetings, including a Journal Club.

Many of the graduate students made presentations at major national and international meetings. Vikki Nolan gave oral presentations at the Society for Epidemiological Research's annual meeting and the annual meeting of the National Sickle Cell Program. Two Program trainees, Hamid Abdolmaleky, a postdoctoral fellow, and Panos Papageorgis, a graduate student, received honorable mention in the Evans Research Days Poster Competition. Mr. Papageorgis was a first-place winner, and Dorothy Pazin, received an honorable mention at the Russek Student Achievement Day competition.

Two students earned Ph.D. degrees this past year. Yan Meng, whose thesis advisor was Dr. Farrer, completed the doctoral degree requirements for the Bioinformatics Program. Her thesis was titled "Multi-locus Approaches to Localizing Genes Associated with Common Human Diseases." Subsequently, Dr. Meng accepted a postdoctoral position at the Broad Institute in Cambridge, MA. Hyunjoo Lee, whose thesis advisor is Dr. Albrecht, is an M.D./Ph.D. student who completed the doctoral degree requirements for the Graduate Program in Molecular Medicine. Her thesis was titled "Identification of Genes Involved in Granulosa Cell Differentiation in Mammalian Sex Determination." She resumed her training at BUSM for the M.D. degree.

Under the direction of Dr. Farrer, Genetics Program faculty members teach the "Genetics & Epidemiology of Disease," a core course in the Graduate Program in Molecular Medicine. Dr. Farrer also teaches a course titled "Genetic Epidemiology" at the Boston University School of Public Health and is the course director and primary lecturer for "Introduction to Human Genetics." Drs. Albrecht, Baldwin, Farrer, Schwartz, and Thiagalingam also deliver between four and thirty-six hours of lectures in numerous courses taught at BUSM.



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The Program's biweekly "Molecular & Quantitative Genetics" seminar series attracted interdisciplinary speakers on topics such as "Huntington's Disease, a Simple Complex Disorder" by Marcy MacDonald, Ph.D., Associate Professor of Neurology and a member of the Center for Human Genetic Research at Harvard Medical School, and "Genomics in Surgical Oncology" by Jennifer Rosen, M.D., Assistant Professor of Surgery. Many of the seminars were "standing room only." Seminar organizers are exploring the possibility of a sponsorship of the seminar series, which would allow them to invite high-profile speakers from outside the Boston area.

### IMMUNOTHERAPY UNIT

It has been two years since the establishment of the Immunotherapy Unit, the main mission of which is the integration of basic research with patient-oriented research. Unit faculty members are developing a comprehensive strategy for the immunotherapy of cancer. Researchers have established a murine model with spontaneous lung metastasis for immunotherapy, with the goal of treating the primary tumor with surgery and lung metastasis with active and/or adoptive immunotherapy. Unit faculty are also investigating the mechanism behind the generation of potent and long-lasting antitumor immunity, focusing on the identification and characterization of the effector T-cells with significant antitumor immunity *in vivo*. If identified, effector T-cells can be used in the adoptive immunotherapy.

Unit researchers have prepared a molecular chaperone vaccine from DC-tumor fusion cells. Heat shock protein 70-peptide complexes (HSP70-PC), prepared from fusion cells, are superior to those from tumor cells. Immunization of mice with HSP70-PC from fusion cells resulted in a T-cell-mediated immune response, including a significant increase of CD8 T-cells and induction of the effector and memory T-cells that was able to break T-cell unresponsiveness to a non-mutated tumor antigen and protect mice

against challenge with tumor cells. These results have been published in the *Journal of Immunology*. In addition, a final patent application for the extraction of HSP70-PC from DC-tumor fusion cells and use of them as a vaccine has been filed.

Unit researchers have made significant progress in the investigation of the role of telomerase and telomeres in the tumorigenesis of spontaneous breast cancer. Unit researchers have generated telomerase-null mice (mTERC<sup>-</sup>/MMT) that carry a potent oncogene. The onset of mammary tumor in mTERC<sup>-</sup>/MMT mice was significantly delayed and the tumor burden significantly decreased, suggesting that telomerase is involved in the formation, progression, and metastasis of breast cancer.

In the coming year, Unit faculty members will continue to develop a HSP70-PC-based tumor vaccine. In addition, they will develop telomerase- and a telomere-based approach in the treatment of breast cancer.

### ION CHANNEL AND CALCIUM SIGNALING UNIT

Research in the laboratory of Victoria Bolotina, Ph.D., Professor of Medicine, Physiology and Biophysics, focuses on the mechanisms of calcium entry and its role in physiological and pathological function of a wide variety of cell types including, but not limited to, vascular smooth muscle cells, platelets, T-lymphocytes, mast cells, beta cells, and neuronal cell lines. Using an integrative multidisciplinary approach and state-of-the-art techniques, this Unit addresses fundamental issues of ion channel function, calcium homeostasis, cellular physiology and signal transduction, and applies them to the organ function and disease models. Advanced patch-clamp techniques are used to monitor the ion channel function, and high-resolution imaging is utilized to track the dynamic changes in intracellular Ca<sup>2+</sup> and to co-localize different molecular determinants of signaling cascades.

To address the questions related to the

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molecular identity and physiological/pathological importance of specific ion channels and their regulatory proteins, a variety of molecular and biochemical approaches is used, including antisense, siRNA, functional inhibition, molecular purification, overexpression, as well as transgenic models. Combining molecular techniques with immunocytochemistry and using high-resolution imaging techniques, Unit researchers study the spatial localization of the ion channels and their regulatory cascades within specialized structural domains in individual cells. This integrative approach allows investigators in Dr. Bolotina's lab to trace each process from individual ion channels (and closely associated regulatory molecules) through the  $\text{Ca}^{2+}$  signaling cascades within single cells to the function of the whole organs.

During the past year, Dr. Bolotina's research focused on the molecular mechanism of store-operated calcium entry (SOCE). It follows the original discovery (made by Dr. Bolotina's group) of a novel cascade of reactions that starts with depletion of intracellular  $\text{Ca}^{2+}$  stores, production of mysterious diffusible calcium influx factor (CIF) that displaces inhibitory calmodulin from plasma membrane-bound  $\text{iPLA}_2$  that leads to its activation, and the production of lysophospholipids, which activate store-operated channels (SOCs) in a variety of excitable and nonexcitable cells.

Recent discoveries of STIM1 as a calcium sensor in endoplasmic reticulum, and Orai1 as a plasma membrane channel activated by depletion of the stores, opened new and exciting possibilities for molecular studies of the details of this pathway. In more recent studies, Dr. Bolotina's group established a novel role of STIM1 as a crucial trigger for CIF production. Molecular knockdown of STIM1 in vascular SMC resulted in disappearance of CIF in extracts from these cells, while STIM1 overexpression produced the opposite effect, and CIF production was amplified several fold. Moreover, researches in Dr. Bolotina's lab identified a neuronal cell line in which SOCE was

impaired, and demonstrated that these cells did not produce CIF and had very low levels of STIM1. Expression of exogenous wild type STIM1 in these cells fully restored CIF production and SOCE. Specific part of STIM1 molecule (intraluminal SAM domain) and specific residues were identified that may be crucial for STIM1 interaction with CIF synthase and triggering CIF production in ER.

Dr. Bolotina's group also found  $\text{iPLA}_2\beta$  to be a central component of SOCE, which is essential for creating a structural complex that forms upon calcium store depletion in puncta structures between ER and plasma membrane, which involves STIM1,  $\text{iPLA}_2\beta$  and Orai1, with CIF and lysophospholipids being second messengers that are mediating the signal transduction.

An important part of the Unit's work focuses on identification of the mysterious CIF molecule. Human platelets are used as a source of CIF; sequential HPLC steps are utilized for its finest purification; mass spectrometry, combined with fragmentation techniques, are used for the determination of its chemical composition; and several advanced bioassay systems are utilized to detect its activity, and to test candidate molecules. James McKnight, Ph.D., Associate Professor of Physiology and Biophysics, is a new collaborator on this project. He will be trying to determine CIF structure using advanced NMR analysis of pure CIF extracts. The molecular identification of CIF and the discovery of the mechanism of its production will be the next breakthrough events and may be the Unit's next major contributions in the fields of  $\text{Ca}^{2+}$  signaling and ion channel regulation.

Another important project completed last year was molecular identification and separation of two important  $\text{Ca}^{2+}$ -conducting channels (Orai1-encoded CRAC that is activated through CIF/ $\text{iPLA}_2\beta$ -dependent mechanism, and TRPC1-encoded  $\text{IP}_3\text{ROC}$ , a channel that is operated via conformational coupling with  $\text{IP}_3$  receptor). This work opened new possibilities for independent studies of these two physiologically

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very important ion channels, which for many years were confused with each other, creating many controversies in the field.

Dr. Bolotina's lab established the role of  $iPLA_2\beta$  in agonist-induced constriction of cerebral, mesenteric, and carotid arteries, in which voltage-gated channels were thought to play the sole role in calcium influx and vascular constriction. A new model was proposed that involves agonist-induced store depletion,  $iPLA_2\beta$ -dependent activation of SOC channels, which produce depolarization and activation of voltage-gated calcium channels. The depolarization and activation may account for an equally important role of SOC and  $Ca^{2+}_L$  channels in cerebral and other resistant vessels.

In a separate project, the role of PKC $\epsilon$  in  $iPLA_2\beta$ -dependent SOCE regulation was established in vascular SMC and related to their proliferation. Dr. Bolotina's group obtained strong evidence that  $iPLA_2$  serves not only as an on/off switch, but also as a fine-tuning device in the store-dependent regulation of SOC channels.  $iPLA_2$  phosphorylation may be crucial for this function.

In new, collaborative studies with the laboratory of Barbara Corkey, Ph.D., Director of the Obesity Research Center at BUSM and the NIH-funded Boston Obesity Nutrition Research Center, and Professor of Medicine and Biochemistry, the role of  $iPLA_2\beta$  in insulin secretion in beta cells was tested. There is accumulating evidence on the crucial role of  $iPLA_2$  in insulin secretion, and Unit researchers believe that their model of  $iPLA_2$ -dependent SOC activation being a trigger for secondary activation of voltage-gates  $Ca^{2+}$  channels may be the missing clue for the roles of  $iPLA_2$  and SOC in beta cell function in normal and diabetic patients and animal models. Preliminary calcium and insulin secretion studies show feasibility and great potential for this hypothesis.

## MOLECULAR GENETICS UNIT

The Molecular Genetics group has two major research teams, one under the direction of Vassilis Zannis, Ph.D., Professor of Biochemistry, and the other under the joint direction of Nelson Ruiz-Opazo, Ph.D., Professor of Medicine, and Victoria Herrera, M.D., Associate Professor of Medicine.

Dr. Zannis and his team focus on the molecular genetics of apolipoproteins and lipoproteins in relation to atherosclerosis and Alzheimer's disease. Ongoing research is studying apolipoprotein gene regulation *in vivo* using antisense and transgenic methodologies and adenovirus-mediated gene transfer. The project focuses on the role of hormone nuclear receptors and factors bound to the apoCIII enhancer on the transcriptional regulation of the apoA-I, apoCIII, and apoA-IV gene cluster.

Elucidation of the structure-function relationship of human apoA-I and apoE and their relevance to cardiovascular disease and Alzheimer's disease, respectively, is the goal. Dr. Zannis is using *in vitro* mutagenesis, transgenic, and gene transfer methodologies. Pertinent questions being considered are the role of apoA-I in the biogenesis and the functions of HDL, the role of apoE in cholesterol and triglyceride homeostasis in the circulation, the role of apoE in lipid homeostasis in the brain, and the pathogenesis of Alzheimer's disease.

The members of Dr. Zannis' team have a wide range of research interests. Kyriakos Kypreos, Ph.D., Instructor of Medicine, is studying the *in vivo* functions of apoE in lipid homeostasis and in atherogenesis, as well as the role of apoCIII in the induction of hypertriglyceridemia. Dr. Kypreos is using *in vitro* studies and adenovirus-mediated gene transfer in mouse models for the latter investigation. The role of the lipid and lipoprotein transport system in obesity, hypertension, and Type 2 diabetes is also under investigation.

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Eleni Zanni, Ph.D., Research Assistant Professor of Medicine, is researching the effect of diet and lipid-lowering drugs on the expression of genes that affect HDL biogenesis and HDL functions in a transgenic mouse model. Irina Gorshkova, Ph.D., Instructor of Medicine, is conducting a physicochemical analysis of the structure and stability of mutants of apoA-I and apoE.

Dr. Duka is studying the *in vitro* and *in vivo* functions of apoA-I using adenovirus-mediated gene transfer. Dr. Duka is also looking at the atheroprotective functions of apoE in mice.

Dr. Zannis' team has made a number of noteworthy achievements, including the generation of transgenic mouse models that reveal how apoA-I is regulated *in vivo*. Investigators are using these mice to switch selectively on apoA-I genes, as well as to increase HDL levels by other mechanisms. In addition, researchers have generated transgenic mice expressing apoE in the brain in order to study the effect of apoE in the pathogenesis of Alzheimer's disease.

In collaboration with Monty Krieger, Ph.D., Whitehead Professor of Molecular Genetics at the Massachusetts Institute of Technology, Dr. Zannis' team has obtained evidence for functional interactions of lipid-bound apoE with the HDL receptor (SR-BI). In addition, the researchers have employed adenovirus-mediated gene transfer of apoE in apoA-I- or ABCA1-deficient mice to establish that both apoA-I and apoE participate in a common pathway that leads to the biogenesis of apoE-containing HDL particles that also requires the functions of the ABCA1 lipid transporter and LCAT.

Studies on the classical HDL pathway by Dr. Zannis' team have shown that apoA-I mutations inhibit discrete steps of the HDL pathway and either lead to rapid catabolism of the intermediate products or lead to their accumulation in plasma. To this point, the

following five discrete categories of mutants have been characterized: (1) mutants that fail to synthesize  $\alpha$ HDL particles but can synthesize pre $\beta$  HDL particles; (2) mutants that cause dyslipidemia; (3) mutants that induce hypertriglyceridemia; (4) mutants that cause LCAT insufficiency and either lead to accumulation of discoidal HDL; and (5) mutants that cause LCAT insufficiency inhibit the formation of discoidal and spherical HDL particles. Mutants in categories four and five can be corrected by treatment with LCAT. The phenotypes produced by targeted mutagenesis of apoA-I will be valuable for the detection of similar phenotypes in humans and can serve as diagnostic and prognostic markers of dyslipidemia and/or atherosclerosis.

In addition, studies with apoE by Dr. Zannis and his colleagues have established that truncated apoE forms correct high levels of cholesterol without causing high triglyceride levels in mice. Using *in vitro* mutagenesis, the researchers have created mutant apoE forms with amino acid substitutions in the 261 to 269 region, which have improved biological functions. They clear cholesterol without induction of hypertriglyceridemia and promote the formation of spherical apoE-containing HDL particles. These truncated and mutant apoE forms may find therapeutic applications in the near future in atherosclerosis and potentially in Alzheimer's disease. A patent application has been submitted.

Dr. Ruiz-Opazo is investigating the molecular genetics of hypertension and novel receptors relevant to hypertension, as well as the genetics of learning and memory. Ongoing research is seeking to identify hypertension susceptibility genes in animal models of this disease, currently focusing on the Dahl S/Dahl R hypertensive rat model and in humans. In addition, the researchers are investigating the identification of susceptibility genes for hypertension target-organ complications like hypertensive renal disease and cardiac hypertrophy. The team is also conducting *in vitro* and *in vivo* functional analysis of novel AngII, AVP, and ET-1



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receptors, including the dual AngII/AVP receptor and the dual ET-1/AngII receptor. Dr. Ruiz-Opazo and colleagues are also looking at genetic determinants of learning and memory in the Dahl S/Dahl R rat model.

In Dr. Herrera's laboratory, the molecular genetics of hypertension and cardiovascular disease are under investigation, as is the molecular basis of endothelial integrity, namely repair/maintenance/dysfunction. The molecular basis of developmental programming of adult-onset disease is also being studied.

Ongoing research in Dr. Herrera's lab includes an investigation of atherosclerosis exacerbation by hypertension, including the dissection of pathways involved in vulnerable plaque development and destabilization through an integrated approach: histopathology, transcriptomics, proteomics, and *in vivo* pathway testing. Researchers are seeking to identify genetic modifiers of hyperlipidemia relevant to gender and genetic background differences through total genome search for putative quantitative trait loci in F2 intercross hybrids and transcription profiling. They are also looking at the identification of key pathways underlying differential susceptibility to coronary lesion development through gene expression profiling.

Dr. Herrera and her colleagues are studying the molecular genetic basis of salt-sensitive hypertension, including the identification of genetic susceptibility pathways underlying salt-sensitive hypertension and its target organ complications through omics-analysis of strategic genetic intercross, congenic, and transgenic rat models. They are also investigating the role of developmental programming of adult-onset disease, including the identification of mechanisms of developmental programming of adult-onset hypertension and its target organ complications. Finally, the team is studying the role of microvascular endothelial function/dysfunction in tissue development, aging, and role in adult-onset disease. Their

work includes identifying the role of endothelium in cardiac and brain development; the role of microvasculature in adult-onset disease; and analysis of novel angiogenesis players in cancer and ischemia.

Dr. Herrera and her colleagues are collaborating on a number of studies, including one that is investigating the role of cardiovascular disease and hypertension susceptibility genes in cognitive impairment. Dr. Ruiz-Opazo is Dr. Herrera's collaborator on this investigation. Dr. Herrera is also working with Dr. Ruiz-Opazo and Dr. Nicola Glorioso, Professor of Internal Medicine at the University of Sassari in Italy, to research susceptibility genes for hypertension and coronary artery disease in humans.

Drs. Herrera and Ruiz-Opazo are working together to investigate the role of the dual ET-1/AngII receptor in the development of the vasculature, neovascularization in coronary artery disease, and neural development and functional impairment. The two, along with Martin Steffen, M.D., Ph.D., Assistant Professor, are studying vascular and microvascular proteomes in cardiovascular and cerebrovascular disease. Drs. Herrera and Ruiz-Opazo are working on three additional studies. The first, pursued in conjunction with John Tonkiss, Ph.D., Associate Professor of Psychiatry, is looking at developmental programming of adult-onset disease and cognitive impairment. A second study, undertaken with James Hamilton, Ph.D., Professor of Physiology and Biophysics, and Jason Viereck, M.D., Ph.D., Instructor of Neurology is investigating MR-microscopy of intracerebral hemorrhage disease course in a stroke-prone transgenic rat model. The third study, done in conjunction with Dr. Wong, is studying endothelial nanomarkers.

#### OBESITY RESEARCH CENTER

The Obesity Research Center comprises faculty members from the Department of Medicine and several basic science departments at BUSM. Barbara E. Corkey,

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Ph.D., Professor of Medicine and Biochemistry, continues to serve as the Director of the Obesity Research Center (ORC) at BUSM and the NIH-funded Boston Obesity Nutrition Research Center (BONRC). Center members include Stephen Farmer, Ph.D., Professor of Biochemistry and Medicine; Paul Pilch, Ph.D., Professor of Biochemistry and Biophysics; and Keith Tornheim, Ph.D., Associate Professor of Biochemistry. James Hamilton, Ph.D., Professor of Biophysics, represents the Department of Biophysics and Physiology. James Kirkland, M.D., M.Sc., Ph.D., Associate Professor of Medicine and Biochemistry, is from the Section of Geriatrics. A total of nineteen publications have resulted from Center activity this year.

Dr. Corkey's laboratory focuses on the metabolic regulation of signal transduction, reactive oxygen and nitrogen species generation, and energy metabolism in fat cells,  $\beta$ -cells, and human fibroblasts. She and her colleagues study fuel-stimulated insulin secretion by the pancreatic  $\beta$ -cell; fuel partitioning in rat and human adipocytes; cytokine signaling; and  $\text{Ca}^{2+}$  transients in human fibroblasts from patients with inborn errors of fatty acid oxidation and Type 1 diabetes. She is Co-Principal Investigator (Orian Shirihai, is the Principal Investigator) in a new NIH R01 grant. In addition, she submitted the 1000 plus competitive application of the Boston Obesity Nutrition Center grant this year, which is currently in its fifteenth year.

Jude Deeney, Ph.D., Assistant Professor of Medicine, is conducting research designed to discern the nutrient-derived metabolic signals leading to glucose- and fatty acid-induced insulin secretion from the pancreatic  $\beta$ -cell. These studies entail the measurement of intracellular calcium, lipids, ATP, and other metabolites, in addition to protein phosphorylation and acylation, which may influence insulin exocytosis.

Wen Guo, Ph.D., Research Assistant Professor of Medicine, is conducting research focusing on three areas: metabolic regulation of adipogenesis and adipocyte function and insulin sensitivity; the regulatory effects of adipose tissue function on atherosclerosis development; and the cross-communication between muscle and adipose tissue.

Dr. Guo uses clonal and primary mouse and human preadipocytes, human bone marrow-derived mesenchymal stem cells, as well as wild-type mice rendered hypoxic by chemical treatment, to study how oxidant stress regulates adipocyte differentiation and adipokine production, and how such modulations influence monocyte to foam cell conversion. As an extension of the latter, Dr. Guo and her colleagues study how modulation of adipose tissue function, either with genetic modification or pharmaceutical manipulation, can affect aorta lesion growth in LDL receptor knockout mice either subjected to Western diet or treated with HIV protease inhibitors. Using a muscle hypertrophic lean mouse (myostatin knockout) model, as well as myostatin antagonists, the team is searching for the myokines that regulate adipose development. Dr. Guo is Principal Investigator for a NIH R01 grant and this year received a pilot grant from BUSM's Department of Medicine for the atherosclerosis project.

In collaboration with Caroline Apovian, M.D., Director of the Center for Nutrition and Weight Management, and Associate Professor of Medicine, Dr. Guo has conducted a successful preliminary study of patients treated with medium-chain fatty acids. Dr. Guo received a third percentile score on her first competitive renewal of her NIH R01 grant this year.

Lina Moitoso de Vargas, Ph.D., Research Assistant Professor of Medicine, is studying pancreatic islet biology and function, particularly the role of calcium influx through voltage-dependent calcium channels in secretagogue-induced insulin secretion.



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Research has been, and continues to be, aided by recent developments in adenoviral gene transfer technology and the ability to express the green fluorescent protein (GFP) of the jellyfish *Aequora victoria* in cells, tissues, and organisms to monitor fluorescence *in situ*.

Distinct GFP variants have been used to allow the visualization of differential gene expression by fusing them to two of the protein subunits of the voltage-dependent calcium channel that mediates the glucose-induced insulin release. New multiple-insert adenoviral vectors have been constructed; these allow the delivery and co-expression of the two differentially fluorescent-tagged channel subunits. Present studies utilize the fluorescent-tagged subunits in heterologous expression systems to conduct a thorough investigation of their functional role, as well as the molecular mechanisms underlying some of the secretagogue-induced insulin secretion pathways.

Gordon Yaney, Ph.D., Assistant Professor of Medicine, is pursuing research that deals with the generation of lipid-signaling molecules arising from the metabolism of glucose and/or complex lipids within the  $\beta$ -cell and their action on various cellular effector systems, including protein kinase C,  $\text{Ca}^{2+}$ -signaling, and exocytosis. He has just completed the second year of his first independent grant from the American Diabetes Association.

Dr. Kirkland is investigating the effects of age and fat deposit sites on adipose function. He has shown that the accumulation of lipid, increases in lipogenic enzyme activities, and changes in differentiation-dependent gene expression are blunted during differentiation of preadipocytes cultured from fat deposits of older individuals, as compared with younger individuals, even after several generations *ex vivo*. Recently, he has found that expression of C/EBP $\alpha$  and PPAR $\gamma$ , key transcription factors in the preadipocyte differentiation program, declines with donor age. Overexpression of C/EBP $\alpha$  and PPAR $\gamma$  by

transient DNA transfection in preadipocytes from older animals restored their capacity to differentiate.

While expression of C/EBP $\alpha$  does not change with age, expression of the dominant negative inhibitor LIP isoform of C/EBP $\alpha$ , which reduces expression of C/EBP $\alpha$  and PPAR $\gamma$ , increases. The goal of current work in Dr. Kirkland's laboratory is to understand the mechanism underlying these changes in transcription factor expression with age. These studies will contribute to understanding of mechanisms of age-related changes in fat tissue function and cell differentiation.

Dr. Tornheim's research deals with regulation of glycolysis and energy metabolism in mammalian systems. His current major project is focused on elucidating the biochemical basis of the oscillatory pattern of insulin secretion that is normally seen *in vivo* and *in vitro* and that is lost or impaired in non-insulin-dependent diabetes. The hypothesis being tested is that oscillations of glycolysis and the ATP/ADP ratio underlie the observed oscillations in intracellular free  $\text{Ca}^{2+}$  and insulin release in pancreatic islets, and that this involves the muscle isoform of the key glycolytic enzyme phosphofructokinase. Recent data have also indicated the possible importance of oscillatory glycolysis for triglyceride synthesis in fat cells. In addition, Dr. Tornheim collaborates with Neil Ruderman, M.D., D. Phil, Director of the Diabetes Research Unit, and Professor of Medicine, Physiology and Biophysics, and his group on studies of vascular metabolism and the effects of diabetes and the regulation of fuel metabolism in various tissues by AMP-activated protein kinase.

## FACULTY

### Professors

Clinton Baldwin, Ph.D.  
Barbara E. Corkey, Ph.D.  
Lindsay Farrer, Ph.D.  
Martin Feelisch, Ph.D.  
Caroline A. Genco, Ph.D.

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**Professors**

Robert Green, M.D., M.P.H.  
Victoria L.M. Herrera, M.D.  
John R. Murphy, Ph.D.  
Nelson Ruiz-Opazo, Ph.D.  
Vassilis I. Zannis, Ph.D.  
Victoria Bolotina, Ph.D.

**Associate Professors**

Margarita Hadzopoulou Cladaras, Ph.D.  
Jianlin Gong, M.D.  
Michael Kirber, Ph.D.  
James Kirkland, M.D., Ph.D.  
Johanna vanderSpek, Ph.D.  
Kenneth Albrecht, Ph.D.

Jude T. Deeney, Ph.D.  
Chee Chew Lim, Ph.D.  
Faina Schwartz, Ph.D.  
Sam Thiagalingam, Ph.D.  
Marsha Wilcox, Ph.D.  
Gordon C. Yaney, Ph.D.

**Research Assistant Professors**

Ajit Bharti, Ph.D.  
Kyriakos E. Kypreos, Ph.D.  
Mark McComb, Ph.D.  
Lina Moitoso de Vargas, Ph.D.  
Caroline Panhuysen, M.D., Ph.D.  
Eleni E. Zanni, Ph.D.

**Instructors**

Lisa Getty, Ph.D.  
Irina N. Gorshkova, Ph.D.  
Ann-Marie Richard, Ph.D.

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# NEPHROLOGY



**SECTION CHIEF**  
*David Salant, M.D.*

## RESEARCH ACTIVITIES

Eleven of the sixteen full-time Section of Nephrology staff based at Boston University Medical Center (BUMC) are extensively involved in research encompassing the fields of autoimmunity; renal immunopathology; cell biology of ischemic and toxic renal injury; renal tubular cell physiology; renal cancer gene regulation and development; polycystic kidney disease; molecular genetics of developmental anomalies of the kidneys and urinary tract; renal amyloidosis; and vascular access patency in hemodialysis patients.

Direct funding from external sources, primarily the National Institutes of Health (NIH) and Veterans Administration, totaled more than \$2 million in 2006-2007 and supported the laboratories of many research faculty members. Six faculty members are Principal Investigators of independent research grants or research training awards from the NIH. Others have career development awards from the American Heart Association, Polycystic Kidney Disease Foundation, and National Kidney Foundation. In addition, VA Boston Healthcare System (VABHS)-based faculty are involved in the VA cooperative studies program, "Multi-center clinical trials of therapy of renal diseases," including the position of study chairmanship of trials, to determine the efficacy of anti-thrombotic agents in maintaining vascular access for d

dialysis and to define the effects of homocysteinemia in patients with kidney failure.

## CLINICAL ACTIVITIES

Renal physicians provide consultative services to Boston Medical Center (BMC) and affiliated programs on a wide range of nephrological problems. They also serve as experts to the eastern New England medical community for complex cases involving autoimmune diseases, renovascular hypertension, amyloidosis, diabetes, kidney stones, and so on.

Over the past fourteen years, the freestanding hemodialysis program has grown from approximately seventy-five patients to the current level of approximately 180 patients. The home peritoneal dialysis program, which is the largest home dialysis program in the Boston area, continues to care for about sixty patients. In collaboration with DaVita, the home dialysis program continues to provide care for many of Boston's underprivileged residents who suffer from kidney failure. Renal staff members visit patients on outpatient hemodialysis weekly and see the home dialysis patients in the clinic every month. They also answer calls from the patients regarding intercurrent problems. Almost all patients from the outpatient program receive their inpatient and other medical care at BMC.

Inpatient visits and procedures, mostly hemodialysis, reflect the high rate of admissions to the care of Section physicians on the end-stage renal disease (ESRD) service. Renal physicians also attend to the medical needs of the inpatient renal transplant patients and operate an active transplant follow-up clinic. A Renal physician devotes 50% effort to the expanding renal transplant program.

Two Renal teams provide consultative and

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acute dialytic services at both the Newton and Menino Pavilions, in particular to the surgical and medical critical care units, but also to pediatrics, high-risk obstetrics, oncology, and other surgical and medical services. Renal physicians oversee the inpatient hemodialysis program operated by DaVita and the Continuous Renal Replacement Therapies (CRRT) in all intensive care units on both campuses.

Two VABHS-based Renal physicians provide consultative inpatient services at the West Roxbury VA, oversee the inpatient and outpatient dialysis unit, and conduct three outpatient clinics per week (renal, hypertension, and transplant) at the Jamaica Plain VA in collaboration with nephrologists from Harvard programs. In addition, VABHS physicians contribute substantial time to general medical activities, including Medical Intensive Care Unit (MICU) and ward attending. Boston University School of Medicine (BUSM) and Harvard Medical School services have been integrated at the West Roxbury VA, and fellows from both schools work as part of a co-operative team.

In addition, the Section provides medical coverage of inpatient hemo- and peritoneal dialysis at the Suffolk County Jail. Two BMC Renal physicians staff a weekly renal clinic at East Boston Neighborhood Health Center.

## EDUCATION

All clinical faculty participate in delivering a total of ten lectures and more than seventy hours of tutorials for BUSM's "Biology of Disease" course. Popular renal clinical electives are offered at VABHS and BMC. In addition, a Renal fellow and attending supervise students on a one-on-one basis. Renal staff members regularly serve as student and junior faculty advisors and sometimes participate as facilitators in the "Integrated Problems" course.

Several investigators have appointments in BUSM's graduate program and serve as thesis

advisors to master's and Ph.D. students; they also interview M.D./Ph.D. candidates. Renal faculty members are actively engaged in tutoring and supervising students in the Graduate Program in Molecular Medicine (GPMM). Herbert Cohen, M.D., Assistant Professor of Medicine, oversees admission to the GPMM and serves as coordinator of the GPMM journal clubs.

The M.D. Nephrology faculty at BUMC contributed eight months of ward attending in the Department of Medicine in 2005-2006, including three months by Steven Borkan, M.D., Firm Chief, and Associate Professor of Medicine, and covered the inpatient dialysis and transplant service. During this time they have very close contact with resident staff. Historically, Renal staff have been sought after to attend on Department of Medicine units because of their clinical and teaching skills. The Nephrology staff members at the VABHS attend for a total of six months in the MICU and on the wards, as well as providing consultative services.

Renal clinical electives are offered at BUMC and VABHS. Residents are given substantial responsibility for working up and following patients on the consult services. They work closely with a Renal fellow and are intensively supervised by an attending. They participate in all clinical conferences and attend all formal teaching sessions, journal clubs, and research seminars.

The Renal fellowship program continues to attract excellent clinical fellows to the four first-year positions distributed between BUMC and VABHS. The Renal fellows are highly regarded by the house staff and provide valuable bedside teaching for medical students, as well as an invaluable service to patients.

An institutional NIH training grant supports the research training program and has been renewed through 2010. All positions were continuously filled through 2006, and 50% of program graduates have academic appointments. Postdoctoral fellows have also

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competed successfully for external support from NIH (National Research Service Award and K08), National Kidney Foundation, American Heart Association, and Polycystic Kidney Disease Foundation.

### MAJOR ACCOMPLISHMENTS

The Institutional Training Grant from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), now in its 34<sup>th</sup> year, was renewed through 2010.

Laurence Beck, M.D., Ph.D., Instructor of Medicine, received a Junior Faculty Development Award from Amgen for his research to define the molecular basis of human membranous nephropathy.

Dr. Borkan received the prestigious Grant V. Rodkey Award from the Massachusetts Medical Society for excellence in teaching.

Dr. Cohen was elected to the American Society of Clinical Investigators (Young Turks).

Laura Dember, M.D., Director of the Dialysis Unit at BMC, and Associate Professor of Medicine, serves on the NIDDK's Dialysis Research Consortium. This consortium will identify and recommend future directions for clinical investigation in chronic dialysis. She also serves as chair of the NIDDK Fistula Study Protocol and Quality Control Committees of the Dialysis Access Consortium. She was appointed as Co-Editor of the *American Journal of Kidney Diseases*.

Andrea Havasi, Research Fellow, received a fellowship grant from the National Kidney Foundation.

Tal Kopel, Research Fellow, received a fellowship grant from the National Kidney Foundation.

Weining Lu, M.D., M.Sc., Assistant Professor of Medicine, received the Pediatric Renal Research award from the National Kidney Foundation of Massachusetts, Rhode Island, New Hampshire and Vermont to study genetic defects in kidney and urinary tract development.

Several Section faculty members serve on editorial boards and as manuscript reviewers for major general and subspecialty journals, and grant reviewers for NIH, Veterans Administration, and foundations. In addition, several members of the faculty presented research seminars, medical grand rounds, and symposium lectures at national meetings, major academic institutions, and postgraduate education courses.

### FACULTY

#### Professors

Edward A. Alexander, M.D.  
Robert J. Hamburger, M.D.  
James S. Kaufman, M.D.  
David J. Salant, M.D.  
John H. Schwartz, M.D.

#### Associate Professors

Steven Craig Borkan, M.D.  
Herbert T. Cohen, M.D.  
Laura M. Dember, M.D.  
Ian R. Rifkin, M.D., Ph.D.

#### Assistant Professors

Vivian E. Abernethy, M.D.  
Weining Lu, Ph.D.

#### Instructors

Omar M. Fituri, M.D.  
Jasvinder Bhatia, M.D.  
Maria Panchenko, Ph.D.  
Zhiyong Wang, M.D., Ph.D.



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# PREVENTIVE MEDICINE AND EPIDEMIOLOGY



**SECTION CHIEF**  
*R. Curtis Ellison, M.D.*

## RESEARCH ACTIVITIES

The Section of Preventive Medicine and Epidemiology is involved in epidemiologic research in the fields of cardiovascular disease, diet, obesity, cancer, and other problems of aging. One of the major research sources is the Framingham Heart Study, organized in 1948 by former Section Chief Thomas R. Dawber, M.D.

R. Curtis Ellison, M.D., M.S., Chief of the Section since 1989, and Professor of Medicine and Public Health, focuses his research primarily on environmental and genetic factors that relate to hypertension and coronary heart disease; the relationship between moderate alcohol consumption and chronic diseases; and the development, early in childhood, of dietary and physical activity habits that relate to obesity and other adult cardiovascular risk factors. Dr. Ellison is a member of the editorial board of *AIM* (Alcohol in Moderation), United Kingdom, which is widely recognized as a key supplier to the public of balanced information on alcohol and health. He is also a member of the Executive Committee and the Advisory Board of the Elizabeth Bishop Wine Resource Center at Boston University.

The Section also directs the Lifetime Health

Study at Framingham, which is evaluating the net lifetime health effects of alcohol use, non-

use, or abuse among the more than 10,000 subjects in the Framingham Study. It also continues to carry out analyses in genetic epidemiology based on data collected in the National Heart, Lung, and Blood Institute (NHLBI) Family Heart Study and the Family Blood Pressure Project.

Since 1994, Section faculty have been members of the Institute on Lifestyle & Health, housed within the Section. Currently, the Institute pursues ongoing surveillance of scientific literature related to various aspects of lifestyle, especially diet, exercise, and the moderate consumption of wine and other alcoholic beverages, habits that relate to the risk of heart disease, cancer, and other chronic diseases. The Institute's critiques of key papers are widely distributed and included in the regular website publications of Alcohol in Moderation (AIM, [www.aim-digest.com](http://www.aim-digest.com)) and Boston University's web-based publications on alcohol abuse, co-edited by Dr. Ellison and Richard Saitz, M.D., M.P.H., Director of the Clinical Addiction Research and Education Unit of the Section of General Internal Medicine at BUMC, and Associate Professor of Medicine.

Section faculty member Lynn L. Moore, D.Sc., Associate Professor of Medicine, researches the development of cardiovascular risk factors during youth and the relationship between obesity and diabetes. During the past year, she continued her work on dietary factors and physical activity during early childhood and their effect on blood pressure and measures of obesity. Dr. Moore also continues to publish on the importance of dairy products in the diet, using data from both the Framingham Children's Study and the National Health and Nutrition Examination Survey (NHANES).

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She recently received funding from the National Institutes of Health (NIH) to evaluate dietary patterns as they relate to obesity and metabolic disease. Dr. Moore is also actively involved in research on environmental toxins and chronic diseases.

Yuqing Zhang, M.D., D.Sc., Professor of Medicine and Public Health, studies the epidemiology of cancer, arthritis, osteoporosis, moderate alcohol consumption, cardiovascular disease, and cognitive function. He has made important contributions to the epidemiology of a variety of bone and joint diseases through collaborative projects with scientists in China. Dr. Zhang continues his Internet-based case-crossover study examining risk factors that trigger attacks of gout, including a report on alcohol consumption and the risk for recurrent gout attacks; he is expanding the approach to address other conditions

Kenneth J. Rothman, Dr.PH., Professor of Public Health and the founding editor of the journal *Epidemiology*, is a senior epidemiologist within the Section and serves as a consultant for studies at many institutions around the world. Dr. Rothman makes major contributions to the scientific literature related to reproductive epidemiology; the epidemiology of the relationship between birth characteristics and adult disease; and environmental epidemiology. He is an active member of the Institute on Lifestyle & Health's faculty, reviewing key new publications on alcohol and health.

Richard H. Myers, Ph.D., Professor of Neurology, carries out research in genetic epidemiology related to Huntington's disease, coronary disease, and hypertension. Jemma B. Wilk, D.Sc., Assistant Professor of Medicine, works on the genetic epidemiology of a variety of types of cardiovascular disease and directs studies of the genetics of pulmonary diseases. Among a number of important research reports from Drs. Myers and Wilk was a report on a gene influencing heart rate on chromosome 5p13-14 in a meta-analysis of genome-wide scans from the

NHLBI Family Blood Pressure Program.

Luc Djoussé, M.D., D.Sc., continues to be a Section faculty member, although his primary appointment is now at Harvard Medical School. Dr. Djoussé researches the epidemiology of cardiovascular disease, moderate alcohol consumption, and other conditions. Dr. Djoussé teaches the Cardiovascular Epidemiology course at Boston University School of Public Health (BUSPH). During the past year, Dr. Djoussé published key papers on mechanisms of cardiovascular disease, heart failure, and genetics of cardiovascular disease, utilizing data from the Framingham Study, the Family Blood Pressure Project, and the Physician's Health Study.

Section members also include Philip A. Wolf, M.D., a neurologist and epidemiologist, and Professor of Neurology and Public Health. As Principal Investigator for the NHLBI contract supporting the Framingham Study and for a number of other key NIH grants, Dr. Wolf continues to make important contributions to the epidemiology of heart disease, stroke, and other chronic conditions. Over the past year, he and other Framingham Study investigators published dozens of papers on many factors related to coronary heart disease and congestive heart failure, as well as on factors related to stroke, carotid disease, and cognitive decline with aging and Alzheimer's disease.

Other senior faculty members associated with the Framingham Study include Emelia Benjamin, M.D., Sc.M., Director of Echocardiography and Vascular Testing for the Framingham Study, a member of the Section of Cardiovascular Medicine and Director of the Ultrasonography Program at Boston Medical Center (BMC), and Professor of Medicine; William B. Kannel, M.D., former Chief of the Section, and Professor of Medicine and Public Health; Daniel Levy, M.D., Director of the Framingham Heart Study, and Professor of Medicine; Joanne Murabito, M.D. Sc.M., a member of the Section of General Internal Medicine at BMC, and Associate Professor of Medicine;

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Christopher O'Donnell, M.D., Assistant Professor of Medicine at Harvard Medical School; and Vasan Ramachandran, M.D., Senior Investigator for the Framingham Heart Study, Co-director of the Echocardiography Laboratory, Co-director of the Framingham Heart Study Fellowship program, and Co-chair of the Framingham Study DNA Committee and Associate Professor of Medicine. [

Section members also include Pantel Vokonas, M.D., Professor of Medicine, who directs the Veterans Administrations Normative Aging Study.

## EDUCATION

While all Section faculty are involved in the teaching of students and house staff, they also work collaboratively with other Boston University faculty, offering expertise and experience in study design and analysis to investigators in their clinical and epidemiological research.

The Section's formal teaching activities over the past year have included primary responsibility for the course in cardiovascular epidemiology (now directed by Dr. Djoussé) and an advanced epidemiological methods course, taught by Dr. Rothman, at BUSPH. Drs. Ellison, Moore, and Zhang are lecturers in several courses through BUSPH. Dr. Moore also teaches the M.D./Ph.D. section of the "Integrated Problems" course at Boston University School of Medicine.

The Section assists in supporting research by General Internal Medicine fellows and Preventive Medicine residents at BMC and collaborates with Dr. Saitz on a number of research and educational projects related to alcohol use and abuse. Most faculty members serve as committee chairs or advisors for master's and doctoral students at BUSPH.

## MAJOR ACCOMPLISHMENTS

Over the past year, a major research accomplishment for the Section has been the

publication of a supplement to the scientific journal *Annals of Epidemiology* titled, "Health Risks and Benefits of Moderate Alcohol Consumption: Proceedings of an International Symposium." This publication, containing twenty-seven articles on moderate drinking, resulted from an international conference sponsored by the Institute in May 2006; the supplement, with Dr. Ellison as Guest Editor, was published in May 2007.

Drs. Kannel and Wolf were recipients of the American Heart Association's 2006 annual awards for important contributions to the science of cardiovascular disease.

## FACULTY

### Professors

Emelia Benjamin, M.D.  
Robert Curtis Ellison, M.D.  
Daniel Levy, M.D.  
Richard Myers, M.D.  
Kenneth Rothman, Ph.D.  
Vasan S. Ramachandran, M.D.  
Pantel Vokonas, M.D.  
Philip Wolf, M.D.

### Associate Professors

Lynn L. Moore, D.Sc.  
Joanne Muribito M.D.  
Munro H. Proctor, M.D., M.P.H.  
Yuqing Zhang, D.Sc.

### Assistant Professor

Jemma Wilk, D.Sc.

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# PULMONARY, ALLERGY, AND CRITICAL CARE MEDICINE



**SECTION CHIEF**  
*David Center, M.D.*

The Section of Pulmonary, Allergy, Critical Care and Sleep Medicine is a multidisciplinary, integrated clinical and scientific division that provides in- and outpatient services to Boston Medical Center (BMC), the VA Boston Healthcare System (VABHS), and affiliated neighborhood health centers. Research faculty are members of the Pulmonary Center at Boston University School of Medicine (BUSM). The Section comprises thirty-seven full-time faculty members and six part-time or adjunct faculty and includes twenty-eight M.D.s, fourteen Ph.D.s, and one M.S.N. Of these, eleven are professors and ten are associate professors.

## RESEARCH ACTIVITIES

The Section's Pulmonary Research Center is divided into seven major groups. Wellington Cardoso, M.D., Ph.D., Professor of Medicine, and Associate Professor of Pathology, heads the research program in developmental biology of the lung. A recently renewed Program Project Grant from the National Institutes of Health's (NIH) National Heart, Lung, and Blood Institute (NHLBI), as well as three R01 awards from the NIH, support the nine M.D. and Ph.D. faculty in this group. Dr. Cardoso is Principal Investigator of the NHLBI grant.

A P01 grant and a new R01, both from NIH, support faculty member Maria Ramirez, Ph.D., Assistant Professor of Medicine, and Assistant Professor of Pathology and Laboratory Medicine. Alan Fine, M.D., Director of the Stem Cell Biology Program, and Associate Professor of Medicine, recently received a new NHLBI-sponsored R21 to study the use of bone marrow-derived stem cells in replacement of damaged airway epithelium. Jining Lu, Ph.D., Assistant Professor of Medicine, recently received a new R01 to study the contribution of microRNAs in lung development.

David Center, M.D., Chief of the Section, Gordon and Ruth Snider Professor of Pulmonary Medicine, and Professor of Medicine and Biochemistry, heads a second research subdivision that studies pulmonary immunology and inflammation. Five R01 awards, three K08 awards, an Asthma and Immunology Center grant from the NIH's National Institute of Allergy and Infectious Diseases (NIAID) support the seven M.D. and Ph.D. faculty members in this group. The Asthma Center grant supports Dr. Center and William Cruikshank, Ph.D., Director of Immunology, and Professor of Medicine, who study the role of interleukin-16 in modulation of asthmatic inflammation, and George O'Connor, M.D., M.S., Professor of Medicine, whose interests are in genetic polymorphisms that predict asthma severity. Drs. Cruikshank and O'Connor are also part of the multi-center URECA study that is seeking to determine the mechanisms of childhood asthma.

K08 faculty research training awards from the NHLBI support Michael Jeong, M.D., Director of the Pulmonary Function Lab at

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BMC, and Assistant Professor of Medicine, and Fred Little, M.D., Assistant Professor of Medicine. Additionally, a Parker B. Francis fellowship supports Dr. Little, who also receives a U01 award from the NIH to study the proteomics of saliva in allergic exacerbations in collaboration with the Boston University Goldman School of Dental Medicine. Funding from the Centers for Disease Control and Prevention (CDC) supports John Bernardo, M.D., Professor of Medicine, and Research Professor of Biochemistry, and Jussi Saukkonen, M.D., Director of the Pulmonary Clinics at the West Roxbury VA Medical Center, and Assistant Professor of Medicine, who are studying the treatment of tuberculosis.

Jeffrey Berman, M.D., Associate Chief of the Medical Service and Chief of Pulmonary and Critical Care for VABHS, Vice Chair for the VA in the Department of Medicine at BUSM, Co-Director of the Pulmonary Fellowship Training Program, and Professor of Medicine, is part of a multicenter trial to study the use of infliximab in pulmonary sarcoidosis.

Ronald Goldstein, M.D., Professor of Medicine, heads the third major research group comprising five faculty members who focus on connective tissue synthesis and repair in the lung. The group is supported by a Reserve Educational Assistance Program (REAP) award from the VA, as well as a clinical trials grant from the NHLBI. The latter grant funds work to study the role of retinoids in emphysema.

Dr. O'Connor heads a research group that studies epidemiology and genetics. This group seeks to determine risk factors for development of COPD; the cardiovascular effects of sleep-disordered breathing; and the factors associated with asthma severity. They are closely aligned with the NHLBI's Framingham Heart Study and the VA Normative Aging Study, in addition to the NHLBI-sponsored study on the effects of retinoids in emphysema. Daniel Gottlieb, M.D., M.P.H., Director of the Sleep Disorders

Center for VABHS, and Assistant Professor of Medicine, serves as Associate Program Director of the General Clinical Research Center. Robert Walter, M.D., M.P.H., Assistant Professor of Medicine, received funding from the Flight Attendant Medical Research Institute to study the epidemiology of smoking-related effects on the airways.

Harrison Farber, M.D., Director of the Pulmonary Hypertension Center at BMC, and Professor of Medicine, heads a fifth group, which studies the pathobiology of the pulmonary vasculature. In addition to their studies on stress responses of the endothelium to low and high oxygen tensions, team members have recognized expertise in treating patients with pulmonary hypertension and acute chest syndrome associated with sickle cell anemia.

Elizabeth Klings, M.D., Assistant Professor of Medicine, receives support from the American Heart Association and the NHLBI in the form of a K23 award.

A sixth group, under the direction of Jerome Brody, M.D., Director of the Pulmonary Center, and Professor of Medicine, focuses on the genetic changes that occur in the airways that predispose an individual to the development of lung cancer and COPD. Working with Avi Spira, M.D., M.Sc., Director of the Bioinformatics and Systems Biology Program, Assistant Professor of Medicine, Pathology and Laboratory Medicine, and Adjunct Professor of Bioinformatics, and Frank Schembri, M.D., Assistant Professor of Medicine, the team has established a bioinformatics program in collaboration with the BU School of Engineering. The team recently published groundbreaking work describing the gene profiles in the airways present in cigarette smokers who develop lung cancer. Dr. Spira's work is supported by a faculty development award from the Doris Duke Society and an NIH R21, as well as an R01 and U01 he recently received.

Hasmeena Kathuria, M.D., Assistant Professor



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of Medicine, focuses on the role of caveolin-1 in lung cancer; a new grant from the American Lung Association funds her work. Dr. Kathuria has developed a clinical referral pathway for lung cancer patients.

Dr. Fine heads the seventh and final group, which studies the contribution of stem cells to the repair of the lung following injury. Dr. Fine's group has substantial interactions with Dr. Cardoso's team, as both look at normal and abnormal repair processes as extensions of the normal developmental process. Darrell Kotton, M.D., Assistant Professor of Medicine, and Andrew Wilson, M.D., Assistant Professor of Medicine, study gene delivery targeted by stem cells. Ross Summer, M.D., Assistant Professor of Medicine, is the recipient of a new K08. He studies hematopoietic stem cells and their trafficking to the lung.

In addition, the Pulmonary Center sponsors a number of clinical trials. Christine Campbell-Reardon, M.D., Associate Director of the Medical Intensive Care Unit and Liaison for the Pulmonary Thoracic Oncology Program at BMC, Associate Director of Fellowship Training in Pulmonary and Critical Care Medicine, and Assistant Professor of Medicine, heads trials of surfactant in acute respiratory disease syndrome (ARDS) and administration of protein C in sepsis. Arthur Theodore, M.D., Director of the Medical Intensive Care Units and Medical Director of Respiratory Therapy at BMC, Director of Medical Education for Pulmonary and Critical Care Medicine, and Associate Professor of Medicine, is Principal Investigator of a multicenter trial of cyclophosphamide in the treatment of systemic sclerosis lung disease.

Helen Hollingsworth, M.D., Clinical Director for the Section, Director of the Pulmonary Function Laboratory at BMC, Director of Allergy and Immunology Fellowship Program, and Associate Professor of Medicine, directs several trials related to the treatment of pulmonary fibrosis. Dr. Berman coordinates a trial of infliximab for sarcoidosis. Dr.

Goldstein; Martin Joyce-Brady, M.D., Associate Professor of Medicine; and Michelle Milic, M.D., Assistant Professor of Medicine, are initiating new trials on mechanical, non-invasive lung reduction in emphysema.

## CLINICAL ACTIVITIES

The Section's clinical programs are extensive and diverse. In spring 2007, Dr. Berman assumed leadership of clinical activities, replacing Dr. Hollingsworth, who is now part-time.

Section faculty provide all the staffing for the Medical Intensive Care Units at BMC and the VABHS, and run active consultation services in each institution. The volume of intensive care patients at BMC alone requires three separate staff and house officer teams. During the past fiscal year, 12,000 inpatient daily visits took place, in addition to 7,000 outpatient visits. One thousand procedures were performed at BMC. Additional clinical activities include staffing the tuberculosis public health clinic. Dr. Bernardo serves as the Tuberculosis Control Officer for the Massachusetts Department of Public Health.

Under Dr. Hollingsworth's direction, outpatient services include subspecialty clinics in asthma and allergy (Drs. Bernardo, Center, Hollingsworth, Jeong, Little and O'Connor) and large referral practices in pulmonary fibrosis (Dr. Goldstein); sarcoidosis (Dr. Berman); scleroderma (Dr. Theodore); amyloidosis (John Berk, M.D., Director of the Bronchoscopy Service at BMC, Director of the Amyloid Airway Clinic, Associate Director of the Pulmonary and Critical Care Medicine Fellowship, Associate Clinical Director of the Amyloid Treatment and Research Program, and Associate Professor of Medicine-pulmonary hypertension and sickle cell anemia chest diseases (Drs. Farber and Klings); COPD (Drs. Goldstein and Theodore); and lung cancer (Drs. Campbell-Reardon and Kathuria). The Section saw its clinical volume rise 10 % this year. Section faculty provide satellite consultation and care at Quincy

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Medical Center, Sturdy Memorial Hospital, East Boston Neighborhood Health Center, South End Community Health Center, South Boston Community Health Center, the Massachusetts Hospital School. They also direct pulmonary rehabilitation at the Radius facilities in Roxbury and Quincy. The Section also provides key administrative support to BMC in a number of venues. Dr. Theodore is director of the Medical Intensive Care Unit and Respiratory Therapy; Dr. Jeong directs the Pulmonary Function Laboratory; and Dr. Milic created a new pulmonary rehabilitation program, of which she is the director, at BMC during the winter.

## EDUCATION

The Section pursues many major educational efforts. Faculty members present a full block to second-year BUSM students in the “Biology of Disease” course and supervise students on clinical and research electives. Eight faculty members participate in the Department of Medicine’s morning report and deliver multiple lectures to house officers.

This year marked the thirty-second year of the Section’s Institutional Training Grant, which provides support for pre- and post-doctoral trainees. Dr. Center is the program’s Principal Investigator. He succeeded Dr. Brody, who piloted the training program during its first twenty-five years. To date, the program has trained more than sixty doctoral students and 130 post-doctoral fellows in multiple disciplines related to the lung. Program graduates include nine Academic Chiefs of Pulmonary Medicine, two Chairs of Medicine, and national and international leaders in virtually every field of pulmonary science, as well as a number of Ph.D. graduates who are now leaders in academia and industry.

In 2003, the Section’s pulmonary fellows established the L. Jack Faling annual teaching award in honor of Jack Faling, M.D., former Director of the Medical Intensive Care Unit at VABHS, and Professor of Medicine. The award is given each year to a Section faculty

member, selected by the pulmonary fellows, who best exemplifies Dr. Faling’s devotion to teaching and clinical practice. Dr. Kotton received this year’s award.

The Section’s flagship educational endeavor is its post-doctoral training program in pulmonary, allergy and critical care medicine. The program has trained more than 150 M.D. clinicians and scientists during the past thirty years. In addition, the Section’s research laboratories are a magnet for visiting scientists and Ph.D. post-doctoral fellows seeking training in disciplines associated with lung diseases. During the past fifteen years, Section faculty have hosted fourteen visiting scientists from Japan, France, Italy, China, Israel, and South America, as well as other institutions in the United States.

Dr. Campbell-Reardon directs the clinical training program, having assumed the role from Dr. Berman, who served in that capacity for the past twenty years. Dr. Center heads the allergy training program and the pulmonary research component of the newly accredited Sleep Medicine Program, which is under Dr. Gottlieb’s direction.

## MAJOR ACCOMPLISHMENTS

On September 11, 2006, the Section hosted the fifth annual Sue Kim Hanson Memorial Lecture. A beloved immunology student enrolled in the Section’s training program, Sue had worked and studied in the Pulmonary Center with her mentor, Hardy Kornfeld, M.D., for more than ten years before her untimely death with her husband and daughter in the World Trade Center tragedy of September 11, 2001. The lectureship is now generously endowed by BU campus members and a number of local philanthropies.

The 2006 was delivered by John Yewdell, M.D., Ph.D., Senior Investigator with the NIAID’s Division of Intramural Research. Prior lectures were delivered by Nobel Laureate Peter Doherty, Ph.D.; Arthur Weiss, M.D.; William Paul, M.D., a former Boston

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University house officer and now Director of NIAID's Laboratory for Immunology; and Brian Seed, Ph.D. Professor of Genetics at Harvard Medical School. The lectureship is held each year on or around September 11.

Section faculty published more than 100 peer-reviewed original papers, invited reviews, editorials, and book chapters this year. Faculty members were invited as visiting professors at fourteen institutions in Asia, Europe, South America, and the United States, and delivered more than fifty invited grand rounds presentations, research presentations, and lectureships. In addition, Section faculty served as officers, chairs, or members for key committees of the NHLBI, American Thoracic Society, American Heart Association, and Massachusetts Thoracic Society. They also participated as peer reviewers or editorial staff members for more than twenty international journals.

After seventeen years as a faculty member, Mary C. Williams, Ph.D., former Pulmonary Center Associate Director, and Professor of Medicine, retired to assume a part-time adjunct position.

The Section recruited Drs. Milic, Schembri, and Wilson as Assistant Professors of Medicine. All three are former B.U. fellows whose research interests focus on rehabilitation medicine, airway genomics, and gene therapy, respectively.

Dr. Center was listed in *America's Best Doctors*.

Dr. Cardoso was promoted to Professor of Medicine.

Dr. Hollingsworth was listed in *America's Best Doctors*, as well as in Boston Consumer's Checkbook.

Dr. Joyce-Brady was named vice president of the medical staff at Radius Specialty Hospital and Chair of the Massachusetts Thoracic Society's Research Grant Committee.

Dr. Saukkonen is President of the Massachusetts Thoracic Society and was elected to the Core Sciences Group, TB Trials Consortium

Kevin Wilson, M.D., Assistant Professor of Medicine, received first place in the Respiratory Disease Young Investigator's Forum and recently became a section editor for *UpToDate*, an evidence-based clinical information resource for clinicians.

## FACULTY

### Professors

Jerome S. Brody, M.D.  
Jeffrey S. Berman, M.D.  
John Bernardo, M.D.  
David M. Center, M.D.  
William Cruikshank, Ph.D.  
L. Jack Faling, M.D.  
Harrison W. Farber, M.D.  
Ronald H. Goldstein, M.D.  
Joel B. Karlinsky, M.D.  
George T. O'Connor, M.D., M.S.  
Mary C. Williams, Ph.D.

### Professor, Emeritus

Gordon L. Snider, M.D.

### Adjunct Professors

Hardy Kornfeld, M.D.  
Robert J. North, Ph.D.

### Associate Professors

John L. Berk, M.D.  
Wellington Cardoso, M.D., Ph.D.  
Alan Fine, M.D.  
Daniel J. Gottlieb, M.D., M.P.H.  
Helen M. Hollingsworth, M.D.  
Martin Joyce-Brady, M.D.  
David Sparrow, D.Sc.  
Arthur C. Theodore, M.D.

### Assistant Professors

Christine Campbell-Reardon, M.D.  
Michael H. Jeong, M.D.  
Jyhchang Jean, Ph.D.  
Hasmeena Kathuria, M.D.  
Elizabeth S. Klings, M.D.  
Darrell Kotton, M.D.  
Frederic F. Little, M.D.  
Jining Lu, Ph.D.  
Anna Pavlova, Ph.D.  
Maria Isabel Ramirez, Ph.D.  
David C. Rishikof, M.D.  
Jussi J. Saukkonen, M.D.

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**Assistant Professors**

Avrum Spira, M.D., M.Sc.

Ross Summer, M.D.

Robert Walter, M.D.

Kevin Wilson, M.D.

YuJun Zhang, Ph.D.

**Adjunct Assistant Professors**

Joseph Macon Keane, M.D.

Anthony O'Regan, M.D.

**Clinical Assistant Professor**

Robert G. Nahill, M.D.

**Research Assistant Professors**

YuXia Cao, M.D.

Konstantin Izvolsky, Ph.D.

Ping Ping Kuang, M.D.

Xinfang Li, Ph.D.

Lin Wei, Ph.D.

**Instructor**

Claire Murphy, N.P.

**Clinical Associate**

Eleana M. Conway, N.P.

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# RHEUMATOLOGY



**SECTION CHIEF, AD INTERIM**  
*Robert Simms, M.D.*

## RESEARCH ACTIVITIES

Building on its strengths in patient care, teaching, and research, the Section of Rheumatology had a strong year on all fronts.

Under the direction of Robert Lafyatis, M.D., Laboratory Director, and Associate Professor of Medicine, the Scleroderma Laboratory Research Program staff includes Raphael Lemaire, Ph.D., Assistant Professor of Medicine; Michael York, M.D., Assistant Professor of Medicine, and a fourth-year Rheumatology fellow; and visiting scholars Julie Bayle, Alessandra Farina, M.D., Research Fellow; and Timothy Radstake, M.D., Research Fellow.

The Scleroderma group focuses on understanding fibroblast biology, the molecular and cellular basis of fibrosis and endothelial cell interactions. The traditional base of the group's research is in fibrosis and matrix biology and is increasingly led by Dr. Lemaire, who works with Dr. Lafyatis to understand the pathogenesis of fibrosis in the tight skin (Tsk) mouse. Over the past year, Drs. Lemaire and Lafyatis made several key observations, including the identification of developmental gene regulators and the factors that stimulate elastogenesis.

Drs. York and Radstake, a research scientist who recently joined the group from the Netherlands, spearhead the second axis of scleroderma research. They are working closely with Ann Marshak-Rothstein, Ph.D., Professor of Microbiology, and Ian Rifkin, M.D., Ph.D., Assistant Professor of

Medicine, and a member of the Section of Nephrology, to further explore innate immunity in scleroderma. Dr. York has shown the effects of  $\alpha$ -satellite DNA and TLR agonists on IFN-regulated genes in leukocytes. These studies promise to clarify whether autoantibodies targeting centromere proteins act as immune adjuvants in scleroderma patients. This work is part of a broader effort to understand the effects of autoantibody immune complexes in scleroderma. It is anticipated that Dr. Radstake's experience in innate immunity in rheumatoid arthritis will accelerate the Section's advances, particularly regarding the importance of monocytes and dendritic cells.

In addition, the Scleroderma group has begun to advance a small group of investigations into vascular disease in scleroderma. In collaboration with Harrison Farber M.D., Director of the Pulmonary Hypertension Center at Boston Medical Center (BMC), Professor of Medicine, and a member of the Section of Pulmonary, Allergy, Critical Care and Sleep Medicine, the Section's Scleroderma researchers have analyzed sera and leukocyte mRNA for biomarkers of pulmonary hypertension in scleroderma patients. Investigators are also collaborating with Dr. Marshak-Rothstein to develop an autoimmune model of pulmonary hypertension; Dr. Farina is working on this project.

Over the past year, the Scleroderma group had several publications, and was awarded a U01 grant, with Dr. Lafyatis as the Principal Investigator. Ongoing support for the group comes from Dr. Lafyatis' R01 grant, grants for biomarker studies from Actelion and Biogen Idec, and grants from the Scleroderma Foundation and the American College of Rheumatology that support Dr. York. Finally, the Scleroderma's laboratory group, under Dr. Lafyatis' direction, submitted a well-scored and possibly fundable CORT grant application, with project components and core labs encompassing all the areas of research described above. If the application isn't funded following the initial submission, it may be resubmitted at a later time.



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In addition to working Dr. Farber, the Section has continued important collaborative efforts with Arthur Theodore, M.D., also a member of the Pulmonary Section, and Director of the Medical Intensive Care Units and Medical Director of Respiratory Therapy at BMC, Director of Medical Education for Pulmonary and Critical Care Medicine, and Associate Professor of Medicine. Drs. Farber and Theodore, as well as Rheumatology investigators, have overlapping clinical and research interests in pulmonary hypertension and interstitial lung disease.

In the area of vasculitis care and research, Peter A. Merkel, M.D., M.P.H., Director of the Boston University Vasculitis Center, Director of Clinical Trials for the Section of Rheumatology, Associate Program Director for the Boston University General Clinical Research Center, and Associate Professor of Medicine, is Principal Investigator of the Vasculitis Clinical Research Consortium, an international research collaboration. Dr. Merkel also leads international outcome studies in vasculitis, is a key investigator in various clinical trials in vasculitis and scleroderma, is conducting genetic and translational biologic studies of vasculitis, and is Principal Investigator of an upcoming international conference on research methodology in rare diseases. Dr. Merkel's work is supported by several grants from various institutes at the National Institute of Health (National Institutes of Arthritis and Musculoskeletal and Skin Diseases; National Center for Research Resources; and National Institute of Allergy and Infectious Diseases). The Boston University Vasculitis Center is the largest program for clinical care and research for vasculitis in the northeastern United States and is an internationally recognized leader in vasculitis research. Eugene Kissin, M.D., Assistant Professor of Medicine; Tuhina Neogi, M.D., Assistant Professor of Medicine; and Robert Simms, M.D, Section Chief *ad interim*, and Professor of Medicine, also participate in the work of the Vasculitis Center and the Arthritis Center.

Clinical research programs in scleroderma continue to be a critical focus for the Section. Dr. Simms is the Arthritis Center Principal Investigator for an NIH-funded, multicenter, randomized trial of stem cell transplantation versus intravenous cyclophosphamide in the treatment of rapidly progressive scleroderma. This trial is now actively enrolling patients. Dr. Lafyatis is an investigator on an ancillary laboratory project that is part of this funded trial. Additional trials being conducted by the Scleroderma Program include the use of an innovative topical therapy for Raynaud's phenomenon, mycophenylate mofetil (an anti-rejection therapy for transplantation) for diffuse scleroderma, as well as several therapeutic trials of vasodilators for pulmonary hypertension, a common complication of scleroderma.

#### CLINICAL ACTIVITIES

The Section's clinical programs continue to benefit from the faculty's outstanding capabilities and the excellent reputation they foster in a wide variety of rheumatic diseases. Specialized areas of interest include vasculitis and scleroderma, which have a national and international referral base. Patients with both vasculitis and scleroderma continue to provide a sizeable number of referrals from outside BMC's network. These patients generate substantial clinical workload and income for other specialties, as well as procedures and laboratory studies for many departments within the hospital.

The Section's clinical activity continues at a high level, and, overall, is almost 7% higher than last year. This figure includes both inpatient and outpatient volume.

#### EDUCATION

The Section continues to direct the musculoskeletal section of the "Biology of Disease" (BOD) course for Boston University School of Medicine students. Directed by Dr. Kissin, this BOD component, which provides one of students' only patient interview

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sessions during the second year, receives excellent reviews. In addition, the Section continues to attract outstanding fellow candidates and had a successful match this year.

Section faculty members contribute substantially to morning report, firm conferences, and resident lectures, both here and at affiliated Veterans Administration locations.

### MAJOR ACCOMPLISHMENTS

Section faculty members have given a large number of invited lectures, including both medical and rheumatology grand rounds, at institutions throughout the country

### FACULTY

#### Professors

David Beller, Ph.D.  
Alan S. Cohen, M.D.  
David T. Felson, M.D., M.P.H.  
Robert W. Simms, M.D.  
Martha M. Skinner, M.D.

#### Professor Emeritus

Alan S. Cohen, M.D.

#### Associate Professors

Robert A. Lafyatis, M.D.  
Caryn Ann Libbey, M.D.  
Peter Merkel, M.D., M.P.H.

#### Research Associate Professor

Saralynn J. Allaire, D.Sc.

#### Assistant Professors

Tuhina Neogi, M.D.  
S. Sohail Ahmed, M.D.  
David Hunter, M.D., Ph.D.  
Eugene Kissin, M.D.  
Raphael Lemaire, Ph.D.  
Kieval Raphael, M.D.  
Russell Widom, Ph.D.

#### Clinical Professor

Burton Sack, M.D.

#### Instructor

Ari J. Schwartz, M.D.

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# VASCULITIS CENTER



## DIRECTOR

*Peter Merkel, M.D., M.P.H.*

## RESEARCH ACTIVITIES

The Boston University Vasculitis Center is the largest clinical and research program in the northeastern United States dedicated to the study of the inflammatory vasculitides. Under the direction of Peter A. Merkel, M.D., M.P.H., Associate Professor of Medicine, the Vasculitis Center continues to grow and expand its research activity, focusing on clinical investigation, including clinical epidemiology, clinical trial design and conduct, and outcome measure development. The Center is also engaged in translational investigation that links the Center's work to vascular biologists and geneticists within the Department of Medicine. In addition to Dr. Merkel, Eugene Kissin, M.D., Assistant Professor of Medicine; Raphael Lemaire, Ph.D., Assistant Professor of Medicine; Tuhina Neogi, MD, Assistant Professor of Medicine; and Robert Simms, M.D., Professor of Medicine are faculty members participating in these research projects.

The most extensive research program within the Vasculitis Center is the Vasculitis Clinical Research Consortium (VCRC). A five-year, \$6.25 million grant from the National Institutes of Health's Rare Disease Clinical Research Network is funding the VCRC. (This grant amount reflects the total cost, and VCRC researchers anticipate it will be renewable for another five years.) A multicenter, international program, the VCRC has developed the infrastructure for comprehensive longitudinal clinical

investigation and clinical trials in several types of vasculitis. The VCRC's goals are to conduct parallel longitudinal cohort studies for the purpose of biomarker discovery; develop a clinical and biological sample repository; pilot clinical trials of promising therapeutic agents for vasculitis; train fellows in clinical investigation in vasculitis; and interact with patient support groups for these diseases.

Dr. Merkel is the international Principal Investigator and Director of the VCRC, and Boston University is the lead center. Other primary centers include the Cleveland Clinic Foundation, Johns Hopkins School of Medicine, and the Mayo Clinic Foundation; these four centers are the leading vasculitis clinical research centers in the United States. Several secondary centers in the United States, Canada, and Europe are also participating in VCRC activities. The VCRC is currently in its fourth year, and research is progressing well. The VCRC now has Longitudinal studies enrolling in 6 type of vasculitis at the 4 Primary VCRC Centers and is starting a therapeutic clinical trial in Wegener's granulomatosis. In addition to the work outlined in the original grant, investigators have been able to leverage this initiative to obtain additional National Institutes of Health (NIH) funding with an R01 grant to study imaging in Takayasu's arteritis for which Dr. Merkel is the Principal Investigator. VCRC investigators have also applied for additional R01 and FDA grants for clinical trials; Dr. Merkel is the Co-principal Investigator on these grants. The VCRC Specimen Repository is located within the Vasculitis Center.

The Vasculitis Center has participated in every major, multicenter clinical trial in vasculitis performed in the United States in the last several years. Additionally, Dr. Merkel is one of the core investigators in the collaborative network that designs and conducts these trials. Among the recently completed trials are: The Wegener's Granulomatosis Etanercept Trial (WGET), the first randomized, double-blind,

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placebo-controlled trial performed in this disease, and the results were published in the *New England Journal of Medicine*. Boston University Medical Center was the fourth leading recruitment site for the WGET. More than a dozen ancillary projects and manuscripts utilizing data and specimens from the WGET either have been published with several more in preparation; Dr. Merkel is the Principal Investigator and lead/senior author on several of these projects. The WGET was funded through grants from the NIH and the Food and Drug Administration. Additionally, the Vasculitis Center was also a participating site for a study of Infliximab for the treatment of giant cell arteritis, the results of which were published this past year in *Annals of Internal Medicine*. This trial was supported by a grant from Centocor Corporation.

The Vasculitis Center is one of eight international centers participating in the Rituximab for ANCA-Associated Vasculitis (RAVE) Study. This NIH-supported clinical trial has garnered significant international interest. In addition to investigating Rituximab's clinical utility, the project has built into it multiple mechanistic studies of great value to vascular biology and immunology. Boston University is the second leading site in terms of enrollment in RAVE. The Vasculitis Center is also a lead site in a proposed trial to study new treatments for Takayasu's arteritis, giant cell arteritis, and is leading in the developmental program for a potential clinical trial for Churg-Strauss Syndrome.

The Vasculitis Center has multiple studies that take advantage of Boston University School of Medicine's expertise regarding clinical epidemiology, including cohort analyses and outcome measure development. A close association between the Section of Rheumatology and the Clinical Epidemiology Unit exists, with several faculty members having appointments in both Sections.

The Vasculitis Center is involved in a variety of studies aimed at developing and improving outcome measures for the study of systemic

vasculitis. Faculty and research fellows in the Vasculitis Center are leading national and international efforts in the revision and expansion of activity measures for vasculitis and are partnering in other studies regarding damage assessment.

Researchers from the Vasculitis Center are partnering with basic investigators at Boston University Medical Center (BUMC) to conduct a series of novel translational research projects. The Vasculitis Center is collaborating with the laboratories of Jane Freedman, M.D., Associate Professor of Medicine, and a member of the Whitaker Cardiovascular Institute, and Joseph Loscalzo, M.D., Ph.D. (Brigham and Women's Hospital), to investigate the interplay between thrombosis and inflammation. This work is supported by a P60 NIH grant from NIAMS. Great potential exists in combining the clinical research strength of the Vasculitis Center with the extensive basic science investigation in vascular biology being conducted at BUMC. Investigators in the Vasculitis Center are also engaged in research into the genetics of vasculitis with several ongoing projects well underway utilizing both site-specific and national data repositories.

Research collaboration is vital to the study of vasculitis, a multi-system disorder. Currently, research within the Boston University Vasculitis Center is performed in conjunction with members of the Cardiology, Pulmonary, and Genetics Sections of the Department of Medicine as well as the Departments of Radiology and Otolaryngology.

### CLINICAL ACTIVITIES

Boston University Vasculitis Center is the largest clinical vasculitis program in the Northeast, and it continues to grow at a steady pace. Clinical volume and new referrals are steadily increasing. The Center receives national and international referrals. Although based in the Section of Rheumatology, the Vasculitis Center has a dedicated team of specialists within the Department of Medicine;

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multiple other BUMC departments have specific faculty members with expertise in vasculitis participating in the Center's clinical activity.

The ability to provide expert consultation in the multiple disciplines necessary for the care of patients with vasculitis increases the referral rate, improves the patients' satisfaction, and contributes to improved quality of care. In particular, clinical associates of the Vasculitis Center are in Cardiology, Gastroenterology, Nephrology, Pulmonology, Vascular Medicine, Dermatology, Cardiovascular Surgery, Otolaryngology, Neurology, Pathology, Radiology, and Vascular Surgery.

The Vasculitis Center's increasing clinical volume is important both for the patient care needs it meets, as well as for the facilitation of recruitment into clinical trials and the development of sources of clinical and biological specimens for the Center's research studies it provides.

## EDUCATION

The Vasculitis Center and its faculty actively participate in Boston University School of Medicine education. Medical students, medical residents, and rheumatology fellows all rotate through the Vasculitis Clinic, and the faculty provides lectures to each type of trainee.

The Vasculitis Center is also strongly involved in community outreach and has developed alliances with vasculitis patient support groups. Through the VCRC, the Vasculitis Center is a major partner with the five major national patient groups for vasculitis: the Vasculitis Foundation, the Polyarteritis Nodosa (PAN) Support Network, the Takayasu's Arteritis Research Association, the Churg-Strauss Syndrome Association, and the National Medical Research Foundation (GCA/PMR). Dr. Merkel serves in an advisory capacity to each of these organizations, and it was partially through the Vasculitis Center's initiatives that the Churg-Strauss Syndrome Association was recently formed. These groups provide an

important source of information for patients with rare diseases.

The faculty and staff of the Boston University Vasculitis Center are the lead group organizing and implementing a new and exciting educational initiative to be launched in the upcoming academic year: a meeting in Bethesda focused on research methodology in rare diseases. The target audience for this meeting includes trainees (fellows) and junior faculty engaged in clinical investigation of rare diseases. Boston University has received a grant from the NIH (NCRR) to support this program as well as funds from a variety of patient support groups.

## FACULTY

### Professor

Robert W. Simms, M.D.

### Associate Professors

Michael LaValley, Ph.D.

Peter A. Merkel, M.D., M.P.H.

Eugene Y. Kissin, M.D.

### Assistant Professors

Raphael Lemaire, PhD.

Tuhina Neogi, M.D.

### Research Associate

Alfred P. Mahr, MD, MPH



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## DEPARTMENT CENTERS

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# ARTHRITIS CENTER



**DIRECTOR, AD INTERIM**  
*Robert Simms, M.D.*

The staff of the Arthritis Center includes seven full-time M.D. faculty, four full-time Ph.D. faculty, four part-time clinical faculty, and five clinical trial coordinators. In addition, during the past year, five rheumatology fellows studied at the Center.

Center faculty members continue to achieve widespread national recognition for both their research programs and their clinical expertise, and they play leading roles in studies of scleroderma, osteoarthritis, and vasculitis. They serve on advisory boards for the National Institutes of Health, the Arthritis Foundation, the Scleroderma Foundation, as well as for biotechnology and pharmaceutical companies. In addition to their clinical, research, and advisory roles, Center faculty pursue educational initiatives and successfully hosted the biennial International Scleroderma Workshop, a weeklong conference for more than 200 basic and clinical scleroderma investigators from around the world.

The Arthritis Center remains a key player in research, clinical activity, clinical investigation, and education programs both nationally and internationally. Growth on all fronts is expected to continue.

## RESEARCH ACTIVITIES

The Center's laboratory research efforts focus on basic biologic mechanisms in the pathogenesis of scleroderma, amyloidosis,

arthritis, and systemic lupus erythematosus. Center faculty members pursue a concordant research effort in the clinical investigation of these disorders, including the testing of novel therapies. Faculty within the Center's Clinical Epidemiology Section carry out groundbreaking research efforts to understand osteoarthritis, the most common type of arthritis.

The Scleroderma Laboratory Research Program is under the direction of Robert Lafyatis, M.D., Associate Professor of Medicine. Dr. Lafyatis' team includes Raphael Lemaire, Ph.D., Assistant Professor of Medicine; Michael York, M.D., a fourth-year Rheumatology fellow, and Assistant Professor of Medicine; and visiting scholars, Drs. Julie Bayle, Alessandra Farina, and Timothy Radstake. This lab focuses on understanding fibroblast biology, the molecular and cellular basis of fibrosis, and endothelial cell interactions.

Fibrosis and matrix biology comprise the lab's traditional research base, and Dr. Lemaire has taken on an ever-greater role in overseeing this research. He continues to work with Dr. Lafyatis to understand the pathogenesis of fibrosis in the tight skin (Tsk) mouse. Several key observations have been made over the past year, including the identification of developmental gene regulators and the factors that stimulate elastogenesis.

Drs. York and Radstake are spearheading the laboratory's second axis of scleroderma research. They are working closely with Ann Marshak-Rothstein, Ph.D., Professor of Microbiology, and Ian Rifkin, M.D., Ph.D., Associate Professor of Medicine, to further explore innate immunity in scleroderma. Dr. York has demonstrated the effects of  $\alpha$ -satellite DNA and TLR agonists on IFN-regulated genes in leukocytes. These studies promise to clarify whether autoantibodies targeting centromere proteins act as immune adjuvants in scleroderma patients. Dr. York's work is part of a broader effort to understand the effects of autoantibody immune complexes in scleroderma.

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It is anticipated that Dr. Radstake's experience in innate immunity in rheumatoid arthritis will accelerate the team's advances, particularly regarding the importance of monocytes and dendritic cells. In addition, the lab has begun to advance a small group of investigations into vascular disease in scleroderma. Arthritis Center researchers, in collaboration with Harrison Farber, M.D., Director of the Pulmonary Hypertension Center at Boston Medical Center, and Professor of Medicine, have analyzed sera and leukocyte mRNA for biomarkers of pulmonary hypertension in scleroderma patients. Finally, collaborative efforts with Dr. Marshak-Rothstein seek to develop an autoimmune model of pulmonary hypertension; Dr. Farina is working on this project as well.

The Scleroderma Laboratory Research Program has achieved a number of successes over the past year, including the generation of several publications; a successful application for a U01 grant, with Dr. Lafyatis serving as the Principal Investigator; ongoing support through Dr. Lafyatis' R01 grant; grants for biomarker studies from Actelion and BiogenIdec; and support for Dr. York through grants from the Scleroderma Foundation and the American College of Rheumatology. Finally, Dr. Lafyatis' laboratory submitted a well-scored (possibly fundable) CORT (on a Program Project scale) grant application this year, with project components and core labs encompassing all the areas of research described above. The application's score (171) suggest possible funding and, if not, motivates a resubmission this winter.

Internationally recognized for its excellence in amyloidosis research and patient care, the Amyloid Treatment and Research Program is under the direction of Martha Skinner, M.D., Professor of Medicine. Using a multidisciplinary approach with investigators in molecular biology, mass spectrometry, immunology, biochemistry, cell biology and pathology, the program focuses on basic and translational research for the systemic forms of amyloidosis. A Program Project Grant from the National Institute of Health's National Heart, Lung, and Blood Institute, as well as grants from private foundations, support this work

During the past year, the Amyloid Program completed a five-year Program Project Grant. Major basic research progress was made toward achieving the following goals: to define the molecular variations in light chains that predispose them to amyloid fibril formation; to define the tissue response to abnormal light chains that permits fibril formation; and, ultimately, to find more effective treatments for AL amyloidosis.

The clinical Amyloid Program has continued competent and efficient patient care and encouraged clinical research studies related to clinical observations. A major international clinical trial for AA amyloidosis using a new drug, Kiacta, was reported in the *New England Journal of Medicine* in June 2007 by Laura Dember, M.D., Director of the Dialysis Unit at Boston Medical Center, and Associate Professor of Medicine, who serves as the Amyloid Program's nephrologist. An international trial for the treatment of familial transthyretin-type amyloidosis, with John Berk, M.D., Director of the Amyloid Airway Clinic, Associate Clinical Director of the Amyloid Treatment and Research Program, Director of the Bronchoscopy Service at Boston Medical Center, Associate Director of the Pulmonary and Critical Care Medicine Fellowship at Boston University School of Medicine, and Associate Professor of Medicine, serving as the Principal Investigator, was launched over the past year and is progressing well.

A key component of the Arthritis Center is the Clinical Epidemiology Research and Training Unit (CERT Unit), a section within the Department of Medicine. Many Unit faculty have secondary appointments in Rheumatology and engage primarily in arthritis-related clinical research, enhancing the Arthritis Center's overall function.

The CERT Unit is under the direction of David Felson, M.D., M.P.H., Chief of the Multidisciplinary Clinical Research Center Grant, and Professor of Medicine and Public Health. The Center Grant, awarded by the

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National Institutes of Health (NIH), encompasses multiple clinical research projects within the Arthritis Center and was renewed within the past year. Other Unit faculty include Saralynn Allaire, Sc.D., M.S.N., Associate Director of the CERT Unit, Research Professor of Medicine, and a leading investigator in work disability in arthritis; Kristin Baker, Ph.D., Instructor of Medicine, an exercise physiologist who has successfully completed exercise trials and trials of biomechanical interventions in arthritis; David Hunter, M.D., Ph.D., Assistant Professor of Medicine, an osteoarthritis trialist and biomechanics specialist; Michael LaValley, Ph.D., Associate Professor of Epidemiology and Biostatistics, a biostatistician whose focus has been on clinical trials methodology and meta-analysis in rheumatology; Tuhina Neogi, M.D., Assistant Professor of Medicine, a rheumatologist; and Yuqing Zhang, Ph.D., Professor of Medicine, a leading quantitative epidemiologist in arthritis who has an interest in Internet-based studies.

Dr. Felson focuses on osteoarthritis epidemiology, including identifying persons at high risk of developing the disease in whom disease can be prevented. He is the Principal Investigator of a sub-study of the Framingham Heart Study, the Framingham Osteoarthritis Study, and is also a Principal Investigator of one large, multicenter observational study of persons at high risk of osteoarthritis, the Multicenter Osteoarthritis Study (MOST).

CERT Unit investigators have been responsible for standardizing outcome measurement in rheumatoid arthritis clinical trials, a process that is ongoing. In addition to the P60 NIH Center Grant, the CERT Unit is funded through five R01 grants, an R03, a K30, and multiple Arthritis Foundation grants. Unit faculty members have a number of recent scientific accomplishments to their credit, including Drs. Felson and Baker's demonstration in a large, randomized trial that wedged shoe inserts, commonly used to treat knee osteoarthritis and thought to work by realigning a knee that is out of proper

alignment, do not work to lessen knee pain.

Dr. Neogi has discovered that deficiency of vitamin K, which is present in many vegetables, may increase the risk of osteoarthritis. Vitamin K is a needed cofactor for some enzymes in cartilage and deficient intake is common. In addition, Dr. Felson, working with Steven Vlad, M.D., Rheumatology Fellow, and Bin Zhang, D.Sc., Research Assistant Professor of Medicine, have done a reanalysis of glucosamine trials and found that glucosamine, widely used to treat osteoarthritis, is not effective. The results of large-scale, publicly funded trials were all negative, whereas the only positive results emanated from a trial conducted by one company and may represent biased publication.

Until now, epidemiologic studies have focused on the causes of new onset disease, but many chronic diseases disable people by causing acute episodes of pain and suffering. Dr. Y. Zhang has refined an existing methodology, the case-crossover study, and developed a method to perform these studies over the Internet, thereby facilitating their dissemination.

The Section of Rheumatology's clinical trial effort continues to grow and active clinical trials in scleroderma and vasculitis are currently ongoing. Robert Simms, M.D., Chief, *ad interim*, of the Section of Rheumatology, and Professor of Medicine, is the regional Principal Investigator for a pivotal, national, multicenter trial of autologous stem cell transplantation versus intravenous cyclophosphamide for poor prognosis diffuse scleroderma. This trial is proceeding to actively enroll patients both regionally and nationally.

Additional trials being conducted by Scleroderma Program faculty include those involving an innovative topical therapy for Raynaud's phenomenon, mycophenylate mofetil (an anti-rejection therapy for transplantation) for diffuse scleroderma, as well as several therapeutic trials of vasodilators

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for pulmonary hypertension, a common complication of scleroderma.

In the area of vasculitis care and research, Peter Merkel, M.D., M.P.H., Director of the Boston University Vasculitis Center, Associate Director of Clinical Trials for the Section of Rheumatology, and Associate Professor of Medicine, is the Principal Investigator of the Vasculitis Clinical Research Consortium, an international research collaboration. Dr. Merkel also leads international outcome studies in vasculitis and is a key investigator in various clinical trials in vasculitis and scleroderma. He is conducting genetic and translational biologic studies of vasculitis, and is the Principal Investigator of an upcoming international conference on research methodology in rare diseases. Dr. Merkel's work is supported by several grants from various NIH institutes (National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Center for Research Resources, and National Institute of Allergy and Infectious Diseases). The Boston University Vasculitis Center is the largest program for clinical care and research for vasculitis in the northeastern United States and is an internationally recognized leader in vasculitis research. Drs. Neogi and Simms, as well as Eugene Kissin, M.D., Assistant Professor of Medicine, all also participate in the work conducted by the Vasculitis Center and the Arthritis Center.

### CLINICAL ACTIVITIES

The Section of Rheumatology's clinical program is a major referral center for autoimmune and rheumatic diseases. Patients with scleroderma, amyloidosis, and vasculitis come from throughout the Northeast, as well as from across the United States and abroad. Total annual clinical volume has grown to more than 7,000 outpatient visits, in addition to several hundred inpatient consultations. Many of these patients have complex medical problems and their referral to Boston Medical Center contributes to substantially to the medical center's reputation and further

enhances clinical collaborative efforts with colleagues in multiple specialties, including Cardiology, Pulmonary, Allergy and Critical Care Medicine, Radiology, and other medical specialties.

### EDUCATION

Arthritis Center faculty members teach the musculoskeletal portion of the "Biology of Disease" course to Boston University School of Medicine students. As part of the course, patients are brought into small group sessions with students to bridge didactic work with clinical contact.

In addition to conducting approximately nineteen hours of formal lectures in the "Biology of Disease" course, Center faculty contributed more than 600 hours of teaching time in the outpatient department and inpatient services for medical students, residents, and fellows. Faculty members have been active in continuing medical education and have given numerous Department of Medicine Grand Rounds, Rheumatology Grand Rounds, and invited lectures at national meetings, including the American College of Rheumatology.

A significant number of medical residents from Primary Care, General Internal Medicine, and Orthopaedics rotate through the Rheumatology Section. During their rotations, residents gain exposure to outpatient medicine in Rheumatology, a goal that is not achieved unless they rotate through the specialty. The Section's fellowship program had a large number of outstanding candidates this year, and two positions for July 2008 were filled with two highly ranked applicants in the new rheumatology match.

### MAJOR ACCOMPLISHMENTS

The Arthritis Center had more than forty original full-length publications, including text chapters and invited reviews, over the past twelve months.



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# CANCER CENTER



**VICE CHAIR, CANCER CENTER**  
*Douglas Faller, M.D., Ph.D.*

## RESEARCH ACTIVITIES

The Cancer Research Center includes more than 115 principal investigators based at Boston University School of Medicine (BUSM), Boston University (BU), and Boston University School of Public Health (BUSPH). Most of the Center's faculty members have their laboratories or research efforts based in their respective departmental space. A number of basic laboratory efforts, however, as well as drug development and the Cancer Clinical Trials office, are within dedicated Cancer Research Center laboratory space.

The Cancer Research Center has established specific research programs, including the Cell Cycle Control and Signaling Program, under the direction of Katya Ravid, D.Sc., Ph.D., Professor of Biochemistry; the Lymphoid Malignancy/Immunotherapy Program, under the direction of Adam Lerner, M.D., Assistant Professor of Medicine and Pathology; the Hormone-Responsive Tumor Program, under the direction of Gail Sonenshein, Ph.D., Professor of Biochemistry; and the Program in Population Sciences/Cancer Control, under the direction of Marianne Prout, M.D., M.P.H., Associate Director of Cancer Control and Prevention, and Associate Professor of Epidemiology. This last program, in particular, is leading the Center's efforts in cancer disparities research.

Now in its sixteenth year, the American Cancer Society Institutional Research Grant

provides pilot grant support to new faculty performing cancer research on a peer-reviewed, competitive basis. Douglas Faller, M.D., Ph.D., Director of the Cancer Research Center, Vice Chairman of the Department of Medicine at Boston Medical Center, and Professor of Medicine, Pediatrics, Biochemistry, Microbiology, Pathology and Laboratory Medicine, is the grant's Principal Investigator. The Center received eighteen applications in 2006/2007, from which four awards were made.

The Carter Family Foundation for Melanoma Research funds novel cancer research programs each year. The American Cancer Society Institutional Grant and the American Society for Hematology and the Grunebaum Foundation provided stipends for research experiences in cancer or hematology for medical students. The Cancer Research Center sponsored the Cooperband Award and the Wein Award to outstanding fourth-year BUSM students involved in cancer research.

Members of the Cancer Research Center continue to be successful in maintaining ongoing support and adding new grant support, despite the major cuts in research funds available from the National Cancer Institute (NCI). Many Cancer Research Center laboratory-based grants and funding from the National Institutes of Health (NIH) have been maintained or expanded, with a number of new R01 grants awarded during 2004-2005. Sources of funding include the NCI, NIH, Department of Defense, Food and Drug Administration (FDA), American Cancer Society, Leukemia Society of America, American Heart Association, and the federal Small Technology Transfer Research/Small Business Research Initiatives (STTR/SBIR). A number of private or corporate sources, including the Mary Kay Ash Foundation, the Susan B. Komen Foundation, the Philip Morris Foundation, and the American Association for Cancer Research, have also

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provided funding. Total annual funding for members occupying dedicated Cancer Research Center laboratory space (K7, K5, L9, or R9) totaled more than \$3.5 million. Total annual cancer-related grant funding for all Cancer Research Center faculty members was approximately \$50 million, with more than \$21 million coming from the NCI.

Training support for members of the Cancer Research Center is provided through the Immunology Training Grant, the Hematology Training Grant, and the Cardiovascular Biology Training Grant.

Because translational research is a priority for the NCI and the Cancer Centers Branch, translational research activities in lymphoma, leukemia, breast cancer, lung and head-and-neck cancer, ovarian cancer, melanoma, and prostate cancer are ongoing. Pilot grants for translational research have been offered to a number of investigators on a competitive basis within each research program to increase both translational research and intra-programmatic interactions. Researchers working in Cancer Research Center core laboratory space have been awarded four new patents through BU in the past year. The patented intellectual property includes new therapeutics, diagnostics, and devices. These patents are currently being licensed and developed through the Boston University Medical Center (BUMC) Technology Transfer Office.

In addition to active participation in national cancer trials, a major focus of the Cancer Research Center is to develop and test new therapeutics developed by BUMC faculty members. New therapies and drugs directed toward chemotherapy-resistant tumors and for the common genetic diseases sickle cell disease and thalassemia, as well as new treatments using novel differentiating and antiviral agents, have been developed by Center investigators and are being evaluated in FDA-registered trials. New therapeutics developed within the Center for the treatment of refractory skin ulcers, acute radiation sickness, cytopenias, and a novel molecular treatment for cystic fibrosis are in, or

entering, clinical trials.

Cancer Research Center efforts over the next year will continue to focus on expanding the grant-supported cancer research base eligible for supplementation under an NCI Cancer Center Support Grant (CCSG) and expanding clinical and translational research to support application for eventual Comprehensive Cancer Center designation by the NCI. To this end, the Cancer Research Center Executive Committee meets regularly to provide evaluation and advice for the Cancer Research Center's research and clinical programs. The Cancer Research Center is also working with the BUMC Cores Committee to reorganize and develop core resources along the lines required for support by the NCI. A new and comprehensive Cancer Research Center website has been designed and will be launched in the coming year to facilitate interactions and access among faculty.

#### CLINICAL ACTIVITIES

The Cancer Research Center pursues clinical activities through the Cancer Prevention and Control Center, which involves both BUSPH and affiliated hospitals. This program is designed to integrate new strategies for cancer control and prevention into general medical care, as well as into the more specialized disciplines of medicine represented at BUMC. It also provides educational and cancer screening services to the community, including providing advice and information to patients on how to alter lifestyles to lower their risk of cancer, and how to work with their own physicians to utilize appropriate cancer detection tests.

The Cancer Center is currently enrolling subjects into national cancer prevention trials, with one focus of prevention efforts to make these trials available to the underserved community cared for through the Cancer Prevention and Control Center's Outreach Program. Outreach efforts are coordinated through the Cancer Center Clinical Trials Office, and include Boston Medical Center, the Cancer Prevention and Control Center, and

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affiliated neighborhood health centers.

Included within the Cancer Research Center is the Bone Marrow/Stem Cell Transplantation Center, which has grown dramatically since its inception seven years ago. The Bone Marrow/Stem Cell Transplantation Center is accredited as a national transplantation center. Cancer Center investigators continue to explore new stem cell transplantation methodologies in the setting of  $\beta$ -cell malignancies, including amyloidosis, with great success.

Through its Center for Cancer and Blood Diseases in the new Joseph Moakley Building, the Cancer Research Center provides a combined oncology/hematology outpatient facility offering medical oncology, surgical oncology, hematology, thoracic surgery, gynecologic oncology, women's health, radiation oncology, rehabilitation, and social work services. A new Cancer Survivorship Program has been developed between the Cancer Center and Boston Medical Center, and it forms the basis of funded research studies by BU faculty.

In addition to its clinical activities, the Cancer Research Center has long been a leader in providing data to the National Surgical Adjuvant Breast and Bowel Project (NSABP), and is a full and active member of the Southwest Oncology Group (SWOG), the Radiation Therapy Oncology Group (RTOG), and the American College of Surgeons Oncology Group (ACOSOG). More than seventy national or investigator-initiated clinical trials are open for enrollment at Boston Medical Center or its affiliates at any one time, allowing patients full access to the most advanced therapies for their diseases. Center faculty are particularly proud of the Center's record of recruitment of minority and disadvantaged patients into national clinical trials, and the Center is one of the leading cancer centers in the country in this respect.

## EDUCATION

The Cancer Research Center continues its educational program for community

physicians and health-care workers, whereby physicians, pharmacists, and nurses are provided with Hematology/Oncology Rounds, Cancer Prevention and Control Grand Rounds, and in-services. In addition, national cooperative cancer protocols being directed through BUMC, including NSABP, SWOG, RTOG, and ACOSOG, have proven valuable tools for improving patient care and education at outlying affiliated institutions. A curriculum for the education of medical students with outcomes assessment, developed through a grant in Cancer Prevention awarded to the Cancer Research Center, has completed its twelfth year of funding.

The goal of the Cancer Research Center is to provide excellent and comprehensive care to patients, while bringing the most advanced treatment modalities available, including new therapeutics and diagnostics developed at BUMC, to bear on their illnesses.

## FACULTY

### Professor

Douglas V. Faller, M.D., Ph.D.

### Associate Professor

Sheng Wang, Ph.D.

### Assistant Professors

Gerald V. Denis, Ph.D.

Sajal K. Ghosh, Ph.D.

### Research Assistant Professor

Yan Dai, Ph.D.

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## CENTER FOR PRIMARY CARE



**DIRECTOR**  
*John Noble, M.D.*

### CENTER FOR PRIMARY CARE

The Robert F. Russell Chapter of the Gold Humanism Honor Society: Boston University School of Medicine received a generous gift from Dr. Robert F. Russell (BUSM Class of 1946) and his family to support the activities of the Center. Dr. Russell was a member of the BUSM Class of 1946. He devoted his career to serving the community of Castine and Penobscot Bay, Maine as a General Practitioner and Surgeon. The Gold Humanism Honor Society Chapter at BUSM has been named in honor of Dr. Russell. The Society inducted its first cohort of students, residents and faculty on November 8, 2006.

A total of 19 third year students, three resident physicians and Elizabeth Abernathy MD, an attending physician in the Department of Medicine were inducted as the Class of 2007 into the Society on April 26, 2007. A series of evening activities are being planned for the fall of 2007.

### BOSTON HEALTHCARE FOR THE HOMELESS

During the past year the Boston Health Care for the Homeless Program (BHCHP) conducted its first capital campaign to renovate the former Mallory Institute of Pathology on the former Boston City Hospital campus. This Egyptian Revival structure was built in 1932 and served as the ambulance bay for the City of Boston as well as the city

morgue. The upper floors of this historic landmark housed the Departments of Pathology of Harvard and Boston University Medical Schools for almost a half century, and several major discoveries were made during that time, including the unraveling of the mysteries of pernicious anemia and much of the pathophysiology of cirrhosis and end-stage liver disease.

BHCHP has raised \$40 million for renovations and preservation of this venerable building. The project will be completed in the spring of 2008. BHCHP will use the large first floor of the Mallory to relocate and expand the current primary care practice in Boston Medical Center. The space will be utilized to implement an innovative clinic that fully integrates medical, mental health, and comprehensive dental services in a single location easily accessible to Boston's homeless men, women, and children.

The location on the campus of Boston Medical Center will foster BHCHP's longstanding collaboration with that outstanding academic medical center. The increase in the number of examination rooms will allow for more education and teaching of residents and medical students in an atmosphere that fosters teamwork and integration of the various clinical disciplines of medicine, psychiatry, nursing, social work. The upper three floors of the Mallory Building will house an expanded 104-bed Barbara McInnis House, BHCHP's medical respite program that has become a national model for the care of ill and injured homeless persons who are too fragile to withstand the rigors of survival on the streets and in the shelters and would otherwise require costly acute care hospitalization.

This program has evolved to become a step-down hospital that provides acute and sub-acute, pre- and post-operative, rehabilitative

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and recuperative, and palliative and end-of-life care for vulnerable persons struggling with illnesses without a home or family supports. The move from the current site of the McInnis House in Jamaica Plain will allow BHCHP to address the increasing acuity of care for patients coming directly from area emergency departments and hospitals, a direct result of the dramatic reduction in the lengths of hospital stays over the past two decades.

The new Mallory Building will allow BHCHP to address the long-cherished goal of providing excellence in clinical care that is fully integrated into the mainstream of Boston's remarkable teaching hospitals, and to participate more fully in the education and training of medical students and residents.

#### MAJOR ACCOMPLISHMENTS

Presentations were made at the Annual Session of the American College of Physicians and at the American Osler Society, in Halifax, Nova Scotia. Dr. Noble was elected to serve as Second Vice President of the American Osler Society. He will be President of the Society in 2010.



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# PULMONARY CENTER



**DIRECTOR**  
*Jerome Brody, M.D.*

## RESEARCH ACTIVITIES

The Pulmonary Center is a centralized, multidisciplinary research center focusing on the study of lung diseases. The faculty of this self-contained lung cell biology department use stem cells and cell-based therapies to study genetics, genomics, epidemiology, proteomics, cell biology, molecular virology and biology, developmental biology, immunology, connective tissue synthesis, and reparative medicine. The Center's more than forty M.D. and Ph.D. faculty members represent five departments, including Medicine, Genetics, Biochemistry, Pathology, and Engineering. Now in its thirty-second year, a multidisciplinary T32 training grant from the National Heart, Lung, and Blood Institute (NHLBI) supports pre- and postdoctoral trainees in the Pulmonary Center. This grant, private funding, and National Institutes of Health (NIH) awards support eight pre-doctoral students, eighteen M.D. and Ph.D. post-doctoral fellows, and two visiting scientists.

The Pulmonary Research Center is divided into six scientific disciplines. Mary Williams, Ph.D., Professor of Medicine and Wellington Cardoso, M.D., Ph.D., Associate Professor of Medicine, head the lung developmental biology research program. An NHLBI Program Project Grant, for which Dr. Williams is the Principal Investigator, as well as two K08 and five R01 awards from the NIH support the nine M.D. and Ph.D. faculty

in this group.

The introduction of a new budget process based on return of indirect costs has energized Pulmonary Center fiscal planning. Committees have been formed to prioritize replacement of aging or non-functioning equipment; a search for new research faculty has been instituted; and plans are being pursued to reorganize and expand research space to accommodate the new Stem Cell program and to move faculty from the laboratory of former Pulmonary Center Associate Director Mary Williams, Ph.D., from the Department of Medicine at Boston Medical Center to Boston University School of Medicine in space adjacent to the Pulmonary Center.

The Center's grants portfolio has remained relatively constant despite a decrease in funds from the National Institutes of Health (NIH). New major grant submissions include a U19 RFA on the regulation of allergic response by David Center, M.D., Chief of the Section of Pulmonary, Allergy, Critical Care and Sleep Medicine, Gordon and Ruth Snider Professor of Pulmonary Medicine, and Professor of Medicine and Biochemistry.

Jerome Brody, M.D., Director of the Pulmonary Center, and Professor of Medicine, and Avi Spira, M.D., M.Sc., Director of the Bioinformatics and Systems Biology Program, Assistant Professor of Medicine, Pathology and Laboratory Medicine, and Adjunct Professor of Bioinformatics, are involved in reorganizing the Genomics and Genetics Department. In addition, Drs. Brody, Center and Spira are participating in an inter-campus initiative in systems biology being led by the new University Vice Provost for Research.

Under the direction of Wellington Cardoso, M.D., Ph.D., Professor of Medicine and, the Lung Development Stem Cell group focuses on mechanisms regulating development of the lung from the endodermal foregut. The group

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includes three young investigators whose projects include microRNAs (Jining Lu, Ph.D., Assistant Professor of Medicine); chromatin remodeling (Maria Ramirez, Ph. D., Assistant Professor of Medicine and Assistant Professor of Pathology and Laboratory Medicine); and regulation of embryonic stem cells as a model of lung development (Darrell Kotton, M.D., Assistant Professor of Medicine). A Program Project Grant that funds study of the developmental biology of the lung received its third renewal. The grant is in its fifteenth year.

Dr. Cardoso has become a recognized authority on early lung development and participates in study sections and workshops for the National Heart, Lung, and Blood Institute (NHLBI). In the coming year, he plans to begin organizing a cross-campus program in development and stem cell biology.

Dr. Center publishes in the area of lung and basic immunology. He is the Principal Investigator on a recently submitted Asthma Center proposal. Dr. Center is on the extramural board of NHLBI advisors and serves on committees for the NIH and other organizations. During the past year, he was appointed Assistant Provost for Translational Research for the Boston University Medical Campus Translational Research Institute.

The Pulmonary Center Stem Cell and Lung Regeneration Program is under the direction of Alan Fine, M.D., Director of the Stem Cell Biology Program, and Associate Professor of Medicine. This group focuses on the development and application of techniques to identify endogenous lung stem cells. Their work has been bolstered by close collaborative interactions with the Center's Lung Development Stem Cell group and is the focus of a new, University-wide initiative on stem cells and lung regeneration being organized by Mark Klempner, M.D., Associate Provost for Research, and Professor of Medicine. Drs. Fine and Kotton are involved with this effort.

Drs. Brody and Spira have developed a

Genomics Lung Cancer Program that focuses on applying gene expression and bioinformatics techniques to develop new diagnostics for lung cancer and to understand the pathogenesis of smoking-related lung diseases. Dr. Spira has received a new grant to develop a lung cancer diagnostic from the National Cancer Institute, as well as a new NIEHS U01 grant from the National Institute of Environmental Health Sciences to develop a biomarker for cigarette smoke exposure. With the help of the BU Entrepreneurial program, Drs. Brody and Spira have started a company, ExProDx to commercialize their lung cancer diagnostic, was published in *Nature Medicine* this year.

In addition, the Center has a number of young investigators who have demonstrated they have promising futures in research. Drs. Kotton and Spira have received external funding and have been invited to NIH workshops. They have also given research seminars at a number of medical centers across the United States. Drs. Lu and Ramirez have received new R01s from the NIH and have projects in the. Andrew Wilson, M.D., Assistant Professor of Medicine, who trained with Dr. Kotton in gene therapy, has received a three-year, \$100,000 grant from the [Flight Attendant Medical Research Institute](#) to study ways to increase the lung's antiprotease activity using lentiviral-based gene therapy.

In conclusion, the faculty and staff of the Pulmonary Center congratulate Dr. Williams on her retirement in June 2007. She came to BU and the Pulmonary Center in 1990 and headed the previous renewal of the Lung Development Program Project Grant. She mentored a number of young investigators and supported young women scientists in the Pulmonary Center. Dr. Williams has been a widely recognized authority on lung development and the biology of alveolar epithelial cells. She served on many NIH committees and was invited to speak at numerous universities and meetings.

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# WHITAKER CARDIOVASCULAR INSTITUTE



DIRECTOR, *AD INTERIM*  
WHITAKER CARDIOVASCULAR INSTITUTE  
DEAN AND PROVOST,  
BOSTON UNIVERSITY SCHOOL OF MEDICINE  
*Karen H. Antman, M.D.*

## RESEARCH ACTIVITIES

The Whitaker Cardiovascular Institute conducts, stimulates, and coordinates research and training related to the etiology, prevention, control, and treatment of cardiovascular disease. More than 125 full-time investigators and technical staff are involved in research, training, and education. Total research support from federal and non-federal sources is in excess of \$33 million per year.

The Institute is currently overseeing four major research programs. Under the direction of Kenneth Walsh, Ph.D., Professor of Medicine, the recently funded five-year Program Project “Endothelial Redox State and Phenotype in Health and Disease” focuses on understanding the biomolecular basis of oxidant signaling, as well as the adaptive and maladaptive consequences of oxidant stress in endothelial biology and vascular disease. Dr. Walsh is also studying signaling pathways in cardiomyocytes and endothelial cells, as well as endovascular stem cell biology, in work funded by the National Institutes of Health (NIH).

The “Structural and Cell Biology in Cardiovascular Disease” Program Project seeks to understand the structural biology of the macromolecules and the macromolecular

complexes involved in the transport of lipids into and out of cells. It is under the direction of David Atkinson, Ph.D., Professor of Physiology and Biophysics, and Research Professor of Biochemistry.

Directed by Herbert Kagan, Ph.D., Professor of Biochemistry, the “Role of the Arterial Wall in Atherogenesis” Program Project is an in-depth study of the causes and prevention of arteriosclerosis at the gross tissue, cellular, and subcellular levels.

Joseph Vita, M.D., Director of Clinical Research for the Department of Medicine, and Professor of Medicine, was recently awarded a five-year Specialized Clinical Center of Research (SCCOR) award from the National Heart, Lung, and Blood Institute (NHLBI), “Vascular Consequences of Insulin Resistance and Obesity.” This SCCOR represents a multidisciplinary examination of the consequences and mechanisms of vascular dysfunction in insulin resistance and obesity. In addition, Dr. Vita is investigating the function of oxidative stress in atherosclerosis using NIH funding.

The NIH is the principal funding source for several other active research efforts, including a newly funded four-year award for Jane E. Freedman, MD, Associate Professor of Medicine and Pharmacology, which studies the role of gene expression in the Framingham Heart Study’s offspring cohort. Dr. Freedman is also studying the role of platelets in arterial thrombosis.

Richard Cohen, M.D., director of the Vascular Biology Unit, and Professor of Medicine, Physiology, and Pharmacology, and the Jay and Louise Coffman Professor of Vascular Medicine at Boston University School of Medicine, is working with Dr. Vita to study endothelial function.

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Wilson Colucci, M.D., Chief of the Section of Cardiovascular Medicine and Co-Director of the Cardiovascular Center at Boston Medical Center (BMC), Head of the Myocardial Biology Unit at Boston University School of Medicine, Thomas J. Ryan Professor of Medicine, and Professor of Physiology, is investigating oxidative stress in myocardial remodeling.

Katya Ravid, D.Sc., Ph.D., Scientific Director of the Central Transgenic Facility at Boston University School of Medicine, and Professor of Medicine and Biochemistry, is conducting research on gene regulation in megakaryocytes.

Nelson Ruiz-Opazo, Ph.D., Professor of Medicine, studies the role of Na<sup>+</sup> transporter genes in essential hypertension.

Vassilis Zannis, Ph.D., Head of the Molecular Genetics Unit, and Professor of Biochemistry, is actively involved with research on gene regulation of apoproteins.

In addition, promising junior investigators continue to be successful in obtaining career development awards, such as the NIH's Clinical Investigator Award and the American Heart Association's Clinical Scientist Development Award and Established Investigatorship. Several have also received R01s from the NIH. Flora Sam, M.D., Associate Professor of Medicine, is studying the role of aldosterone on cardiac remodeling. Noyan Gokce, M.D., Associate Director of Echocardiography at BMC, and Associate Professor of Medicine, is investigating the relationships between adiposity and vascular function with a particular focus on the effects of weight loss on the vasculature.

### CLINICAL ACTIVITIES

Over the past year, the Whitaker Cardiovascular Institute continued its activities in NHLBI-sponsored clinical trials of cardiovascular disease.

Led by Alice Jacobs, M.D., Director of the

Cardiac Catheterization Laboratory and Interventional Cardiology at BMC, and Professor of Medicine, the "Bypass Angioplasty Revascularization Investigation 2 Diabetes" (BARI2D) trial is an NHLBI-sponsored trial investigating the benefits of coronary artery bypass surgery versus those of percutaneous transluminal coronary (balloon) angioplasty in diabetics.

Dr. Jacobs is also leading a Phase 2 investigation of nitric oxide synthase inhibition in the treatment of cardiogenic shock (SHOCK-2) and will soon commence a full-scale Phase 3 trial on this topic (TRIUMPH). Finally, Dr. Jacobs is also completing an NHLBI-sponsored registry to track outcomes of drug-eluting stents, known as the DEScover Registry.

In studies of vasopressin, a pressor hormone that elevates blood pressure, Haralambos Gavras, M.D., Chief of the Section of Hypertension at BMC, and Professor of Medicine, and his associates have developed peptides that counteract the vasopressin-1 (V1) receptor. The researchers have demonstrated that approximately 30% of patients with severe heart failure experience an improvement in circulatory function following administration of the peptide antagonist. Recently, the laboratory has synthesized several other peptides inhibiting both V1 and V2 receptors, the V2 receptors being responsible for water absorption by the kidney. Clinical trials are now underway for studies of the new V1 antagonist in patients with hypertension or heart failure and for the dual V1-V2 blocker in patients with fluid retention or edema. In addition, Dr. Gavras and Irene Gavras, M.D., Professor of Medicine, have carried experimental testing through Phase 3 clinical studies on the effects of new renin inhibitors, ACE inhibitors, and calcium channel blockers.

Studies led by Drs. Colucci and Sam are examining the role of aldosterone in regulating myocardial systolic and diastolic function, pulmonary vascular tone, and coronary blood

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flow reserve under physiologic and pathophysiologic conditions, and, in particular, in patients with dilated cardiomyopathy.

Dr. Colucci's group is also conducting several trials of new therapeutic agents for patients with heart failure. Drugs under study include adrenergic receptor and endothelin receptor antagonists, natriuretic peptides, and drugs that increase myocardial cell calcium sensitivity.

## EDUCATION

Educational programs, particularly in research training of both pre- and postdoctoral students, are consistent with the Institute's mission to further the conquest of cardiovascular diseases through the preparation of research leaders. The Whitaker Cardiovascular Institute has been involved in teaching through its weekly Tuesday lecture series, which invites a series of local and international speakers. Outside speakers also visit with Whitaker labs, trainees, and investigators during their visit.

The Cardiovascular Research Training Grant also funds the Institute's teaching activities. Now in its thirty-first year, the Basic Science Cardiovascular Postdoctoral Training Program (Multidisciplinary Training in Cardiovascular Research), under the direction of Dr. Freedman, offers research training in hypertension, atherosclerosis, and ischemic heart disease. This single program

has graduated more than one hundred and six students, most of whom hold academic positions.

Institute trainees attend weekly lectures and separate luncheon meetings. This "Work In Progress" seminar series is within the Institute's current seminar series, during which trainees will present their work to colleagues and receive constructive feedback. In the upcoming year, other topics for the trainees will include basic statistics and a paper writing workshop.

## MAJOR ACCOMPLISHMENTS

The Institute is currently interviewing for a new director.

Dr. Freedman was awarded a four-year R01 titled "Gene Expression and Thrombosis in a Community-Based Cohort Study."

Dr. Gokce was awarded a five-year R01 titled "Inflammation and Vascular Dysfunction in Obesity."

Noriyuki Ouchi, M.D., Ph.D., Assistant Professor of Medicine, was awarded an American Heart Association Scientist Development Award.



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## AFFILIATED HOSPITALS

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# BOSTON VETERANS ADMINISTRATION HEALTHCARE SYSTEM



**ASSOCIATE CHIEF, MEDICAL SERVICE**  
*Jay Orlander, M.D., M.P.H.*

The VA Boston Healthcare System (VABHS) is the primary tertiary care referral center for five New England states, as well as a leading provider of care to veterans in eastern Massachusetts. VABHS comprises three main campuses: Jamaica Plain (JP), West Roxbury (WX), and Brockton. The system also includes six outpatient clinics in the Greater Boston area.

VABHS has a total bed capacity of 647. The West Roxbury campus houses the acute inpatient medical, surgical, neurological, and rehabilitation services. Acute psychiatry, a spinal cord program, an inpatient hospice program, a transitional care unit, a nursing home unit, and specialized substance abuse programs reside at the Brockton campus. The Jamaica Plain campus is primarily an outpatient and research facility and has the majority of specialized clinical services and significant research initiatives.

VABHS' medical service is closely affiliated with the Departments of Medicine at Boston University School of Medicine (BUSM) and Harvard Medical School (HMS). Many faculty members at both schools have full- or part-time appointments at VABHS, where they practice, teach, and conduct some or all of their research. VABHS is a major site for the clinical education of residents and fellows

from Boston Medical Center (BMC), Brigham and Women's Hospital (BWH), and Beth Israel Deaconess Medical Center (BIDMC), as well as for students from BUSM and HMS.

The prolonged conflict in the Persian Gulf has created clinical needs and financial pressures that impact VABHS. Evolving patient needs, new clinical and research priorities from Washington, and constant changes in health care are evident in the VABHS' patient population, programs, and initiatives.

## RESEARCH ACTIVITIES

VABHS' research program continues to succeed even in this era of fiscally stringent research resources nationally.

With current funding that exceeded \$5 million during Fiscal Year 2007, the Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC) continues to be a leading center of research excellence for VABHS. MAVERIC oversees three major research-related programs and is one of only three Epidemiology Research Centers of Excellence that the VA has nationwide. MAVERIC researchers have special expertise in pharmaco-epidemiology and are currently pursuing thirty individual studies in this core area.

MAVERIC is also one of five national Cooperative Studies Program Coordinating Centers (CSP CC) involved in planning and running a variety of clinical trials. While

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VABHS is one of the newest CSP CCs, having joined the program in 2002, it has coordinated more than twenty large-scale trials and epidemiology studies in a wide range of chronic disease areas, including cancer, cardiovascular disease, renal disease, osteoporosis, mental illness, pulmonary disease, aging, exceptional longevity, diabetes, hypertension, and neurodegenerative diseases. This group is currently running or planning six large clinical trials. The newest study, led by Mary Brophy, M.D., Assistant Professor of Medicine, and a member of the Section of Hematology/Oncology, is a North American RCT involving VA, as well as non-VA, sites in the United States and Canada. Dr. Brophy and her colleagues are comparing new treatment regimens for rheumatoid arthritis.

The leadership of MAVERIC has been acknowledged for its creative and successful data management systems and approaches to analysis of the large VA datasets. Michael Gaziano, M.D., Louis Fiore, M.D., M.P.H., Co-director of MAVERIC, Chief of the Section of General Internal Medicine and Clinical Epidemiology at VABHS, and Associate Professor of Medicine, has been named Chief of Informatics for the National VA Cooperative Studies Program.

Dr. Fiore has been recognized for the creative and novel approaches to data management that MAVERIC has taken. Under Dr. Fiore's direction, MAVERIC has installed state-of-the-art electronic systems that allow for real-time data management and clarification with less paperwork. New applications utilize Web-based technology to offer unique, easy-to-use, and secure approaches to the management of clinical trial information. Because of the initiatives Dr. Fiore has pursued, research nurses at VA hospitals across the country now send information about patients enrolled in clinical trials to MAVERIC through the VA Intranet and the Internet. A second electronic tool currently used at MAVERIC, also launched under Dr. Fiore's initiative, is an electronic clinical trial management system that helps researchers locally and nationally

share information and documents about a particular research project. At present, MAVERIC is deploying video conferencing equipment to all participating CSP CCs to facilitate investigator communication. Together, these tools allow the VA to conduct research safer, faster, and less expensively.

Dr. Brophy oversees MAVERIC's third and final component, a national serum and tissue repository to support VA investigations across the country. Dr. Brophy recently completed a \$650,000 renovation of the lab, which will add state-of-the-art genomic research capabilities in the coming year.

A novel offshoot of the successful biorepository site has been the funding of a collaborative studies program titled, "Veteran's Affairs' Biorepository Trust," or VABT. Dr. Fiore is the Principal Investigator, and Dr. Brophy is Co-Principal Investigator. This project seeks to collect residual surgical tissue, blood, and longitudinal clinical information from veterans for future translational research. MAVERIC will coordinate the study. Surgical tissue will be housed in a repository at the Phoenix VA site, with blood and DNA banked in the MAVERIC Lab.

More than half of VABHS' Medical Service sections have staff leading or collaborating on research projects in MAVERIC and cross-disciplinary research, particularly with colleagues in mental health. Research within the clinical subspecialties is also prevalent. The Jamaica Plain campus is home to a new Clinical Studies Unit (CSU) for outpatient clinical trials funded by biotech companies or PHARMA. Newly renovated, the unit is staffed by nurse researchers and an administrator who assist with the process of conducting outpatient clinical trials. To support junior investigators, VABHS provides assistance with contracting, negotiating, and working with funders. VABHS also provides biostatistical assistance to investigators who are preparing a submission to a funding agency and helps to analyze any findings obtained. In addition, the CSU serves more-senior

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investigators who are involved in multi-site clinical trials as part of their research program at VABHS.

The Section of General Internal Medicine houses the VA Normative Aging Study. Pantel Vokonas, M.D., Professor of Medicine and Public Health, directs the study, and David Sparrow, Sc.D., is Associate Director. This prospective epidemiologic study recruited more than 2,000 veterans in 1963 for study and continues to this day. Researchers in the Normative Aging Study collaborate with investigators across disciplines at the VA and at several Boston-area teaching hospitals. They have published more than 400 manuscripts. Core funding for the project is now linked through MAVERIC, while individual project grants linked to this project total more than \$2 million.

Antonio Lazzari, M.D., Assistant Professor of Medicine, is leading three studies that focus on the assessment, risks, and treatment of osteoporosis in men. One study examines the impact of anticonvulsants on bone density. In addition, Anand Kartha, M.D., M.Sc. Assistant Professor of Medicine, is involved in a collaborative project with the pharmacy to improve medication reconciliation.

The Division of Cardiology's research activities include basic research into mechanisms of cardiac fibrosis and failure, as well as clinical trials testing newer approaches to managing heart failure. The heart failure clinical trials are under the direction of Jacob Joseph, M.D., Director of the Heart Failure Program, and Associate Professor of Medicine.

Endocrinology is the VABHS' smallest section, but under the leadership of Paul Conlin, M.D., Associate Professor of Medicine at HMS, it is a national leader in telemedicine research and applications. Dr. Conlin's work in diabetic eye screening using tele-imaging was so successful that he now oversees a national program using the technology. Several studies testing diabetic control through use of

laptop computers deployed to patients are underway.

Daniel Jacobson, M.D., Chief of the Section of Oncology, and Professor of Medicine, studies amyloidosis. Three new clinical trial protocols – in prostate cancer, lung cancer, and colon cancer, respectively – have been launched over the past year by Valia Boosalis, M.D., Assistant Professor of Medicine. Nikhil Munshi, M.D., M.B.B.S., Associate Professor of Medicine at HMS, leads a fifteen-center consortium within the VA that is studying new molecules in the treatment of multiple myeloma.

In Pulmonary, Daniel Gottlieb, M.D., M.P.H., Associate Program Director of the General Clinical Research Center at BUSM, and Associate Professor of Medicine, directs the Sleep Disorders Center at VABHS. Eric Garshick, M.D., Associate Professor of Medicine at HMS, studies the impact of spinal cord injury and environmental toxins on lung function. Marilyn Moy, M.D., Assistant Professor of Medicine at HMS, is a career development awardee studying the impact of exercise on COPD.

The Department of Veterans Affairs, the National Institute of Diabetes and Digestive and Kidney Diseases, and industry sources are funding research being conducted by the VABHS' Renal Section. Current studies include dialysis vascular access; the role of homocysteine in cardiovascular disease in patients with chronic kidney disease; research concerning a new agent for the treatment of diabetic nephropathy; and studies of a new erythropoietic-stimulating agent. James Kaufman, M.D., Professor of Medicine and a member of MAVERIC, is actively involved in epidemiologic studies of chronic kidney disease. Based on his research, Dr. Kaufman co-authored a paper that appeared in the Journal of the American Medical Association that demonstrated for-profit dialysis facilities give patients larger doses of Epogen (EPO) than nonprofit centers. This treatment is likely to have significant implications for the

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management and financing of chronic dialysis. David Mount, M.D., Assistant Professor of Medicine at HMS, is investigating chloride transport, a mechanism that appears to be relevant in both kidney and brain tissue.

Many members of the VABHS' Section of Gastroenterology have ongoing investigations addressing a range of health issues. Satish Singh, M.D., Associate Professor of Medicine, is researching new imaging technologies for colorectal cancer. Hiroshi Mashimo, M.D., Assistant Professor of Medicine at HMS, is studying esophageal motility. Viral hepatitis is the subject of work being done by Marcos Pedrosa, M.D., M.P.H., Associate Professor of Medicine. Raj Goyal, M.D., M.B.B.S., Mallinckrodt Professor of Medicine at HMS, is studying Barrett's esophagus.

### CLINICAL ACTIVITIES

During the past fiscal year, more than 55,000 patients received care in the VABHS system, accounting for more than 500,000 total visits to primary and specialty clinics across all disciplines.

Returning Gulf War veterans and their special needs have resulted in necessary enhancements to clinical services. Because of a high prevalence of soldiers experiencing a traumatic brain injury (TBI), all staff have undergone formal training in TBI. A new, multidisciplinary program for screening, diagnosis, and treatment for TBI was established over the past year.

The Section of General Internal Medicine and Clinical Epidemiology assume responsibility for patient care, training, and research responsibilities. Traditional continuity clinic precepting, general medicine consultation service, and a hospitalist program are included. Faculty members train residents and fellows for academic careers in research; provide specialized clinical care, such as women's health; and offer guidance for careers in medical education through the BU Master Education Training (MET) fellowship

program. Dr. Kartha has been named as the new Director of the General Internal Medicine Consult Service. In addition, Richard Serrao, M.D., Assistant Professor of Medicine, now directs the Ambulatory Diagnostic Treatment Center (ADTC).

Under Dr. Kartha's leadership, a full-time physician assistant has been introduced to each of two of the VABHS' four General Internal Medicine ward teams. These new staff members have rapidly developed a detailed knowledge of the VA systems of care, and they have facilitated and provided discharge planning, patient education and direct care. Housestaff and attending evaluation of their impact on patient care efficiency, patient satisfaction, and the housestaff educational experience is ongoing. The goal of these additions is to improve clinical efficiency, effectiveness and positively impact the educational environment for trainees.

The Cardiology Service at VABHS is a tertiary referral center for VA facilities throughout New England. This year, the division welcomed a new chief, David Faxon, M.D., Lecturer on Medicine at HMS. Dr. Faxon is a pioneer in the field of interventional cardiology, where he investigated early angioplastic techniques while on the BUSM faculty. He later served as Chief of Cardiology first at the University of Southern California and then at the University of Chicago. He has held numerous roles in professional organizations, such as the American Heart Association, of which he is a past president.

Cardiology divisional activities include inpatient and outpatient cardiology; a large Heart Failure Program; cardiac catheterization and interventional cardiology, including peripheral interventions and atrial septal defect closure; advanced echocardiography and nuclear imaging; stress testing; and interventional electrophysiology, including ablation procedures and biventricular pacing for heart failure. The Division added a third electrophysiologist, Peter Hoffmeister, M.D., during the past year, and launched a vascular



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medicine clinic under the direction of Scott Kinlay, M.B.B.S., Ph.D., Assistant Professor of Medicine at HMS, an interventional cardiologist. The Division has created a nurse practitioner-led program for same day-cardiac catheterization patients, known as the CAPE Service, which allows trainees rotating to the VA to focus more of their efforts on sicker and educationally valuable patient care activities.

The Pulmonary, Critical Care and Sleep Service at VABHS underwent several leadership changes this past year. Ronald Goldstein, M.D., Professor of Medicine, now leads the Section. Jussi Saukkonen, M.D., Assistant Professor of Medicine, joined the Section this past year and is Director of the Outpatient Clinics. In addition, Joel Karlinsky, M.D., a long-standing member of the Section, took over as Director of the ICU.

The Pulmonary Section manages inpatient and outpatient consultation services, which are centered at the West Roxbury campus. The Section also performs in- and outpatient bronchoscopies (approximately 200 procedures per year); manages respiratory therapy; oversees a busy eight-bed Medical Intensive Care Unit (MICU); and conducts inpatient consultations. In addition to outpatient Continuity Clinics for patients with pulmonary diseases, the Pulmonary Acute Care Clinic is an important referral center for veterans with pulmonary diseases from throughout New England. This clinic is staffed by attending physicians, interns, residents, and fellows who meet daily. With more than 2,000 patients visits last year, the clinic is aimed at patients who need rapid diagnostic and therapeutic interventions.

A new pulmonary hypertension clinic was developed under the leadership of Jeffery Berman, M.D., Associate Chief of the Medical Service and Pulmonary Section Chief, Vice Chair for the VA for the Department of Medicine at BUSM, Co-Director of the Pulmonary Fellowship Training Program, and Professor of Medicine, a multidisciplinary

program involving Interventional Cardiology's Scott Kinlay, Ph.D., M.B.B.S., Assistant Professor of Medicine at HMS, was also launched.

Under Dr. Gottlieb's direction, the Pulmonary Section has expanded its Sleep Medicine program and recruited a new sleep medicine physician, Hassan Chamis, M.D., who is joining the Section at the beginning of the academic year. Dr. Chamis will pursue both clinical work and sleep research. A new Pulmonary HTN clinic was launched this year in collaboration with Interventional Cardiology. Plans are underway to expand the Allergy program.

The VA's Sleep Program, consisting of sleep clinics and a sleep laboratory, is a referral center for patients from throughout New England. Its goal is to diagnose and treat a variety of sleep disturbances. The Sleep Clinic receives upwards of eighty consults a month, which reflects the prevalence of sleep disorders among veterans. Located at the VA's Brockton campus, the sleep laboratory performs nearly 700 sleep studies per year and is undergoing an expansion from four beds to six, which will permit 1,000 studies to be performed each year. In addition to his work directing the Sleep Medicine program, Dr. Gottlieb also manages an active clinical and research program.

The VABHS' Hematology and Oncology Services work closely on Ward 9D of the Jamaica Plain campus. The Section maintains an extensive program of education, patient care, and research. The staff includes seven attending physicians affiliated with BUSM: Dr. Jacobson leads the Oncology Division, while Kenneth Bauer, M.D., Professor of Medicine at HMS, heads the Hematology section. Hematology/Oncology physicians regularly attend various multidisciplinary tumor conferences, including the ENT Tumor Board, Pulmonary Tumor Board, General Surgery Tumor Conference, and Genitourinary Tumor Board. Other conferences in which Section faculty members

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participate include weekly clinic management conferences; weekly hematopathology conference; bimonthly thoracic oncology management conference; and a weekly outside speaker conference. Faculty members participate in the residents' morning report, medical grand rounds, and weekly "medical forum" conferences.

BUSM oncology fellows spend 50% of their time during their first two years at the VA; typically four fellows are at the VA at one time. Other staff members include six oncology nurses, an oncology pharmacist, and an oncology social worker. The Section is the designated Comprehensive Cancer Treatment Center in the New England region.

Michelle Hankins, M.D., Director of Clinical Oncology, collaborates with the Geriatrics Service and is a participating hospitalist in a new Palliative care consultation service that was launched this year.

The Infectious Diseases (ID) Service at VABHS is responsible for a busy inpatient consultative service; outpatient clinics, including the multidisciplinary HIV Clinic; and management of infection control and hospital epidemiology. The VA is an important training venue for ID fellows from BUSM.

The VABHS' Renal Service provides inpatient consultation and dialysis services at the West Roxbury campus and directs a chronic outpatient dialysis unit at the Jamaica Plain campus. Section faculty members attend four half-day clinic sessions a week at the Jamaica Plain campus, where they see 150 to 200 return visits. They also conduct thirty to forty new patient consults a month; many of these patients have chronic kidney disease, resistant hypertension, or nephrotic syndrome. All Section members participate in the training of fellows, residents, and students.

Rheumatology is a small but active service with an ambulatory clinic at each of the

VABHS' three main clinics. BUSM fellows rotate to largest clinic in the system, located at the Jamaica Plain campus. During the past year, a full-time rheumatologist, Samar Gupta, M.D., was recruited to the service. Dr. Gupta has enhanced the clinical program through a newly developed Rheumatology/Orthopedics clinic that is embedded in the Jamaica Plain campus' Orthopedics clinic. In addition, he has expanded the curriculum for residents on the consultation service and brought an HMS fellow into the West Roxbury clinics.

Although it is the smallest section, Endocrinology remains active. Plans to expand and DM consult service with clinical pharmacists or mid-level providers are in development.

The section Medical service is grateful to Elihu Schimmel, M.D., Professor of Medicine, and Dr. Pedrosa for leading the Section following the loss of its Associate Chief, Chi-Chuan Tseng, M.D., Ph.D., M.P.H., a cherished and valued Section member, and during an ongoing search for Section chief. Despite these challenges, the Section carries on with an ever-increasing number of procedures and ambulatory visit. At the end of academic year, a newly renovated endoscopy suite opened at the West Roxbury campus. This new unit will provide all inpatient procedures. All outpatient advanced endoscopy will transition here over the coming months.

## EDUCATION

Together, BMC, BWH, and BIDMC rotate more than 200 interns and residents and eighty medical students through the VABHS each year. David Thornton, M.D., Assistant Professor of Medicine and a member of the Section of Infectious Diseases, oversees BMC housestaff and BUSM student rotations, while Sarah Grudberg, M.D., Instructor in Medicine at HMS and a hospitalist in the Section of General Internal Medicine, is the point person for the HMS-affiliated residency programs. Jamil Kirdar, M.B.CH.B., Assistant Professor of Medicine at HMS and member of the

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Section of Cardiology, oversees the HMS students.

Each affiliate sends a Chief Medical Resident, which means that three Chief Residents, as well as a Primary Care Chief Resident, are on site at all times. Under the direction of the BUSM and HMS residents and student program directors at the VA, these individuals work together to present a cohesive educational program and to support housestaff, regardless of affiliation.

Fifty-two BUSM students spent part of their core third-year medicine clerkships at VABHS; a similar number receive training in ambulatory medicine. Second-year students from both medical schools receive training in physical diagnosis at the VA. Bedside and didactic interaction of trainees and students has proven to be one of high points of the medical service's integration.

Clinical and research fellows in General Medicine, Women's Health, Informatics, Cardiology, Pulmonary, Infectious Diseases, Gastroenterology, Hematology/Oncology, Rheumatology, and Renal Medicine all receive significant training at VABHS.

One unique clinical training rotation is the Ambulatory Diagnostic Treatment Center (ADTC), now led Dr. Serrao. This block clinical rotation provides expeditious evaluation and intensive ambulatory treatment for complex medical issues and poorly controlled chronic conditions. The clinic serves as a training site for medical residents and third-year clerks.

A new Ambulatory and Patient Safety rotation developed by Drs. Kartha and Thornton, as well as by Ashish Jha, M.D., Assistant Professor of Medicine, was introduced into the medicine residency program this year. Trainees rated it highly, and the program was highlighted at the second annual John McCahan Health Science Education Day in June 2007. Because of its success, the program will be expanded in the coming year.

Morning report is held daily, and a noontime didactic conference is held four days a week. An interactive case conference, with input from multiple services, has begun one day per week and is well attended. Current educational initiatives are focusing on improving didactic teaching in the intensive care units, as well as the appropriate training and certification of housestaff in central line insertion and other invasive techniques.

### MAJOR ACCOMPLISHMENTS

Over the past year, the VABHS has achieved a number of noteworthy goals, including the development of an inpatient Palliative Care Consult Service; the addition of two inpatient nurse practitioners to two General Internal Medicine ward teams in a demonstration project; the creation of three new ambulatory clinics that enhance clinical care: Vascular Medicine, Rheumatology/Orthopedics and Pulmonary HTN; the introduction of a new ambulatory and patient safety rotation for BUSM residents; the recruitment of two new section chiefs, Kalpana Gupta, M.D., M.P.H., for Infectious Diseases and Gyorgy Baffy, M.D., Ph.D., for Gastroenterology; and MAVERIC's successful competition for a five-year renewal as a Cooperative Studies Program Coordinating Center.

Robert Hamburger, M.D., Chief of the Renal Section, won the Lippman Award for 2006 as the Teacher of the Year at VABHS

Brian Hoffman, M.D., C.M., Chief of the Medical Service and Professor of Medicine at HMS, was appointed as Adjunct Professor of Medicine at BUSM. He was honored as the Maurice B. Strauss Professor of Medicine at VA Boston, a title bestowed by both BUSM and HMS.

Jay Orlander, M.D., M.P.H., Associate Program Director of the BU Residency Program, Associate Director in Charge of Education for the General Internal Medicine Fellowship, and Associate Professor of Medicine, assumed the role of Associate Chief

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of Medicine this year.

Kevin Tucker, M.D., Assistant Professor of Medicine at HMS and a member of the Renal Section, won the Partners Teaching Award for Nephrology.

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# QUINCY MEDICAL CENTER



**CHIEF OF MEDICINE**  
*Thomas Barber, M.D.*

## RESEARCH ACTIVITIES

Quincy Medical Center (QMC) is a private, non-profit, 232-bed community teaching hospital affiliated with Boston Medical Center (BMC) and Boston University School of Medicine (BUSM). Founded in 1888 as a cottage hospital to care for workers in the local granite quarries, the hospital soon broadened its mission to serve the acute care needs of residents of Quincy and surrounding South Shore communities. Until its privatization and affiliation with BMC/BUSM in 1999, the hospital was a municipal institution run by the city of Quincy.

QMC has had a longstanding commitment to improving the health of all individuals in its community regardless of ability to pay, a mission that continues to this day. In the years since the affiliation between QMC and BMC, the two institutions have developed a strong and growing partnership, with benefits to both. QMC and BMC have jointly developed many clinical and educational programs, and dozens of BMC physicians provide patient care and medical education at QMC. QMC and the South Shore have become major sources of referrals to BMC for tertiary services.

In 2005, Gary Gibbons, M.D., was appointed CEO and President of QMC. Dr. Gibbons is an internationally known vascular surgeon who has been a pioneer in the care of the diabetic foot. He is also a senior surgeon at BMC and Professor of Surgery at BUSM. Senior leaders at BMC and BUSM – including Karen Antman, M.D., BUSM Dean and Provost, Elaine Ullian, BMC President and CEO, and Paul Drew, Executive Vice President – serve on the QMC Board of Trustees, which also includes a diverse group of physicians and business leaders from the Quincy community.

QMC offers a broad array of inpatient and outpatient services. The Emergency Department treats approximately 34,000 patients annually, and the inpatient services care for more than 8,000 patients each year on the medical, surgical, critical care, and geriatric psychiatry units. During the past year, QMC closed its transitional care unit, and the Radius Specialty Hospital opened a new long-term acute care unit in its place. BMC pulmonologists staff this unit, as they do the Radius unit in Roxbury. The hospital's financial situation remains challenging, despite steady progress in expanding clinical services, increasing patient volume, building medical education programs, and enhancing the quality, safety and efficiency of patient care. The city of Quincy and the Commonwealth of Massachusetts have supported the hospital financially since its privatization, but expected federal support has not materialized. During the past year, QMC engaged FTI Cambio, a healthcare consulting firm, to assist in reorganizing care delivery to further enhance quality while improving profitability. Steady gains have been made from rigorous oversight of clinical utilization patterns, as well as the establishment and maintenance of carefully



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developed productivity standards.

### RESEARCH ACTIVITIES

BUSM's Institutional Review Board (IRB) supports research studies based at BMC and BUSM that enroll patients at QMC. Robert Dart, M.D., Chief of Emergency Medicine at QMC, and Associate Professor of Emergency Medicine, chairs the Clinical Research Advisory Board, which reviews and approves proposals for clinical research programs at QMC. Research studies not based at BMC must undergo review and approval by an extramural IRB.

### CLINICAL ACTIVITIES

In the highly competitive South Shore healthcare environment, QMC has chosen to focus primarily on the provision of general medical, surgical, psychiatric, and emergency medical services. QMC's clinical programs are designed to provide for the outpatient and inpatient hospital-based healthcare needs of the community, with particular focus on the needs of the elderly and Quincy's large and growing Asian population.

QMC supports programs in diagnostic imaging, radiation therapy, laboratory medicine, occupational health, geriatric care, women's health, rehabilitation, pain management, back and spine care, nutrition, diabetes management, neurology, cardiovascular programs, stroke care, cancer care, tuberculosis control, and a broad range of other primary care and specialty medical, surgical, and psychiatric services. It maintains close links with a network of private practices, community health centers, emergency medical, and public health services. QMC also sponsors the South Shore Women, Infants and Children (WIC) program, the Quincy/South Shore AIDS Consortium, a Veterans Administration clinic, health services and interpreter services for Asian patients, and many health education programs for the public.

Primary care services are provided in affiliated private group practices, in the Manet Community Health Center system, and in a satellite clinic of the Boston University Medical Group in Quincy. The medical staff is predominantly made up of private physicians in the various medical and surgical specialties, as well as psychiatry.

Strong relationships have also grown between many QMC and BMC clinical departments. BMC provides contracted services to QMC in Emergency Medicine and in Radiology, which is headed by Jose Varghese, M.D., Associate Professor of Radiology. The Department of Psychiatry is under the direction of James Evans, M.D., Assistant Professor of Psychiatry. The Anesthesiology Department, headed by Mark Levin, M.D., is run by Anaesthesia Associates of Massachusetts, which also staffs BMC's anesthesiology's program. BMC's Department of Surgery operates BMC Surgical Associates in Quincy, a multidisciplinary surgical program comprising general surgeons, vascular surgeons, podiatrists, otolaryngologists, thoracic surgeons, and neurosurgeons, all of whom also practice at BMC.

During the past year, QMC has seen rapid growth in the new tuberculosis clinic, staffed by John Bernardo, M.D., Tuberculosis Control Officer for the Department of Public Health, Professor of Medicine, Research Professor of Biochemistry, and a member of BMC's Section of Pulmonary, Allergy, and Critical Care Medicine, and Claire Murphy, R.N.P. With the assistance of BMC's Department of Cardiology and Ravin Davidoff, M.D., Director of Clinical Cardiology and Director of the Echocardiography Program at BMC, Executive Director of Clinical Affiliations for Boston University Medical Center, and Professor of Medicine, QMC and BMC have enhanced collaborations in interventional cardiology, electrophysiology, cardiac rehabilitation, and ambulatory cardiac testing. Anaesthesia Associates of Massachusetts has taken on a growing role in QMC's critical care program. QMC has been particularly

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successful this year in recruiting new primary care physicians, several of whom are bilingual and bicultural in Chinese and English, to its staff. Promising opportunities exist for further collaborations between QMC and BMC.

in improving systems for reporting critical lab results.

## EDUCATION

QMC hosts BUSM students for “Introduction to Clinical Medicine I and II” and for clinical rotations in Psychiatry and Emergency Medicine. QMC provides inpatient rotations for residents in Psychiatry, General Surgery, Family Medicine, Emergency Medicine, Physical Medicine and Rehabilitation, and Anesthesia. In collaboration with BUSM’s Continuing Medical Education program, QMC offers a wide range of rounds and meetings, both on campus and in local conference centers, to support the educational needs of South Shore healthcare providers. QMC is the only community hospital on the South Shore that provides medical educational programs open to all healthcare providers free of charge.

## MAJOR ACCOMPLISHMENTS

QMC performed exceedingly well during its most recent, and unannounced, Joint Commission survey in November 2006. The hospital has received outstanding ratings in recent surveys by the American College of Surgeons Cancer Care Accrediting Group, the ISO 9001 inspection of QMC’s Occupational Health Services, and the College of American Pathologists’ survey of the clinical laboratories. The Massachusetts Department of Public Health has accredited QMC as a Primary Stroke Center.

QMC is a member of the Hospital Quality Alliance, the Institute for Health Care Improvement’s 100,000 Lives Campaign, and the Massachusetts Hospital Association’s Patients First project. It has fully implemented the Joint Commission’s National Patient Safety Goals. The hospital has been recognized by the Massachusetts Coalition for the Prevention of Medical Errors for its work

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# ROGER WILLIAMS MEDICAL CENTER



CHAIRMAN,  
DEPARTMENT OF MEDICINE  
*Alan Weitberg, M.D.*

Roger Williams Medical Center is a 256 bed acute care institution in Providence, Rhode Island with academic training programs in Internal Medicine, Dermatology, Dermatopathology, Surgical Oncology, Hematology, Medical Oncology, Pulmonary Medicine, Infectious Diseases, Rheumatology and Podiatric Medicine. The medical center is a major teaching affiliate of the Boston University School of Medicine.

In addition to the main campus, there is a 16 acre campus nearby which is the site of the Radiation Oncology facility, a hospice unit, a nursing home and an assisted care living facility managed by the hospital. There is also a medical office building for the University Medical Group and significant laboratory space for faculty investigators. The Adele DeCof Cancer Center is located on this site, having been established with a \$2 million donation.

Roger Williams serves as a training facility for third-year clinical clerks in Medicine and Surgery from the Boston University School of Medicine. These students are housed on campus for the duration of their clerkship. In addition, there are 46 residents in Internal Medicine with whom the students interact as well as with fellows in the majority of the

medical subspecialties.

The research program at Roger Williams Medical Center focuses on several important areas. The Center for Stem Cell Research is developing new biomedical technologies for treating diseases such as muscular dystrophy, myocardial infarction and pulmonary injury. Wound healing research is being done in the Departments of Dermatology, Surgery and Medicine. Other laboratories are involved in cell signaling research, the study of HIV and AIDS, carcinogenesis and immunology. A large clinical research effort involves all of the clinical departments.

The medical center provides high quality medical-surgical care to the community. The state's only blood and marrow transplantation program is housed at Roger Williams in a 5 bed transplant unit with a plasmapheresis laboratory. Also unique is the hospital's inpatient alcohol and substance abuse unit. One of the few inpatient geritopsychiatry units in Rhode Island also is based at Roger Williams. Also recognized in the community are the hospitals' dermatology services, active endoscopy suite, sleep laboratory, bone and mineral metabolism program and rheumatology program.

## MAJOR ACCOMPLISHMENTS

Dr. Alan Weitberg, Chairman of the Department of Medicine, was named an Assistant Dean for Academic Affairs at Boston University School of Medicine by Dean Antman.

Dr. Joseph Tucci, Director of the Division of Endocrinology, was named as one of Rhode Island's best doctors in Rhode Island Monthly Magazine. He also received a grant from GSK Laboratories to study the effect of oral Ibandronate versus placebo in men with osteoporosis.

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Dr. LuGuang Luo, a member of our research division, received a grant from the Juvenile Diabetes Research Foundation in the amount of \$487,355 for three years. He also presented invited presentations at the American Diabetes Associate Annual Meeting in Chicago and at the Cambridge Healthtech Institute in Boston.

The Division of Pulmonary Medicine published a number of research papers on topics including interstitial lung disease, pulmonary manifestations of rheumatologic diseases and the use of stem cells in pulmonary medicine.

The training programs in internal medicine, rheumatology, hematology/oncology, pulmonary medicine and infectious diseases, successfully completed site visits by the Accreditation Council on Graduate Medical Education. Their respective program directors are Alan Weitberg, M.D., Bernard Zimmerman, M.D., Frank Cummings, M.D., Michael Passero, M.D. and Gail Skowron, M.D.

Dr. Marc Weinberg was invited to participate in a broadcast of a panel discussion on the use of high dose angiotensin receptor blockers for hypertension in New York City. He also was an invited speaker at several international venues on the same topic.

## **FACULTY**

### **Professors**

Joseph R. Tucci, M.D.  
Alan B. Weitberg, M.D.

### **Clinical Professor**

Marc S. Weinberg, M.D.

### **Adjunct Professor**

Stephen H. Zinner, M.D.

### **Associate Professors**

Francis J. Cummings, M.D.  
Michael A. Passero, M.D.  
Gail Skowron, M.D.  
Bernard Zimmerman, M.D.

### **Research Associate Professor**

A. Raymond Frackelton, Ph.D.

### **Assistant Professors**

Mehrdad Abedi, M.D.  
Alan Epstein, M.D.  
Rakesh Gupta, M.D.  
Cynthia Holzer, M.D.  
Shahid Malik, M.D.  
Joseph Meharg, M.D.  
Ritesh Rathore, M.D.

### **Clinical Associate Professors**

Michael B. Macko, M.D.  
John Stoukides, M.D.

### **Clinical Assistant Professor**

Mark E. Braun, M.D.  
Parul Shah, M.D.





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## VICE CHAIR FOR CLINICAL AFFAIRS REPORT

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# CLINICAL AFFAIRS REPORT



VICE CHAIR, CLINICAL AFFAIRS  
*Jack Ansell, M.D.*

## CLINICAL ACTIVITY SUMMARY

The Department of Medicine's clinical activities continue to grow at a steady pace. Department faculty deliver inpatient care at Boston Medical Center (BMC) and ambulatory care at four BMC sites: the Doctor's Office Building (DOB), the Preston Family Building, the Yawkey Ambulatory Care Center (YACC), and the newly opened Moakley Building. Additional sites of care include the Commonwealth Medical Group (CMG), a satellite practice on Commonwealth Avenue; Quincy Medical Center (QMC); a number of affiliated neighborhood health centers; and selected private practice locations in the Greater Boston area.

## AMBULATORY CARE

The ambulatory program experienced 218,412 visits in Fiscal Year 2007, a figure that represents a growth of 3.9% over the preceding year (*Figure 1*). Thirty-four percent of visits were in the YACC; 26% in the DOB; 19% in the Preston building; 15% in the Moakley building; 3.2% in the CMG practice; and 2.3% at QMC (*Figure 2*).

With 42% growth in volume, the Cardiology practice experienced the largest increase in the number of patients seen, followed by the Nephrology practice at 25%, and the Endocrinology practice with 19%. As *Figure 3* demonstrates, activity in the **medical** specialty practices showed a 3.8% increase, while primary care fell by 4%. Demand for primary

care remains strong, but its lack of growth can be attributed to limited capacity.

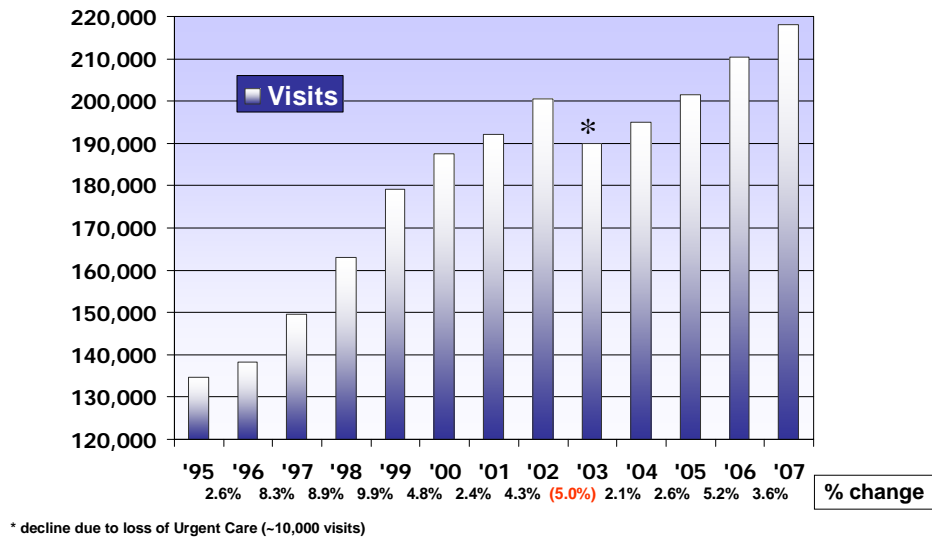
## INPATIENT CARE

The Department of Medicine saw a 3% increase in inpatient growth in FY07, with admissions and observations numbering 18,353 cases admitted to its service (*Figure 4*). Approximately half of all admissions to BMC are to the Department of Medicine service. Despite the heavy patient flow, faculty attendings and housestaff continue to work efficiently and maintain the overall length-of-stay (LOS) at slightly less than 5.0 days.

To handle the high volume of admissions and to comply with residency rules regarding the 80-hour workweek, the Department of Medicine created an uncovered hospitalist team that cares for patients without housestaff coverage. This team, along with the previously established physician assistant team, has enabled the Department to comply with residency work rules and significantly enhanced the inpatient service's teaching program.

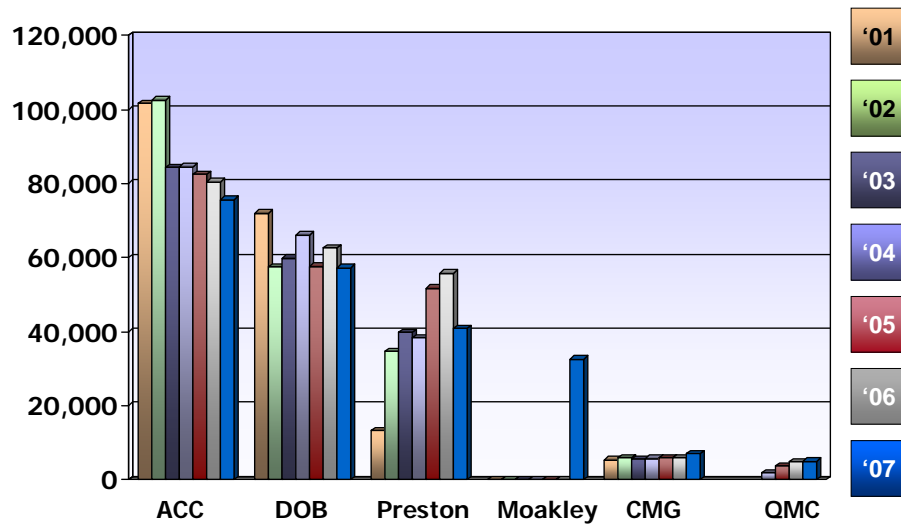
## Department of Medicine Ambulatory Visits

FY '95 - '07

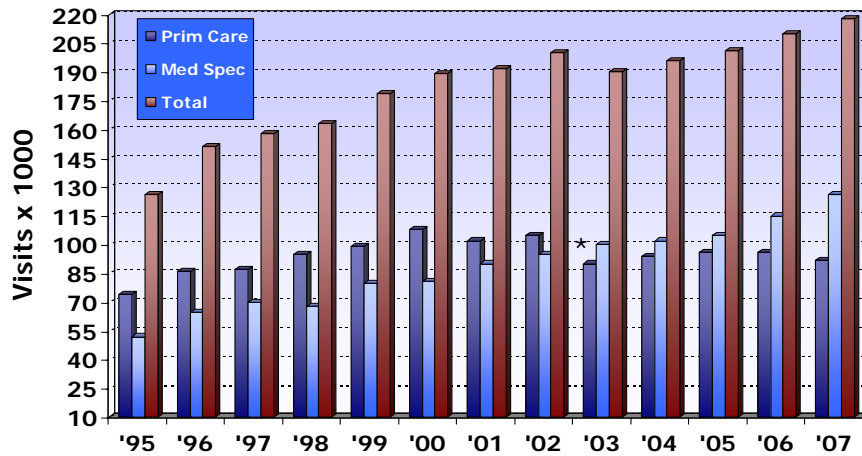


## Visits per Clinic Site

FY '01 - '07

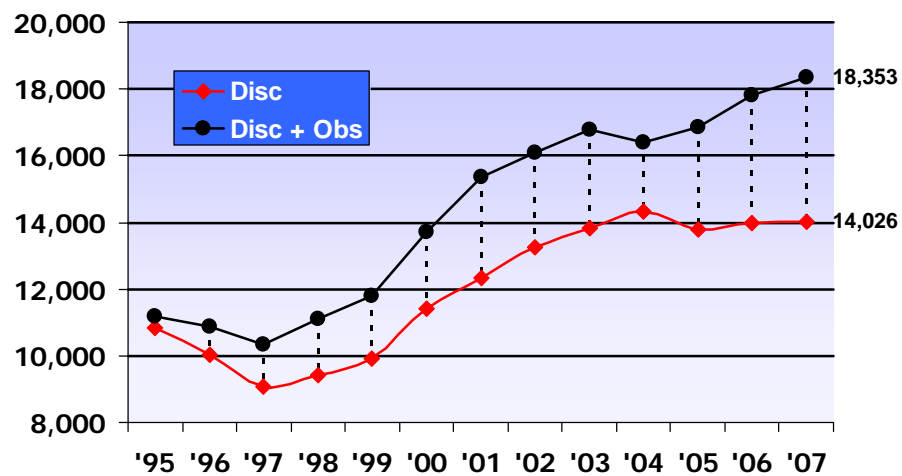


## Primary Care vs Medical Specialty Visits FY '95 - '07



\* decline due to loss of Urgent Care

## Department of Medicine Discharges + Observations FY '95 - '07



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## VICE CHAIR EDUCATION REPORT



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# EDUCATIONAL PROGRAMS



VICE CHAIR, EDUCATION  
*David Battinelli, M.D.*

## RESIDENCY PROGRAM IN MEDICINE

### EDUCATION 2006

Integrated in 1992, the Boston University Medical Center Residency Program takes full advantage of the complementary strengths of the Department of Medicine and all its major resources including the Boston Medical Center (BMC), the Boston Veterans Administration Health Care System (BVAHCS), the Boston Health Net, and affiliated community hospitals. In addition to their clinical experiences, selected residents participate actively in research and play a key role in educating Boston University School of Medicine (BUSM) students. BUSM's residency program offers one of the largest and most diverse educational experiences in the nation, providing clinical and research training in all areas of internal medicine. The diverse and complementary experiences in affiliated major teaching hospitals, together with the guidance and supervision of our medical school faculty, ensure that house officers obtain skills in all aspects of patient care.

Residency training is organized around several key principles:

- The triad of patient care, education, and research forms the foundation for the department.
- Clinical experience is the house officer's most effective teacher.

- House officer training must be diverse, flexible, and individualized.
- Training program must offer personal as well as professional support.

This philosophy serves the residency program well helps guide ongoing program development. High-quality house officers currently represent more than fifty medical schools. House officers are attracted to the BUSM residency program because of department strengths, as well as the missions of both BMC and BVAHCS.

The medical service at BMC is geographically located on 2 campuses in close proximity to each other, namely The East Newton and Harrison Avenue Campuses. There are 8 general medicine teams on Harrison Avenue, and 4 general medicine teams on East Newton. In addition, there are 3 subspecialty services on East Newton on which the house staff rotate, namely Renal, Heme-onc, and Geriatrics.

Our general medicine teams are staffed by a number of dedicated hospitalists, as well as general internists from BMC, and selected subspecialty attendings with a strong record of teaching. The attending serves as the attending of record for the majority of the ward patients on the general medicine teams, as well as the teaching attending, thereby improving the teaching and communication for team members at all educational levels (resident and students). Evans Educators, who are chosen for their teaching and leadership skills and are master clinicians, work in close association with the clinical and educational directors on both campuses. In addition to attending on the wards a number of months each year, they have had a major positive impact on the structure and curriculum of our attending rounds and Wednesday Firm Conferences. The introduction of "hospitalists" as specialized

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clinicians and teachers continues to enrich the clinical service.

The consolidation of all VA inpatient services to the West Roxbury VA campus and the integration of both the Boston University and Harvard University teaching services have been a major success. Boston University and Harvard University both contribute 50% of the student, resident, and fellow trainees in the integrated VA health care system. All trainees learn side-by-side with their medical school counterparts on fully integrated ward, unit, and consult teams. VA faculty who have either a Boston University or Harvard University medical school appointment supervise the trainees. Chief residents from both schools also work collaboratively to provide the highest quality academic and educational program. The feedback has been exceptional and this integration elevates BUSM's VA experience to one of the best and richest in the nation.

For the 2006-2007 academic year there are fifty-eight PGY-1 interns, eleven of whom are in the preliminary program and forty-two of whom (five primary care trainees and forty-two traditional track trainees) are in the categorical program. The PGY2 year has forty-six trainees, (five in primary care and forty-one traditional); the PGY3 year has forty-four trainees (six primary care and thirty-eight traditional). Six chief medical residents-five inpatient chief residents, and one ambulatory chief resident round out the staff.

### INTERNSHIP

The internship includes rotations in emergency medicine, inpatient general medicine, inpatient sub-specialty medicine, medical intensive care, coronary care, ambulatory care, night float, and vacation. Each categorical intern has a weekly continuity clinic experience.

### JUNIOR AND SENIOR RESIDENCY

The program's second and third years allow house officers some flexibility to design their experience in accordance with individual needs and preferences. These two years are organized as continuum, with certain rotations considered integral to each year, while others are scheduled per house officer request and program availability. Residents organize their elective time depending on their career interests. Residents may choose to arrange blocks of elective time devoted to the pursuit of one area in depth, such as a specific research interest or intensive training in a clinical subspecialty or clinical practice.

### POST-RESIDENCY TRAINING POSITIONS

House officers continue to obtain prestigious fellowship positions across the country. In addition, approximately 20% of BUSM's trainees enter generalist careers in academic internal medicine, hospital medicine, private practice, geriatrics, and general internal medicine fellowships. This diversity is a result of a wide array of educational opportunities that enable house officers to choose among subspecialty or generalist careers without undue curricular pressures (see the attached list of Post-Graduate Positions 2006-2007).

### PROGRAM TRACKS

The **preliminary program** is under the guidance and direction of Beth Manning, M.D., M.P.H., Associate Program Director, and Assistant Professor of Medicine. This program includes two elective blocks, as well as the option of a continuity clinic experience, depending on individual trainee's preferences. These options, along with a broad representation of clinical experiences, continue to attract a group of PGY1 house officers interested in a comprehensive year of internal medicine training prior to advanced specialty training. The preliminary program works closely with other BU- sponsored programs, including emergency medicine, neurology, ophthalmology, and anesthesiology.

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The **primary care training program (PCTP)** is under the guidance and direction of Angela Jackson, M.D., Associate Program Director and Associate Professor of Medicine. The PCTP has continued to attract high-quality house officers from across the country. The PCTP builds upon the categorical program's core curriculum and provides residents with an enriched and expanded experience in ambulatory medicine through the use of ambulatory blocks, elective blocks, ambulatory seminar series, and special outpatient rotations. The ambulatory curriculum was expanded to include the 24 half-day seminars to provide ample teaching time to cover ambulatory topics in sufficient depth, along with opportunity for skills practice and application. With the opportunities for continuity clinic experiences in inner-city neighborhood health centers and the BMC campus, the PCTP focuses on the needs of an underserved patient population.

Under Dr. Jackson's direction, the residency program has successfully competed for Title VII federal funding, providing support for BUSM's unique training in an urban health network comprised of BMC and its community partners: Codman Square Health Center, Dorchester House Multi-Service Center, East Boston Neighborhood Health Center, South Boston Community Health Center, and Whittier Street Neighborhood Health Center. This year, despite a top score by peer reviewers, there were no HRSA funds for new proposals. Dr. Jackson has been actively involved in lobbying efforts in Congress to increase funding, and we hope to regain grant funding for the 2008-11 period.

In the **categorical traditional track**, 80% of our residents continue to enter prestigious sub-specialty fellowship programs both here at BUSM and across the country. Traditional track residents interested in intensive training in either clinical or research take advantage of the research opportunities within the department. In addition, residents and fellows have the opportunity to participate in the Clinical Research and Scholar's Track

(CREST), an NIH funded program run in conjunction with the Boston University School of Public Health (SPH). Selected program trainees spend the summer learning critical research skills and working on a clinical research project during their second and/or third years. BUSM also offers the ABIM research pathway. In the 2006-2007 academic year, residents have made important contributions doing basic science and clinical research in a number of subspecialty areas and have presented at the Evans Day Research Meeting, Senior Resident Academic Day, and national meetings. The residency program continues to support these activities as integral to the development of future clinician investigators.

Fully integrated for over 10 years, the residency program has continued to emphasize balancing the inpatient and ambulatory experiences to ensure a diverse curriculum and prepare trainees for careers as generalists or future subspecialists. The program continues to adapt to integrated clinical services and focus on enhanced teaching of medical students and residents, curriculum development, IM-RRC requirements, and establishing a national reputation. Residents continue to obtain high-quality fellowship programs, meet national standards for promoting generalism and professionalism, and do so with a greater than 95% pass rate on the ABIM exam. A strong group of incoming house officers has recently been recruited and another prosperous academic year lies ahead.

#### UNDERGRADUATE MEDICAL EDUCATION

The Department of Medicine is a major contributor to the undergraduate education at BUSM. The department's clinical and research faculty teaches throughout all four years of the medical school curriculum and serve as student advisors and mentors for a large proportion of the medical school class. In the first two years of medical school, faculty members teach the "Introduction to Clinical Medicine" course, covering both patient interviewing and physical diagnosis. In

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addition, faculty teach in the “Integrated Problems” course and the “Biology of Disease” course (BOD). For more than 15 years, the BOD course remains the most highly rated course in the first two years of medical school.

The third-year clinical clerkship experience provides BUSM students with a rich, diverse, and challenging opportunity to learn clinical medicine. The eleven-week clerkship is divided into a seven-week inpatient experience and a four-week ambulatory experience. Students rotate between the BMC and the BVAHCS campuses. Students work side-by-side with housestaff, faculty, and fellows and are provided a hands-on clinical experience where they are active, responsible members of the health care team. Many students return to the wards during their fourth year to complete an acting internship, during which they are given responsibilities commensurate with intern-level patient care. Selected students participate in the competitive advanced acting internship and work in place of interns providing them an

even more advanced level of responsibility. Other students rotate on to subspecialty electives, learning consultative medicine in the inpatient and outpatient rotations.

The Department offers a number of faculty development programs to improve the clinical teaching of students and other trainees. All housestaff in the Department of Medicine participate in a seven-session course addressing teaching and leadership skills. This course begins with a day-long retreat and is supplemented by additional sessions integrated into the academic year. All faculty have the opportunity to participate in the Stanford Faculty Development Course in Clinical Teaching offered by two Stanford trained facilitators within the Department of Medicine. The Department is proud of the large number of our faculty who are awarded numerous medical school and university awards for excellence in teaching and patient care.

### PROGRAM PERSONNEL

David L. Battinelli, M.D.	Vice-Chairman for Education Program Director
Joel Caslowitz, M.D.	Associate Program Director
David Halle, M.D.	Associate Program Director
Angela Jackson, M.D.	Director, Primary Care Training Program Associate Program Director
Beth Manning, M.D., M.P.H.	Director, Preliminary Program Associate Program Director
Jay Orlander, M.D.	Associate Program Director
David Thornton, M.D.	Associate Program Director Director, Medical Student Education (VABHCS)
Warren Hershman, M.D.	Director, Medical Student Education
Robert Levin, M.D.	Director, Medical Student Program (HAC)
Eleanor Paglia, M.D.	Co-Director, Medical Student Program

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## BOSTON UNIVERSITY RESIDENCY PROGRAM IN MEDICINE 2006-2007

<b>Chief Residents</b>		<b>Medical School</b>	<b>Post Graduate Position</b>
Jameel Ahmed		Boston University School of Medicine	Cardiology Fellowship, Boston University
Jonathan Berz		Tufts University School of Medicine	General Internal Medicine Fellowship, Boston University
Lee Gazourian		Boston University School of Medicine	Pulmonary/Critical Care Fellowship MGH and Harvard Medical School
Craig Noronha		Boston University School of Medicine	General Internal Medicine Faculty Boston Medical Center
Paru Patrawalla		Brown Medical School	Pulmonary/Critical Care Fellowship New York University
Satyam Sarma		Jefferson Medical College	Cardiology Fellowship, Baylor University, TX
<b>Senior Residents</b>		<b>Medical School</b>	<b>Post-Graduate Position</b>
Bindu	Akkanti	University of Texas, Southwestern	Pulmonary and Critical Care Fellowship Baylor University, Houston, TX
Miguel	Ariza	Boston University School of Medicine	Endocrine Fellowship Boston University
Urmila	Bajpai	University of Massachusetts Medical School	Rheumatology Fellowship University of California, San Francisco
Indraneel	Chakrabarty	Boston University School of Medicine	Gastroenterology Fellowship Lahey Clinic, Burlington, MA
Jeannie	Chao	Boston University School of Medicine	Rheumatology Fellowship University of California, San Diego
Marjory	Charlot	University of Iowa College of Medicine	Hematology/Oncology Fellowship Boston University
Robert	Chehade	University of Massachusetts Medical School	Gastroenterology Fellowship Dartmouth-Hitchcock Medical Center
Karen	Choong	McGill University Faculty of Medicine	Endocrine Fellowship Boston University
William	Chung	Albert Einstein College of Medicine/ Yeshiva University	Cardiology Research Associate Boston University
Ellen	Cowen	Jefferson Medical College/Thomas Jefferson University	General Internal Medicine Fellowship Boston University
Peter	Grayson	Medical University of South Carolina College of Medicine	Rheumatology Fellowship Boston University
Clare	Horkan	Trinity College, Ireland	Radiology Fellowship Beth Israel Deaconess Medical Center
Vera	Kandror	Boston University School of Medicine	Gastroenterology Fellowship Massachusetts General Hospital, Boston
Colleen	Keyes	Boston University School of Medicine	Pulmonary/Critical Care Fellowship Boston University
Airie	Kim	Baylor College of Medicine	Pulmonary/Critical Care Fellowship University of California, Los Angeles
Susan	Kim	Temple University School of Medicine	Hematology/Oncology Fellowship Tufts New England Medical Center
Robert	Klett	Wake Forest University School of Medicine	Amyloid Fellowship Boston University
Gowri	Kularatna	University of Maryland School of Medicine	Gastroenterology Fellowship Washington University, St. Louis, MO



Lien	Le	Brown Medical School	GIM Faculty Dartmouth-Hitchcock Medical Center
Chris	Leung	University of Medicine & Dentistry of New Jersey/ R.W. Johnson Med School	Gastroenterology Fellowship Boston Medical Center
Benjamin	Levin	Boston University School of Medicine	Hospitalist Beth Israel Deaconess Medical Center
Jennifer	Lo	Louisiana State University Medical Center School of Medicine in Shreveport	Hospitalist PACE Program, BWH, Boston, MA
Manish	Maski	University of Wisconsin Medical School	Nephrology Fellowship Beth Israel Deaconess Medical Center
Priya	Mitra	Northeastern Ohio Universities College of Medicine	Radiation Oncology Fellowship University of Virginia
Francesc	Nesta	Universita Di Brescia, Italy	Cardiology Fellowship Beth Israel Deaconess Medical Center
Karen	Patterson	University of Rochester School/Medicine and Dentistry	Pulmonary Fellowship University of Chicago
Ivonne	Ramirez	Columbia University College of Physicians and Surgeons	Gastroenterology Fellowship Boston University
Cameron	Ramsay	Temple University School of Medicine	Cardiology Fellowship University of Massachusetts, Worcester
Lars-Eric	Reinhold	Boston University School of Medicine	Primary Care Physician South Boston Health Center
Jeremy	Richards	Washington University School of Medicine	Pulmonary/Critical Care Fellowship MGH and Harvard Medical School
Ian	Rogers	University of Connecticut School of Medicine	ABIM Research Pathway Cardiology Research Associate Massachusetts General Hospital
Daniil	Rolshud	Mount Sinai School of Medicine/New York University	Gastroenterology Fellowship Johns Hopkins University, Baltimore
David	Schopfer	Finch University of Health Sciences/ Chicago Medical School	Cardiology Fellowship University of Illinois-Chicago
Tseganesh	Selameab	University of Minnesota- Minneapolis School of Medicine	Primary Care Physician University of Minnesota, Minneapolis
Neha	Shah	New York Medical College	EIS Fellowship, Centers for Disease Control, Atlanta, GA
Alex	Shpilman	Finch University of Health Sciences/ Chicago Medical School	Cardiology Fellowship University of Massachusetts, Worcester
Adel	Tabchy	American University of Beirut, Beirut	Hematology/Oncology Fellowship MD Anderson Cancer Center, Houston
Thomas	Tadros	University of Massachusetts Medical School	Cardiology Fellowship Boston University
Evelyn	Taiwo	Temple University School of Medicine	Hematology/Oncology Fellowship University of Texas-Southwestern
Versha	Taparia	Northwestern University - Pulmonary/ The Feinberg School of Medicine	Critical Care Fellowship New York University, New York
Samir	Thadani	New York University School of Medicine	Cardiology Fellowship Pacific Medical Center, San Francisco
Hillary	Tompkins	Boston University School of Medicine	Gastroenterology Fellowship Boston University
Eugene	Valsky	New York Medical College	ABIM Research Pathway Cardiology Fellowship Boston University



Ariel Weissmann\* Harvard Medical School  
Edwin Zishiri University of Zimbabwe

Cardiology Fellowship  
Cleveland Clinic, Cleveland, OH

*\*Dr. Ariel Weissmann passed away suddenly in July 2006 in his third year of residency. The Department of Medicine has established a Resident Teaching Award in his memory.*

## Juniors

## Medical School

Renata Aguiar	Universidade Federal Do Rio De Janeiro, Brazil
Tahamtan Ahmadi	Universitat Zu Koln, Germany
Suma Amarnath	University of Michigan Medical School
Anthony Annese	Boston University School of Medicine
Ogheneruona Apoe	Tufts University School of Medicine
Daniel Arnold	Tulane University School of Medicine
Annemieke Atema	Boston University School of Medicine
Donette Campbell	Stony Brook University Health Sciences School of Medicine
Phil Cefalo	University of Massachusetts Medical School
Jorge Chaves	University of Texas Medical School at Houston
Eddy Chen	Keck School of Medicine of the University of Southern California
Regine Cherazard	Temple University School of Medicine
Warren Chuang	Boston University School of Medicine
Aine Clements	Brown Medical School
William Cooney	Boston University School of Medicine
Damian Crawford	University of Maryland School of Medicine
Carrie Daniel	University of Kansas School of Medicine-Kansas City
David Denmark	New York Medical College
Mustali Dohadwala	Medical College of Wisconsin
Peter Everett	Boston University School of Medicine
Celia Garner	University of Minnesota Medical School
Geoffrey Gibney	University of Connecticut School of Medicine
Rejane Guerrier	UMDNJ-New Jersey Medical School
Eiman Jahangir	University of Tennessee Health Science Center College of Medicine
Jaime Jenkins	University of North Carolina at Chapel Hill School of Medicine
Aarti Kakkar	Emory University School of Medicine
Andrew Kim	Boston University School of Medicine
Jeffrey King	University of Massachusetts Medical School
Myung Lee	New York Medical College
Janette Lin	Brown Medical School
Yannbor Lin	Boston University School of Medicine
Christine Liu	Temple University School of Medicine
Sezmin Noorani	Medical College of Georgia School of Medicine
Nitin Patel	UMDNJ-Robert Wood Johnson Medical School Piscataway
William Rabitaille	New York Medical College
Alan Rosen	Boston University School of Medicine
JOHN RYAN	UNIVERSITY COLLEGE CORK, IRELAND
Paul Schulze	Universitat Leipzig, Germany
Jennifer Sinclair	Boston University School of Medicine
Amulya Siram	Boston University School of Medicine
Peter Soderland	University of Massachusetts Medical School
David Solarz	University of Cincinnati College of Medicine
Lesley Stead	New York Medical College
Sohera Syeda	Rush Medical College of Rush University Medical Center
Megan Titas	Emory University School of Medicine

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Sara-Maiz Thomas  
Tonslyn Toure  
Pantila Vanichakarn

University at Buffalo State University of New York School of Medicine  
Brown Medical School  
University of Chicago, Division of the Biological Sciences

#### INTERNS

Onyinyechi Agbara  
Solmaz Amirnazmi  
Dominique Bayard  
Priti Bijpuria  
Patrick Boland  
Khalilah Brown  
Stephanie Christenson  
Amy Clark  
Jason Craft  
Mircea-Cristian Dobre  
Maureen Dubreuil  
Toru Endo  
Joao Daniel Fontes  
Mark Franciosa  
Neel Gandhi  
Anthony Garcia  
Sandeep Ghai  
Saulius Girnius  
Kelly Hannigan  
Vu Ho  
Jason Homsy  
Tinatin Khizanishvili  
Woojin Kim  
Bruce Kovalenko  
Joann Kwah  
John Lee  
Megan Leo  
Wrenn Levenberg  
Suru Lin  
Maria Lopez  
Jason Luke  
Hector Marquez  
Jana Montgomery  
Thandeka Myeni  
Cassandra Pierre  
Ava Port  
Rajeev Prabakaran  
Sujata Ramamurthy  
Anjana Ranganathan  
Judith Richards  
Eric Ritter  
Belinda Rivera  
Daniel Roseman  
Marla Scriffignano  
Alefiya Shakir  
Torfay Sharifnia  
Rohit Sharma  
Rebecca Summers

#### MEDICAL SCHOOL

Wayne State University School of Medicine  
Jefferson Medical College of Thomas Jefferson University  
Mount Sinai School of Medicine of New York University  
University of Maryland School of Medicine  
Jefferson Medical College of Thomas Jefferson University  
Howard University College of Medicine  
Medical College of Wisconsin  
Milton S. Hershey Medical Center, Pennsylvania State University  
Brown Medical School  
University of Minnesota-Minneapolis School of Medicine  
University of Connecticut School of Medicine  
Tufts University School of Medicine  
Universidade Federal Do Rio de Janeiro  
Boston University School of Medicine  
University of Tennessee College of Medicine  
Tufts University School of Medicine  
Wayne State University School of Medicine  
University of Cincinnati College of Medicine  
Royal College of Surgeons of Ireland  
Temple University School of Medicine  
University of Rochester School of Medicine and Dentistry  
Medical College of Virginia of Virginia Commonwealth University  
Brown University School of Medicine  
New York School of Medicine  
Drexel University College of Medicine  
Dartmouth Medical School  
University of Florida College of Medicine  
University of Chicago Pritzker School of Medicine  
Northwestern University- The Feinberg School of Medicine  
University of Puerto Rico School of Medicine  
Rosalind Franklin University of Medicine and Science/Chicago  
University of Medicine & Dentistry of New Jersey  
Boston University School of Medicine  
Medical College of Georgia  
State University of New York at Buffalo School of Medicine  
University of Medicine & Dentistry of New Jersey  
University of Miami School of Medicine  
Northeastern Ohio Universities College of Medicine  
University of Pittsburgh School of Medicine  
SUNY Downstate College of Medicine  
Meharry Medical College School of Medicine  
Universidad Central Del Caribe  
Rush Medical College  
Boston University School of Medicine  
Boston University School of Medicine  
Tulane University School of Medicine  
University of Texas Southwestern Medical School at Dallas  
Tufts University School of Medicine

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Suzuko Suzuki	Boston University School of Medicine
Morsal Tahouni	Boston University School of Medicine
Benjamin Vaghari	Mount Sinai School of Medicine of New York University
Andrew Van Vugt	Boston University School of Medicine
Santosh Varkey	Boston University School of Medicine
Amanda Vest	Imperial College School of Medicine, London
MaryAnn Williamson	University of Medicine & Dentistry of New Jersey
Shruti Wilson	University of Minnesota-Minneapolis School of Medicine
Kar-mun Woo	Columbia University College of Physicians and Surgeons
Megan Young	University of Chicago Pritzker School of Medicine

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## VICE CHAIR PUBLIC HEALTH REPORT

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# PUBLIC HEALTH REPORT



**VICE CHAIR, PUBLIC HEALTH**

*Jeffrey Samet, M.D., M.A., M.P.H.*

As befits a major teaching hospital, the Department of Medicine plays a substantial role in advancing a public health mission. Department faculty members and staff are active in a variety of clinical, teaching, and research projects that address local, state, national, and international public health issues. To fulfill these roles, important relationships have been developed with the Boston Public Health Commission (BPHC), the Massachusetts Department of Public Health (DPH), and the federal government.

Many Department faculty members have secondary appointments at the Boston University School of Public Health (BUSPH), a vibrant institution located on the campus of Boston University Medical Center. Likewise, many BUSPH faculty have secondary appointments in the Department of Medicine. Collaborations among these faculty and staff facilitate a spectrum of public health projects that address the needs of local individuals while creating models of care and prevention.

During the past year, the federal Substance Abuse and Mental Health Services Administration (SAMHSA) awarded a competitive \$14 million grant to the Massachusetts Bureau of Substance Abuse Services. Daniel Alford M.D., M.P.H., Associate Professor of Medicine, is leading this five-year project's \$12 million subcontract to

Boston Medical Center (BMC). Theresa Kim, M.D., Assistant Professor of Medicine, is the Associate Director of this project, which is referred to as MASBIRT (Massachusetts Screening, Brief Intervention and Referral to Treatment). Both of these physicians are members of the Section of General Internal Medicine (GIM). The funding will enable dissemination of screening and brief intervention for alcohol, tobacco, and drug use. Multiple faculty members from BMC and several neighborhood health centers are involved.

Another accomplishment in the public health realm was the appointment of Michele David M.D., M.P.H., M.B.A., Co-Director of the Haitian Health Institute at BMC, Assistant Professor of Medicine, and a member of the Section of GIM, as a member of the Massachusetts Public Health Council. The Public Health Council is the DPH's policy arm and consists of only fourteen members; Dr. David is the designated member from the academic medical centers.

Anita Barry, M.D., M.P.H., Assistant Professor of Medicine, and a member of the Section of Infectious Diseases at BMC, directs municipal public health efforts to address infectious diseases. As Director of Communicable Disease Control for BPHC and Medical Director of the BPHC Tuberculosis Clinic at BMC, she is instrumental in developing the city's emergency preparedness activities. Brant Viner, M.D., Associate Professor of Medicine, and a member of the Section of GIM, and John Bernardo, M.D., Professor of Medicine, Research Professor of Biochemistry, and a member of the Section of Pulmonary, Allergy, and Critical Care Medicine, provide clinical leadership in local and state tuberculosis control efforts. Dr. Bernardo is Tuberculosis Control Officer for DPH.

Department of Medicine faculty members have

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assumed leadership roles in the BPHC. Nancy Norman, M.D., M.P.H., a member of the Section of GIM, serves as the BPHC's Chief Medical Officer and, for a six-month period, was the acting Director. In these roles, she provides leadership for a wide spectrum of Boston's public health campaigns.

Jeffrey Samet, M.D., M.A., M.P.H., Vice Chairman of Medicine for Public Health, Chief of the Section of GIM at BMC, and Professor of Medicine and Public Health, serves as the Medical Director of the Substance Abuse Prevention and Treatment Services Division (SAPTSD) for the BPHC. Other GIM faculty work in SAPTSD. In recent months, Dr. Alford transitioned away from his role as Medical Director of the BPHC's Methadone Treatment Program (MTP), a position he had held for the past decade. During this time, he was chosen by the American Association for the Treatment of Opioid Dependence to receive its national award, the National Nyswander Dole Award, which is given to outstanding individuals for exceptional contributions to the care of patients with opioid dependence.

Sheila Chapman, M.D., Assistant Professor of Medicine, is the Medical Director of the Pregnant Women's Program, the Methadone Maintenance Treatment Program at the Boston Public Health Commission. Sandra Gordon, M.D., Assistant Professor of Medicine, provides care to the patients in the MTP. Alex Walley, M.D., M.Sc., a new member of the GIM, has taken over the role of MTP Director.

The DPH has supported a number of initiatives involving Department faculty at BMC, including support from the AIDS Bureau to promote enhanced HIV testing at BMC. The DPH's Bureau of Substance Abuse Services supports the Department of Medicine and BMC's efforts to enhance current capacity to address the state's opioid-dependence epidemic. These efforts include the promotion, throughout Massachusetts, of the use of buprenorphine, a relatively new medication for this disease. Colleen LaBelle, R.N., from the

Section of GIM, has led this initiative in collaboration with Dr. Alford, Health Care for the Homeless, neighborhood health centers, the BMC's HIV program, and the Department of Family Medicine.

Working with faculty in the Section of GIM Women's Health Unit, the DPH has provided breast cancer screenings to underserved populations. Chava Chapman, M.D., M.P.H., Associate Professor of Medicine, has worked with the Women's Health Network to provide uninsured women with comprehensive cancer screenings.

Many Department of Medicine faculty members are integrated into several of BUSPH's departments, thereby giving BUSPH a strong clinical perspective. BUSPH Dean Robert Meenan, M.D., M.P.H., is a Professor of Medicine at BUSM in the Section of Rheumatology. BUSPH statisticians play integral roles in a wide spectrum of research projects led by Department of Medicine faculty, and many have joint appointments in the Department. Faculty in BUSPH's Departments of Social and Behavioral Sciences, Epidemiology, and Health Policy & Management are active Co-investigators or Principal Investigators of projects involving Department of Medicine faculty. The multiple interrelationships between BUSM's Department of Medicine and the BUSPH faculty add a richness to an environment in which public health issues can be addressed in clinical settings.

Disparity issues in healthcare delivery have been explored by Department faculty. Nancy Kressin, Ph.D., Associate Professor of Medicine in the Section of GIM, has led several initiatives to address disparities in outcomes between racial groups for specific outcomes, such as hypertension.

The international arena provides yet another sphere in which public health issues can be addressed by Department faculty. Drs. Samet and Walley, as well as Debbie Cheng, Ph.D., Associate Professor of Biostatistics at SPH,



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who has a secondary Department of Medicine appointment, are pursuing research concerning HIV prevention in St. Petersburg, Russia.

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## VICE CHAIR RESEARCH REPORT

# RESEARCH SUMMARY



**VICE CHAIR, RESEARCH**  
*Barbara Corkey, Ph.D.*

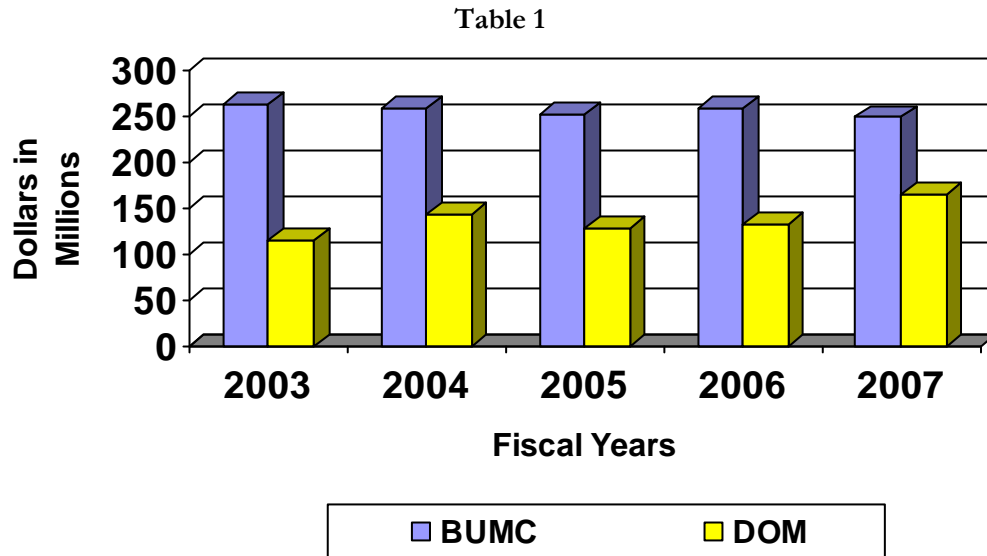
## OVERVIEW OF DEPARTMENT RESEARCH PORTFOLIO

Although competition has been more intense for available research funding for the past several years, FY07 Department of Medicine research base showed a 43% increase. There are several separate institutions to which DOM research funds are awarded based upon where the projects are actually conducted. Table 1 below highlights the number of awards and total dollars by awardee institution for the past three fiscal years.

Table 1

Awardee Institution	FISCAL 2005			FISCAL 2006			FISCAL 2007		
	Awards	Dollars	%	Awards	Dollars	%	Awards	Dollars	%
Boston Medical Ctr	204	55,177,053	43%	196	49,754,876	38%	156	41,477,301	25%
BU Charles River	1	32,349	0%	0	-	0%	0	-	0%
BU Medical Campus	266	68,162,209	53%	242	75,573,999	57%	220	115,058,488	69%
Evans Medical Fdn	2	28,656	0%	1	10,850	0%	3	53,256	0%
Roger Williams Hosp	13	3,051,654	2%	16	4,992,957	4%	18	7,133,573	4%
VA Health System	3	2,244,028	2%	5	2,326,657	2%	2	2,047,307	1%
<b>Total:</b>	<b>489</b>	<b>128,695,950</b>	<b>100%</b>	<b>460</b>	<b>132,659,338</b>	<b>100%</b>	<b>399</b>	<b>165,769,925</b>	<b>100%</b>

**Figure 1: DOM Research Base Compared to BUMC Research Base**



As demonstrated by Figure 1, the DOM research portfolio constitutes a significant portion of the entire BU Medical Campus research portfolio which includes awards to the Schools of Medicine, Dental Medicine, Public Health, and the Boston Medical Center. Please note that BUMC FY2004 does not include the 128M award for the biocontainment laboratory.

In FY02, the Department revised the data analysis methodology for its research base data collection and initiated tracking the number and dollar value of subcontracts funded by DOM research awards. As demonstrated in the table 2 below, for the past five fiscal years, the Department has received over 100 million dollars in research awards in net total cost after subtracting subcontractor costs allocated to other institutions.

**Table 2: Net DOM Research Award Dollars**

Fiscal Year	Total Direct Cost	Number of Subcontracts	Subcontractor Cost	Net Direct Cost	% Change	Net Indirect Cost	Net Total Cost
FY02	81,851,359	107	8,871,465	72,979,894	base year	28,503,647	101,483,541
FY03	85,667,712	110	8,098,692	77,468,210	6%	29,491,922	106,960,132
FY04	105,927,841	138	12,051,271	90,465,596	16%	37,006,045	127,471,641
FY05	97,732,638	131	10,971,050	87,479,562	-10%	30,963,312	118,442,874
FY06	100,110,383	117	9,796,988	92,684,277	6%	32,548,955	125,255,232
FY07	142,660,432	123	9,844,013	132,983,333	43%	32,786,592	165,769,925

The five year trend data which analyzes both sponsor type and research type is based upon total dollars for consistency with data reporting of comparable institutions. Averaged over the past five years, 89% of the DOM research base has been funded by federal sources as shown in table 3

below. Industrial awards have averaged 4%, private foundations 5% and state/city health services delivery awards 2% over the past five years.

**Table 3: Research Base by Sponsor Type**

Year	2003		2004		2005		2006		2007						
Sponsor Type	Total	Cost	% of Total	Total	Cost	% of Total	Total	Cost	% of Total	Total	Cost	% of Total			
Federal	100,385,849		87%	127,053,161		89%	114,534,336		89%	119,432,195		90%	152,867,896		92%
Industry	4,605,424		4%	5,244,783		4%	5,578,688		4%	4,925,278		4%	4,113,496		2%
Private	8,518,151		7%	9,058,317		6%	6,609,901		5%	6,134,295		5%	6,135,683		4%
State/City	1,650,210		1%	1,577,626		1%	1,973,025		2%	2,167,570		2%	2,500,171		2%
Totals:	115,159,634		100%	142,933,885		100%	128,695,950		100%	132,659,338		100%	165,617,246		100%

Figure 2, shows the preponderance of federal funding in the DOM research portfolio.

Although there are thirteen different federal research sponsors which have funded the DOM research portfolio, seven of those twelve are part of the Department of Health and Human Services: Administration on Aging, AHRQ, CDC, DHHS, FDA, HRSA and NIH. It is not surprising in an academic medical center that in FY07, 90% of the federal awards were provided by those DHHS sponsors, principally by NIH, which has funded 86% of the DOM research portfolio for the past five fiscal years. Table 4, on the following page, shows the distribution of DOM federal sponsors.

**Figure 2: DOM Research Portfolio by Sponsor Type**

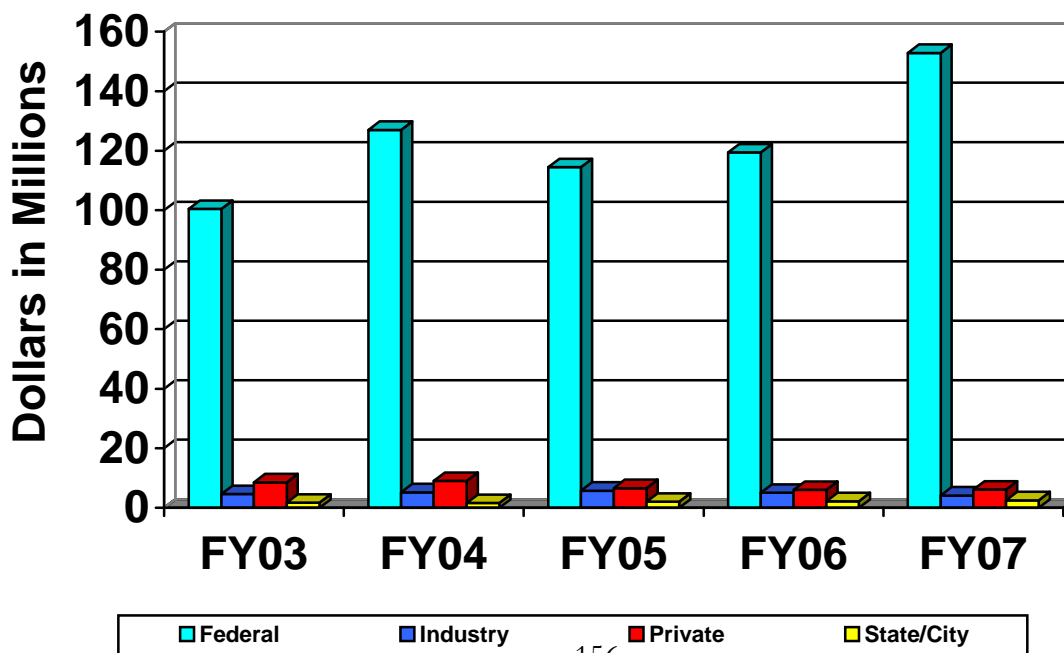


Table 4

Federal Sponsor Name	FY03		FY04		FY05		FY06		FY07	
	No of Awards	% of Total	No of Awards	% of Total	No of Awards	% of Total	No of Awards	% of Total	No of Awards	% of Total
Administraion on Aging (AoA)	-	0.00%	1	0.30%	-	0.00%	-	0.00%	-	0.00%
Agency for Health Care Research & Quality (AHRQ)	1	0.30%	2	0.61%	2	0.64%	2	0.71%	1	0.42%
Center for Disease Control (CDC)	4	1.40%	2	0.61%	3	0.96%	4	1.42%	4	1.67%
Department of Defense (DOD) US Army	12	4.10%	12	3.64%	10	3.21%	9	3.20%	5	2.09%
Department of Education (DOEd)	0	0.00%	0	0.00%	2	0.64%	2	0.71%	2	0.84%
Department of Health & Human Services (DHHS)	5	1.70%	5	1.52%	4	1.28%	3	1.07%	1	0.42%
Food & Drug Administration (FDA)	3	1.00%	1	0.30%	2	0.64%	4	1.42%	5	2.09%
Health Resources & Services Administration (HRSA)	6	2.00%	7	2.12%	9	2.88%	9	3.20%	3	1.26%
National Institutes of Health (NIH)	254	85.80%	286	86.67%	273	87.50%	240	85.41%	213	89.12%
National Aeronautics & Space Administration (NASA)	1	0.30%	1	0.30%	1	0.32%	1	0.36%		0.00%
National Science Foundation (NSF)	1	0.30%	3	0.91%	1	0.32%	1	0.36%		0.00%
Office of Naval Research (ONR)	4	1.40%	4	1.21%	-	0.00%	-	0.00%	-	0.00%
Veterans Administration (VA)	5	1.70%	6	1.82%	5	1.60%	6	2.14%	5	2.09%
<b>Total Federal Awards</b>	<b>296</b>	<b>100%</b>	<b>330</b>	<b>100%</b>	<b>312</b>	<b>100%</b>	<b>281</b>	<b>100%</b>	<b>239</b>	<b>100%</b>

Table 5, on the following page, contains a detailed analysis of DOM NIH awards by funding mechanism and NIH Institute, both for number of awards and net total dollars.



Table 5 below shows the distribution of FY07 DOM NIH awards by award type and NIH Institute.

NIH Institute	FY 07 NIH AWARD TYPE									Total Awards	Net Total** Dollars
	F	K	M	N	P	R	S	T	U		
NCI	-	2			-	17			1	20	5,257,275
NCRR	-	-	1		2	-			1	4	7,252,214
NEI	-	-			-	1			-	1	201,875
NHLBI	-	9			8	41		3	13	74	32,159,333
NIA	-	2			-	15			5	22	8,155,575
NIAAA	-	2			-	5			-	7	2,782,722
NIAID	-	-		2	1	11		1	5	20	71,989,297
NIAMS	-	-		1	1	7			1	10	3,067,530
NICHHD	-	1			-	5			-	6	1,581,239
NIDA	-	2			-	7			-	9	2,760,134
NIDCR	-	-			-	3			2	5	1,127,252
NIDDK	1	3			1	21		2	1	29	6,504,367
NIEHS	-	-				2				2	295,174
NIGMS	-	-				-				-	
NIMH	-	-				1				1	107,446
NINDS	-	-				1				1	661,512
NLM	-	-				-		1		1	161,966
<b>Total</b>	<b>1</b>	<b>21</b>	<b>1</b>	<b>3</b>	<b>13</b>	<b>137</b>	<b>-</b>	<b>7</b>	<b>29</b>	<b>212</b>	<b>144,064,911</b>
Net total by Grant Type \$\$	54,352	3,555,364	2,205,400	1,079,510	17,025,878	43,945,462		3,108,367	73,090,578	144,064,911	
Average Award Size \$\$	54,352	169,303	2,205,400	359,837	1,309,683	320,770		444,052	2,520,365	679,551	

\*\* net = total cost less subcontracts

Not surprisingly, the “R” series of individual, investigator-initiated research grant remains by far the most popular funding mechanism for Department of Medicine investigators. Table 6 shows the number of awards per faculty member.

Table 6

Number of NIH Awards	FY 04		FY 05		FY 06		FY 07	
	No of PI's	% of total	No of PI's	% of total	No of PI's	% of total	No of PI's	% of total
1	75	54%	71	55%	70	56%	66	42%
2	26	19%	22	17%	26	21%	45	28%
3	15	11%	12	9%	15	12%	20	13%
4	13	9%	13	10%	7	6%	8	5%
5	6	4%	7	5%	4	3%	8	5%
6	2	1%	1	1%	2	2%	3	2%
7	2	1%	3	2%	-	0%	2	1%
8	1	1%	1	1%	1	1%	3	2%
9	-	0%	-	0%	1	1%	1	1%
>10	-	0%	-	0%	-	0%	2	1%
<b>Total:</b>	<b>140</b>	<b>100%</b>	<b>130</b>	<b>100%</b>	<b>126</b>	<b>100%</b>	<b>158</b>	<b>100%</b>

Over the past four years, the number of DOM faculty with NIH awards has remained fairly constant. Table 6, to the left, shows the number of faculty by number of NIH awards. The number of faculty with a single award has averaged 53% to 56% of NIH awardees. In FY07, there has been a slight increase in the number of faculty with two and three NIH awards.

DOM faculty are asked to classify their research awards in one of four major categories as outlined in the table below. Over the past five years, basic research has averaged 65% of the DOM research portfolio while clinical research has averaged 25%. Health services research training and career development awards have remained constant at 3% to 4% and 7% to 8% respectively.

**Table 7: Research Portfolio by Research Type**

Year	2003		2004		2005		2006		2007	
Research Type	Total Cost	% of Total	Total Cost	% of Total	Total Cost	% of Total	Total Cost	% of Total	Total Cost	% of Total
Basic	70,681,679	61%	90,754,124	63%	80,810,756	63%	85,847,971	65%	119,250,881	72%
Clinical	30,883,058	27%	37,124,387	26%	33,375,080	26%	33,118,237	25%	37,207,622	22%
Health Svc	4,478,884	4%	3,812,389	3%	5,049,602	4%	3,755,142	3%	2,466,421	1%
Training	9,116,013	8%	11,242,985	8%	9,460,512	7%	9,937,989	7%	6,845,002	4%
Totals:	115,159,634	100%	142,933,885	100%	128,695,950	100%	132,659,338	100%	165,769,926	100%

**Figure 3: DOM Research Portfolio by Research Type**

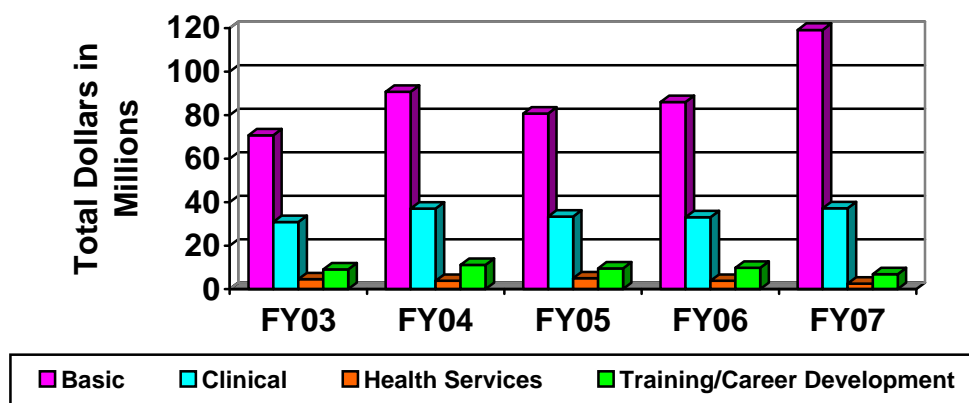


Figure 3 shows the growth of basic research over the past four years with a 6% increase in FY07.

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## PILOT PROJECT GRANT PROGRAM

The goal of the DOM Pilot Project one-year grant program is to explore new, currently unfunded avenues of research with the goal of acquiring sufficient preliminary data to apply for extramural funding. Applicants must have a full-time faculty appointment in the DOM to be eligible to apply for pilot project funding. Awards range from \$ 10,000 to \$ 25,000 and can be used for any purpose except faculty salary support. Funding criteria include the following:

- (1) expectation that the project will lead to a fundable extramural grant application
- (2) the project fosters inter-sectional collaboration
- (3) the project advances existing DOM research programs.

In FY07, there were a total of 27 applications submitted for review by the Research Review Committee which functions as NIH-type internal study section. Ten awards, to eight different Sections, were funded at \$ 15,000 each for a total DOM financial commitment of \$ 150,000. FY2007 Pilot Project Recipients are listed in the table 8 below.

**Table 8**

<b>Awardee</b>	<b>Section</b>	<b>Project Title</b>
Laurence Beck, MD, PhD	Renal	Identification of the membranous nephropathy antigen(s)
Yan Dai, PhD	Cancer Research Center	Molecular Mechanisms mediating resistance to androgen antagonists
Caroline Genco, PhD	Infectious Disease	The role of Nod Proteins in macrophages and endothelial cell activation
Elaine Hylek, MD, MPH	General Internal Medicine	The effect of rapid heart rate on endothelial function and thrombogenicity
Guangmu, Li, MD	Renal	Identification of interacting proteins for ATP6V1B2 as a novel survival factor
Paola Massari, PhD	Infectious Disease	Effect of <i>N. lactamica</i> porin porB on cell activation
Ross Summer, MD	Pulmonary	Adiponectin in the lung
Ellen Weinberg, PhD	CVI	Role of Interlukin-33 in ST2 receptor signaling
Michael Wolfe, MD	Gastroenterology	Immunologic mechanisms mediating the effects of NSAIDS on colorectal cancer
Xuemei Zhong, PhD	Immunobiology	Study of heart specific immune regulation in autoimmune myocarditis

Table 9 below displays Pilot Project demographics for fiscal years 2002 through 2007.

**Table 9: Pilot Project Award Data**

Fiscal Year	APPLICATIONS		AWARDS					
	Submitted	Awarded	Amount	Total Amount	MD	PhD	MD, PhD	Other**
FY 02	34	11	15,000	\$165,000	7	3		1*
FY 03	22	9	\$ 15,000	\$ 135,000	4	3	2	
FY 04	22	11	\$ 14,000	\$ 154,000	5	3	2	1*
FY 05	38	10	\$ 14,000	\$ 140,000	5	3	3+	
FY 06	31	8	\$ 15,000	\$ 120,000	4	1	2	1
FY 07	27	10	15,000	\$150,000	3	5	1	1
<b>Total</b>	<b>174</b>	<b>59</b>	<b>N/A</b>	<b>\$ 864,000</b>	<b>28</b>	<b>18</b>	<b>10</b>	<b>3</b>

\*\* = Other includes DSc and MD, MPH.

\* = Same faculty member received two separate awards in two different fiscal years.

+ = Two faculty members collaborating on one pilot project.

The DOM makes a significant financial investment in the pilot project program as noted in the chart above. Through the competitive award process, fifteen DOM Sections have received pilot project grants during fiscal years 2002 through 2007 as outlined in table 10 below.

**Table 10: Pilot Project Distribution by Section**

Section Name	FY02	FY03	FY04	FY 05	FY06	FY07	Total Awards	Total Dollars
Cancer Research Center	1	1				1	3	\$ 45,000
Cardiovascular Medicine	1		1	1.5	1		4.5	\$65,000
Cardiovascular Institute		1				1	2	\$ 30,000
Clinical Epidemiology & Training Unit				1			1	\$ 14,000
Endocrinology	1	1	2		.5		4.5	\$ 65,500
Gastroenterology	2	1	1	1	2	1	8	\$118,000
General Internal Medicine		1	2		1	1	5	\$ 73,000
Geriatrics			1		1		2	\$ 29,000
Hematology-Oncology	1		1	1.5			3.5	\$ 50,000
Immunobiology	1					1	2	\$30,000
Infectious Disease	2			1		2	5	\$ 74,000
Molecular Medicine/Genetics Unit		1	1		1		3	\$ 44,000
Molecular Medicine/Obesity Center				1	.5		1.5	\$ 21,500
Nephrology	1	1		1	1	2	6	\$ 89,000
Preventive Medicine & Epidemiology	1		1				2	\$ 29,000
Pulmonary		1	1	1		1	4	\$ 58,000
Rheumatology		1		1			2	\$ 29,000
<b>TOTAL AWARDS</b>	<b>11</b>	<b>9</b>	<b>11</b>	<b>10</b>	<b>8</b>	<b>10</b>	<b>59</b>	<b>\$ 864,000</b>

At the conclusion of their grant, each pilot project recipient is required to submit an NIH style progress report describing their research findings as well as grant proposals submitted, papers or abstracts prepared, and new collaborations or mentoring relationships facilitated by the funds provided. From FY02 through FY07, additional extramural funding resulting from pilot project

awards totals: \$ 5,314,604 direct cost dollars plus \$ 1,687,122 indirect cost dollars for a total of \$7,001,726.

The outcomes from FY02 through FY07 pilot project recipients are highlighted in table 11.

**Table 11: Pilot Project Outcomes FY02 – FY07**

Publications		Grant Applications		New Collaborations	Trainees
In preparation	12	Pending	1	New collaborations initiated = 41	Technical Staff, Graduate students or post-docs mentored = 14
Papers	30	Not Funded	27		
Abstracts	34	Funded	27		

### EVANS SEMINAR SERIES

In the twelfth annual Evans Seminar series, there were a total of eight seminars given by guest faculty from a variety of research institutions. These visiting scientists, listed below, met with faculty and trainees and presented talks on a variety of topics.

**Table 12: Evans Seminar Speakers**

Date	Speaker	Topic	Institution
12/14/06	C. Ronald Kahn, MD	Insulin signaling and diabetes	Joslin Diabetes Center, Harvard Medical School
12/21/06	David Altshuler MD, PhD	Genetic basis of disease	Broad Institute of Harvard and Massachusetts Institute of Technology, Harvard Medical School
1/18/07	Paul Ridker, MD	Epidemiology of vascular disease and inflammation	Brigham Women's Hospital, Harvard Medical School
2/22/07	Michael Welsh, MD	Cystic fibrosis	University of Iowa, Carver College of Medicine
3/8/07	Joseph Sodroski, PhD	HIV infection and Virology	Dana-Farber Cancer Institute, Harvard Medical School
4/12/07	Mark Gladwin, MD,	Nitric oxide biology, hemoglobin	National Heart Lung Blood Institute
5/17/07	Stefan Somlo, MD	Polycystic kidney disease	Yale University School of Medicine
5/31/07	Aravinda Chakravarti, PhD	Genetic basis of disease, population genetics	Johns Hopkins, Bloomberg School of Public Health

### EVANS DAYS

Evans Days were held November 1 through November 3, 2006. Program events were orchestrated by Vice Chair for Research, John F. Keaney, Jr. MD, his staff and Debbie Hall. This annual three-day event highlights both the clinical and basic research accomplishments of Department of Medicine faculty. There are both poster sessions and oral presentations where faculty and trainees can share their knowledge with one another and with the distinguished visiting faculty. The Ingelfinger Visiting Professor (clinical science) was Bradford Berk, M.D., PhD, Chairman Department of Medicine, University of Rochester School of Medicine. The Wilkins Visiting Professor (basic science) was Richard Lifton, M.D., PhD. Chairman, Genetics Department, and Yale University. Both visiting



professors met with faculty and trainees to discuss a variety of research topics.

## MAJOR ACCOMPLISHMENTS

Despite slower growth of NIH grant resources, DOM faculty have continued to successfully compete for research funding. In FY 07, noteworthy new research awards as well as competing renewals are listed in table 13 below.

**Table 13: New FY07 DOM ROI Research Awards**

Investigator	Section	Sponsor & Award #	Project Period	Total Cost	Project Title
Emelia Benjamin	Cardiovasc Med	AG028321	09/1/06 06/30/11	\$ 1,099,007	Aging and Inflammation: Longitudinal Markers and Genetics in the Framingham Study
Lindsay Farrer	Molecular Medicine	AG25259 01A2	9/22/06 8/31/11	\$1,681,062	Multi-ethnic Genome-wide Alzheimers Association
David Felson	Clin Epi & Training	AR62668 01	9/30/05 8/31/11	\$ 1,707,891	Relation of Alignment and Other Risk Factors to Knee OA
Jane Freedman	Cardiovasc Med	HL087201	4/1/07 11/3/10	\$ 1,671,379	Gene Expression and Thrombosis in a Community Based Cohort Study
Robert Friedman	GIM	HL081380-01A1	7/1/06 4/30/10	\$ 2,478,193	Improving Dietary Behavior Through Tailored Messages
Frank Gibson	Infectious Diseases	DE018318-01	2/1/06 1/31/10	\$ 1,610,000	Infections-Elicited Oral Bone Loss: TLR2, Ontogeny and Porphyromonas Gingivalis
Noyan Gokce	Cardiovasc Med	HL084213	2/20/07 1/31/12	\$ 1494283	Inflammation and Vascular Dysfunction in Obesity
Jining Lu	Pulmonary	HL081800	5/1/06 2/28/11	\$ 1,098,900	MicroRNA-mediated Gene Regulation in Lung Development
Marisa Ramirez	Pulmonary	HL083034	7/1/06 6/30/11	\$ 1,250,000	Lung Alveolar Type I Cell Morphogenesis
Jeffrey Samet	GIM	AA16059	7/1/05 6/30/09	\$ 2,599,711	Maximizing Opportunity-HIV Prevention in Hospitalized Russian Drinkers
Vita, Joseph	Cardiology	HL083269	9/1/06 6/30/10	\$1,220,629	Determinants of Shear Stress Mediated Arterial Remodeling
Kenneth Walsh	CVI	HL86785	7/1/06 6/30/11	\$ 1,250,000	Molecular Control of Myo/Angiogenesis

## New FY07 DOM R21 Research Awards

Investigator	Section	Sponsor & Award #	Project Period	Total Cost	Project Title
Alan Fine	Pulmonary	HL082778	8/1/06 6/30/08	\$ 275,000	Characterization of a Lung Mesenchymal Progenitor Cell
Darrell Kotton	Pulmonary	HL086414	9/30/06 7/31/08	\$ 275,000	Cell-specific Delivery of RNAi to Pulmonary Alveolar Macrophages in vivo
Lynn Moore	Prev Med & Epi	DK75068 01A1	4/1/07 3/31/09	\$ 288,145	Dietary Patterns, Obesity, and Associated Metabolic Outcomes in Adolescents

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## GRANTS

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## CANCER CENTER

### Gerald Denis

Cancer Center

Agency: American Cancer Society

Project Title: Molecular Analysis of BRD2 Signaling and B Cell Function

Total Direct Cost: \$600,000 1/1/2005 - 12/31/2008

Direct Cost Current Year: \$150,000

### Gerald Denis

Cancer Center

Agency: NCI

Project Title: Proteomic Biomarkers for Lymphoma

Total Direct Cost: \$100,000 6/1/2007 - 5/31/2009

Direct Cost Current Year: \$50,000

### Douglas Faller

Cancer Center

Agency: NCI

Project Title: Signal Transduction by Androgen Antagonists in Prostate Cancer

Total Direct Cost: \$676,898 7/1/2004 - 4/30/2008

Direct Cost Current Year: \$188,752

### Douglas Faller

Cancer Center

Agency: NCI

Project Title: Ras Oncoprotein-Targeted Therapy For Cancer

Total Direct Cost: \$952,157 9/1/2005 - 6/30/2010

Direct Cost Current Year: \$195,180

### Douglas Faller

Cancer Center

Agency: Department of Defense- Army

Project Title: Targeting The Telomere as a Therapeutic Approach To Prostate Cancer

Total Direct Cost: \$281,250 3/1/2006 - 2/28/2009

Direct Cost Current Year: \$93,750

### Susan Perrine

Cancer Center

Agency: NIDDK

Project Title: Novel Globin Gene Modulators

Total Direct Cost: \$1,404,831 6/1/2003 - 5/31/2008

Direct Cost Current Year: \$205,343

### Susan Perrine

Cancer Center

Agency: NHLBI

Project Title: Sickle Cell - Butyrate Study

Total Direct Cost: \$695,881 7/1/2003 - 3/31/2008

Direct Cost Current Year: \$150,627

### Douglas Faller

Cancer Center

Agency: American Association for Cancer Research

Project Title: PKC-DELTA as a Therapeutic Target in Colon Cancer

Total Direct Cost: \$231,482 7/1/2006 - 6/30/2008

Direct Cost Current Year: \$115,741

## CARDIOVASCULAR MEDICINE

### Emelia J. Benjamin

Cardiovasc Med

Agency: NIA

Project Title: Aging and Inflammation: Longitudinal Markers and Genetics in the Framingham Study

Total Direct Cost: \$1,099,007 9/1/2006 - 6/30/2011

Direct Cost Current Year: \$223,406

### Emelia J. Benjamin

Cardiovasc Med

Agency: NHLBI

Project Title: Framingham: Inflammation, Genes & Cardiovascular Disease

Total Direct Cost: \$1,988,794 6/1/2004 - 5/31/2009

Direct Cost Current Year: \$487,615

### Kai Chi

Cardiovasc Med

Agency: American Heart Association

Project Title: Molecular and Functional Analysis of Endothelial

Total Direct Cost: \$236,364 7/1/2003 - 6/30/2007

Direct Cost Current Year: \$59,091

### Wilson Colucci

Cardiovasc Med

Agency: NHLBI

Project Title: Mechanisms of Oxidant Signaling in Post-MI Remodeling

Total Direct Cost: \$1,250,000 12/1/2003 - 11/30/2007

Direct Cost Current Year: \$250,000

### Wilson Colucci

Cardiovasc Med

Agency: NHLBI

Project Title: ACTION-A CHF Trial Investigating Outcomes of Exercise

Total Direct Cost: \$901,423 9/30/2002 - 7/31/2008

Direct Cost Current Year: \$104,767

### Wilson Colucci

Cardiovasc Med

Agency: ACG

Project Title: The Impact of Patient Education on IBS

Total Direct Cost: \$150,000 7/1/2006 - 6/30/2008

Direct Cost Current Year: \$75,000

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**Ravin Davidoff**

Cardiovasc Med  
Agency: BUSM  
Project Title: Cardiology Course  
Total Direct Cost: \$24,388 7/1/2006 - 6/30/2007  
Direct Cost Current Year: \$24,388

**Jane Freedman**

Cardiovasc Med  
Agency: NHLBI  
Project Title: Multidisciplinary Training in Cardiovascular Research  
Total Direct Cost: \$3,313,920 7/1/2006 - 6/30/2011  
Direct Cost Current Year: \$662,784

**Jane Freedman**

Cardiovasc Med  
Agency: PDL  
Project Title: A randomized, double blind, multicenter study of visilizumab versus placebo in subjects with intervenous steroid refractory ulcerative colitis previously responsive in visilizumab study  
Total Direct Cost: \$1,650 3/29/2006 - 2/28/2011  
Direct Cost Current Year: \$1,650

**Jane Freedman**

Cardiovasc Med  
Agency: NHLBI  
Project Title: Gene Expression and Thrombosis in a Community Based Cohort Study  
Total Direct Cost: \$1,671,379 4/1/2007 - 11/30/3010  
Direct Cost Current Year: \$439,676

**Noyan Gokce**

Cardiovasc Med  
Agency: NHLBI  
Project Title: Inflammation and Vascular IDysfunction in Obesity  
Total Direct Cost: \$1,494,283 2/20/2007 - 1/31/2012  
Direct Cost Current Year: \$286,292

**Noyan Gokce**

Cardiovasc Med  
Agency: NHLBI  
Project Title: Obesity, Adipocytokines, and Endothelial Dysfunction  
Total Direct Cost: \$1,378,373 8/15/2003 - 7/31/2008  
Direct Cost Current Year: \$292,368

**Naomi Hamburg**

Cardiovasc Med  
Agency: ACC/Merck  
Project Title: Effects of Physical Inactivity on Insulin Sensitivity and Vascular Function  
Total Direct Cost: \$60,000 7/1/2006 - 6/30/2007  
Direct Cost Current Year: \$60,000

**Alice K. Jacobs**

Cardiovasc Med  
Agency: NHLBI Arginox Pharmaceuticals  
Project Title: SHOCK II Phase 2 Trial  
Total Direct Cost: \$5,923 11/1/2003 - 10/30/2006  
Direct Cost Current Year: \$385

**Alice K. Jacobs**

Cardiovasc Med  
Agency: NHLBI  
Project Title: BARI 2D  
Total Direct Cost: \$208,556 6/1/2001 - 5/31/2008  
Direct Cost Current Year: \$44,595

**Alice K. Jacobs**

Cardiovasc Med  
Agency: NHLBI St. Luke's-Roosevelt Hospital  
Project Title: Occluded Artery Trial (OAT)  
Total Direct Cost: \$17,000 2/1/2001 - 10/31/2007  
Direct Cost Current Year: \$345

**Alice K. Jacobs**

Cardiovasc Med  
Agency: NHLBI  
Project Title: BARI PTCA Registry  
Total Direct Cost: \$135,606 7/1/1997 - 6/30/2009  
Direct Cost Current Year: \$10,850

**Alice K. Jacobs**

Cardiovasc Med  
Agency: Intermune Pharmaceuticals, 007  
Project Title: IPF Study-007  
Total Direct Cost: \$107,335 1/1/2004 - 12/31/2009  
Direct Cost Current Year: \$21,467

**John F. Keaney**

Cardiovasc Med  
Agency: NIA  
Project Title: NOX Isoforms and Vascular Cell Phenotype  
Total Direct Cost: \$1,000,000 2/15/2005 - 1/31/2010  
Direct Cost Current Year: \$195,300

**John F. Keaney**

Cardiovasc Med  
Agency: NHLBI  
Project Title: Endothelial Redox State & Phenotype in Health & Disease  
Total Direct Cost: \$8,378,700 9/1/2005 - 9/1/2010  
Direct Cost Current Year: \$1,173,042

**John F. Keaney**

Cardiovasc Med  
Agency: NHLBI  
Project Title: Hypoclorite-Mediated Impairment of endothelial  
Total Direct Cost: \$1,250,000 3/15/2003 - 2/28/2008  
Direct Cost Current Year: \$244,125

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**Michael K. Klein**

Cardiovasc Med  
Agency: AstraZeneca  
Project Title: Knee Osteoarthritis MRI Semi-Quantitative Scoring  
Total Direct Cost: \$12,864 10/29/2004 - 3/31/2005  
Direct Cost Current Year: \$12,649

**Kevin M. Monahan**

Cardiovasc Med  
Agency: Luitpold  
Project Title: Phase III Study of Taxorexin Injection vs. Dacarbazine in Patients with Metastatic Malignant Melanoma  
Total Direct Cost: \$15,500 8/1/2006 - 7/31/2009  
Direct Cost Current Year: \$6,100

**Kevin M. Monahan**

Cardiovasc Med  
Agency: Guidant Corp  
Project Title: REASSURE  
Total Direct Cost: \$29,535 9/1/2004 - 8/31/2008  
Direct Cost Current Year: \$922

**Kevin M. Monahan**

Cardiovasc Med  
Agency: Guidant Corp  
Project Title: PEGASUS CRT Study  
Total Direct Cost: \$13,835 6/1/2005 - 6/30/2008  
Direct Cost Current Year: \$1,308

**David R. Pimentel**

Cardiovasc Med  
Agency: NHLBI  
Project Title: Ventricular Remodeling from H2O2 in Mechanical Overload  
Total Direct Cost: \$587,000 9/30/2005 - 8/31/2010  
Direct Cost Current Year: \$117,400

**Flora Sam**

Cardiovasc Med  
Agency: NHLBI  
Project Title: Role of Aldosterone in Cardiac Remodelling  
Total Direct Cost: \$1,000,000 6/1/2005 - 4/30/2009  
Direct Cost Current Year: \$195,300

**Deborah Siwik**

Cardiovasc Med  
Agency: American Heart Association  
Project Title: Role of EMMPRIN in Hydrogen Peroxide Stimulated Matrix  
Total Direct Cost: \$236,364 7/1/2003 - 6/30/2007  
Direct Cost Current Year: \$59,091

**Joseph A. Vita**

Cardiovasc Med  
Agency: NHLBI  
Project Title: Clinical Utility of Endothelial Function in PAD  
Total Direct Cost: \$3,215,055 9/22/2003 - 8/31/2008  
Direct Cost Current Year: \$617,508

**Joseph A. Vita**

Cardiovasc Med  
Agency: NHLBI  
Project Title: BUMC Leadership Program in Vascular Medicine  
Total Direct Cost: \$3,721,665 2/8/2007 - 1/31/2012  
Direct Cost Current Year: \$349,969

**Joseph Vita**

Cardiovasc Med  
Agency: NHLBI  
Project Title: Determinants of Shear Stress Mediated Arterial Remodeling  
Total Direct Cost: \$1,220,629 9/1/2006 - 6/30/2010  
Direct Cost Current Year: \$294,181

**Joseph Vita**

Cardiovasc Med  
Agency: NHLBI  
Project Title: Vascular Consequences of Insulin Resistance and Obesity  
Total Direct Cost: \$7,075,655 5/1/2005 - 4/30/2011  
Direct Cost Current Year: \$1,242,286

**Joseph Vita**

Cardiovasc Med  
Agency: Ocean Spray  
Project Title: Effects of Cranberry Juice on Endothelial Function in Patients with CAD  
Total Direct Cost: \$33,566 7/1/2006 - 6/30/2007  
Direct Cost Current Year: \$33,566

**Cardiology**

Cardiovasc Med  
Agency: Abbott Laboratories  
Project Title: Levosimendan: Mechanisms of Action in chronic myocardial failure  
Total Direct Cost: \$202,500 7/24/2006 - 12/31/2007  
Direct Cost Current Year: \$101,250

**Cardiology**

Cardiovasc Med  
Agency: Donations  
Project Title: Research donations  
Total Direct Cost: \$1,265 7/1/2006 - 6/30/2007  
Direct Cost Current Year: \$1,265

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## CLINICAL EPIDEMIOLOGY RESEARCH AND TRAINING UNIT

### **Saralynn Allaire**

Clin Epi & Training

Agency: DOE

Project Title: Development of Materials and Methods Needed to Deliver a Proven Job Retention Vocational Rehabilitation

Total Direct Cost: \$245,839 11/1/2004 - 10/31/2008

Direct Cost Current Year: \$81,946

### **Saralynn Allaire**

Clin Epi & Training

Agency: American College of Rheumatology

Project Title: Meeting Job Accommodation Needs: A Tool for Rehabilitation Professionals to use with Patients with Rheumatic Disease

Total Direct Cost: \$100,000 7/1/2005 - 6/30/2008

Direct Cost Current Year: \$50,000

### **Kristin Baker**

Clin Epi & Training

Agency:

Project Title: The Relationship of n-3 Fatty Acids with Pain & Synovium in Knee OA

Total Direct Cost: \$475,000 7/11/2006 - 6/30/2010

Direct Cost Current Year: \$118,750

### **Kristin Baker**

Clin Epi & Training

Agency: Arthritis Foundation

Project Title: Long Term Strength Training for Knee Osteoarthritis: Can We Improve Upon Adherence

Total Direct Cost: \$97,221 1/1/2005 - 12/31/2007

Direct Cost Current Year: \$48,610

### **Per M. England**

Clin Epi & Training

Agency: Arthritis Foundation

Project Title: The Role of Meniscal Pathology in Incident and Progressive Knee OA

Total Direct Cost: \$100,000 7/1/2006 - 6/30/2008

Direct Cost Current Year: \$50,000

### **David Felson**

Clin Epi & Training

Agency: Arthritis Foundation

Project Title: Activities, Anatomic Abnormalities, Disability and Cartilage Loss in the Knee

Total Direct Cost: \$154,209 7/1/2002 - 12/31/2006

Direct Cost Current Year: \$38,552

### **David Felson**

Clin Epi & Training

Agency: Arthritis Foundation

Project Title: Correlates of Articular Cartilage Volume and Thickness in Framingham Subjects

Total Direct Cost: \$324,690 9/1/2001 - 8/31/2006

Direct Cost Current Year: \$54,115

### **David Felson**

Clin Epi & Training

Agency: Arthritis Foundation

Project Title: Effective Vitamin K Supplementation on OA

Total Direct Cost: \$185,186 1/1/2005 - 12/31/2007

Direct Cost Current Year: \$44,752

### **David Felson**

Clin Epi & Training

Agency: NIA

Project Title: The Framingham Osteoarthritis Study

Total Direct Cost: \$3,806,730 7/1/2000 - 4/30/2008

Direct Cost Current Year: \$96,892

### **David Felson**

Clin Epi & Training

Agency: NIA

Project Title: Multicenter Osteoarthritis Study (MOST)

Total Direct Cost: \$1,908,242 9/30/2001 - 6/30/2008

Direct Cost Current Year: \$719,500

### **David Felson**

Clin Epi & Training

Agency: NIAMS

Project Title: Data Coordinating for Osteoarthritis Initiative

Total Direct Cost: \$288,550 7/1/2002 - 6/30/2009

Direct Cost Current Year: \$41,221

### **David Felson**

Clin Epi & Training

Agency: NIAMS

Project Title: Multidisciplinary Clinical Research Center at Boston University

Total Direct Cost: \$3,367,214 9/24/2001 - 8/31/2011

Direct Cost Current Year: \$660,776

### **David Felson**

Clin Epi & Training

Agency: NIAMS

Project Title: (BOAMRI) Biomarkers in Osteoarthritis MRI Studies

Total Direct Cost: \$930,343 9/30/2003 - 8/31/2007

Direct Cost Current Year: \$148,807

### **David Felson**

Clin Epi & Training

Agency: NIAMS

Project Title: Structural Correlates of Knee Pain

Total Direct Cost: \$813,548 8/11/2006 - 7/31/2009

Direct Cost Current Year: \$200,363



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**David Felson**

Clin Epi & Training  
Agency: NIAMS  
Project Title: Relation of Alignment and Other Risk Factors to Knee OA  
Total Direct Cost: \$1,707,891 9/22/2006 - 8/31/2011  
Direct Cost Current Year: \$189,201

**David Felson**

Clin Epi & Training  
Agency: NICHD  
Project Title: Laxity and Malalignment in a Large Cohort Study of OA  
Total Direct Cost: \$155,007 9/26/2002 - 8/31/2007  
Direct Cost Current Year: \$31,001

**David Felson**

Clin Epi & Training  
Agency: NHLBI  
Project Title: Boston University Clinical Research Training (CREST) Program  
Total Direct Cost: \$1,399,450 6/1/1999 - 5/31/2010  
Direct Cost Current Year: \$279,890

**David Felson**

Clin Epi & Training  
Agency: NIA  
Project Title: Inflammation and Knee Osteoarthritis  
Total Direct Cost: \$247,620 9/30/2006 - 6/30/2011  
Direct Cost Current Year: \$27,054

**David Felson**

Clin Epi & Training  
Agency: ATC, Limited  
Project Title: Pulmonomics Laboratory Fund  
Total Direct Cost: \$53,127 2/1/2006- -  
Direct Cost Current Year: \$53,127

**David Felson**

Clin Epi & Training  
Agency: Scois, Inc  
Project Title: Clinical Trail  
Total Direct Cost: \$25,200 2/1/2003 - 12/31/2006  
Direct Cost Current Year: \$25,200

**Kevin D Gross**

Clin Epi & Training  
Agency: Arthritis Foundation  
Project Title: Foot Structure and Knee Pain, Function, and Cartilage Thickness  
Total Direct Cost: \$100,000 7/1/2006 - 6/30/2008  
Direct Cost Current Year: \$50,000

**David Hunter**

Clin Epi & Training  
Agency: Merck & Co.  
Project Title: Analysis of FIT for Osteophytes  
Total Direct Cost: \$26,446 5/7/2004 - 5/6/2006  
Direct Cost Current Year: \$24,105

**David Hunter**

Clin Epi & Training  
Agency: Pfizer Inc.  
Project Title: Osteoarthritis, Comorbidity and Disability  
Total Direct Cost: \$72,727 1/1/2002 - 12/1/2004  
Direct Cost Current Year: \$72,727

**David Hunter**

Clin Epi & Training  
Agency: Momenta  
Project Title: Inhibition of Thrombosis in Atherosclerosis Mouse Model  
Total Direct Cost: \$59,675 1/31/2007 - 1/31/2008  
Direct Cost Current Year: \$59,675

**David Hunter**

Clin Epi & Training  
Agency: Novartis  
Project Title: A randomized, double blind, placebo controlled, multicenter phase II/III study to evaluate the efficacy and safety of tegaserod  
Total Direct Cost: \$12,814 4/10/2006 - 7/10/2008  
Direct Cost Current Year: \$12,814

**David Hunter**

Clin Epi & Training  
Agency: OJ Grant/MinuteMaid  
Project Title: OJ Grant/MinuteMaid contract w/ BU  
Total Direct Cost: \$80,000 9/1/2006 - 9/1/2007  
Direct Cost Current Year: \$80,000

**David Hunter**

Clin Epi & Training  
Agency: Wallace H. Coulter  
Project Title: Knee Osteoarthritis Brace  
Total Direct Cost: \$76,203 4/1/2007 - 3/31/2008  
Direct Cost Current Year: \$19,050

**David Hunter**

Clin Epi & Training  
Agency: Intermune Pharm 006  
Project Title: IPF Study-006  
Total Direct Cost: \$19,231 1/1/2004 - 1/1/2009  
Direct Cost Current Year: \$3,846

**David Hunter**

Clin Epi & Training  
Agency: DOE  
Project Title: A Randomized Trial of Realignment Therapy for Treatment of Medial Knee OA - NIDRR  
Total Direct Cost: \$346,155 12/1/2004 - 11/30/2007  
Direct Cost Current Year: \$115,385

**Leonid Kalichman**

Clin Epi & Training  
Agency: Arthritis Foundation  
Project Title: Posterior Column Disorders and Low Back Pain: The Framingham Study  
Total Direct Cost: \$100,000 7/1/2006 - 6/30/2008  
Direct Cost Current Year: \$50,000

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**Tuhina Neogi**

Clin Epi & Training

Agency: NIAMS

Project Title: Predictors and Consequences of  
Subchondral Bone Attrition in Osteoarthritis

Total Direct Cost: \$504,479 7/1/2007 - 6/30/2012

Direct Cost Current Year: \$7,504

**Tuhina Neogi**

Clin Epi & Training

Agency: Abbott Labs

Project Title: Vitamin K Deficiency, Chondrocalcinosis,  
and Osteoarthritis-Abbott

Total Direct Cost: \$231,000 7/1/2004 - 6/30/2007

Direct Cost Current Year: \$82,000

**Yuquing Zhang**

Clin Epi & Training

Agency: American College of Rheumatology

Project Title: Alcohol Consumption, Statin Use and  
Risk of Repeat Gout Attacks - ACR

Total Direct Cost: \$100,000 7/1/2005 - 6/30/2007

Direct Cost Current Year: \$50,000

**Yuquing Zhang**

Clin Epi & Training

Agency: Roche

Project Title: A Randomized, controlled, open label  
study of CERA in patients

Total Direct Cost: \$119,740 2/1/2005 - 1/31/2007

Direct Cost Current Year: \$59,870

**Yuquing Zhang**

Clin Epi & Training

Agency: Keryx Biopharmaceut.

Project Title: The effect of sulodexide in overt type 2  
diabetic nephropathy

Total Direct Cost: \$91,035 10/3/2005 - 9/2/2009

Direct Cost Current Year: \$22,759

**WHITAKER CARDIOVASCULAR INSTITUTE****Kenneth Walsh**

CVI

Agency: NIA

Project Title: Regulation OF Vessel Wall Apoptosis

Total Direct Cost: \$1,250,000 2/1/2003 - 12/31/2007

Direct Cost Current Year: \$250,000

**Kenneth Walsh**

CVI

Agency: NHLBI

Project Title: Endothelial Redox State & Phenotype in  
Health & Disease

Total Direct Cost: \$8,378,700 9/1/2005 - 8/31/2010

Direct Cost Current Year: \$1,173,042

**Kenneth Walsh**

CVI

Agency: NHLBI

Project Title: Signaling Pathways in Heart Failure

Total Direct Cost: \$1,926,984 3/1/2005 - 2/28/2010

Direct Cost Current Year: \$385,061

**Kenneth Walsh**

CVI

Agency: NHLBI

Project Title: Molecular Control of Myo/Angiogenesis

Total Direct Cost: \$1,250,000 7/1/2006 - 6/30/2011

Direct Cost Current Year: \$250,000

**ENDOCRINOLOGY, DIABETES, AND  
NUTRITION****Caroline Apovian**

Endocrinology

Agency: Orexigen Therapeutics

Project Title: Orexigen

Total Direct Cost: \$78,530 5/17/2006 - 5/16/2008

Direct Cost Current Year: \$39,265

**Caroline Apovian**

Endocrinology

Agency: Eli Lilly

Project Title: Exenatide

Total Direct Cost: \$90,219 10/27/2006 - 10/26/2007

Direct Cost Current Year: \$90,219

**Caroline Apovian**

Endocrinology

Agency: Sanofil-Aventis

Project Title: Victoria

Total Direct Cost: \$153,937 2/1/2006 - 2/28/2008

Direct Cost Current Year: \$76,969

**Michael Holick**

Endocrinology

Agency: Randy Kendricks

Project Title: Evaluation of Vitamin D or Ultraviolet  
irradiation in men with metastatic prostate cancer

Total Direct Cost: \$180,000 3/1/2007 - 3/1/2009

Direct Cost Current Year:

**Shalender Bhasin**

Endocrinology

Agency: Merck

Project Title: Determination of Minimal Clinically  
Important Differences in Physical Function Measures in  
Older Individuals

Total Direct Cost: \$392,966.00 4/1/2007 - 3/31/2008

Direct Cost Current Year: 392966

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**Shalender Bhasin**

Endocrinology  
Agency: Ardana  
Project Title: ARD-0403-AAA  
Total Direct Cost: \$175,205.00 10/24/2006 - 10/23/2007  
Direct Cost Current Year: 175205

**Shalender Bhasin**

Endocrinology  
Agency: Solvay Pharmaceutical  
Project Title: TEEAM Study  
Total Direct Cost: \$833,334 11/4/2005 - 10/1/2009  
Direct Cost Current Year: \$333,333

**Shalender Bhasin**

Endocrinology  
Agency: CDC  
Project Title: Generation of Reference Limits for Total Testosterone Levels  
Total Direct Cost: 398413 3/1/2007 - 2/28/2008  
Direct Cost Current Year: 395413

**Shalender Bhasin**

Endocrinology  
Agency:  
Project Title: Testosterone Dose Response in Surgically Menopause Women  
Total Direct Cost: \$250,000 10/1/2006 - 7/31/2008  
Direct Cost Current Year: \$125,000

**Shalender Bhasin**

Endocrinology  
Agency: NIA  
Project Title: Testosterone Supplementation for Aging-Associated Sarcopenia  
Total Direct Cost: \$2,287,101 7/1/1997 - 2/28/2010  
Direct Cost Current Year: \$404,983

**Shalender Bhasin**

Endocrinology  
Agency: NIDDK  
Project Title: Mechanisms of Testosterone Effects on Body Composition  
Total Direct Cost: \$1,175,000 9/30/2004 - 6/30/2008  
Direct Cost Current Year: \$235,000

**Shalender Bhasin**

Endocrinology  
Agency: NICHD  
Project Title: Role of 5-Alpha Reductase in Testosterone Action  
Total Direct Cost: \$707,246 4/1/2003 - 3/31/2008  
Direct Cost Current Year: \$225,000

**Shalender Bhasin**

Endocrinology  
Agency: NICHD  
Project Title: Testosterone Modulation of Response to Phosphodiesterase  
Total Direct Cost: \$1,050,300 9/7/2005 - 7/31/2010  
Direct Cost Current Year: \$206,719

**Wen Guo**

Endocrinology  
Agency: NIDDK  
Project Title: Lipid Metabolism in Fat Cells  
Total Direct Cost: \$920,000 6/1/2000 - 12/31/2010  
Direct Cost Current Year: \$184,000

**Michael Holick**

Endocrinology  
Agency: Natl Dairy Council  
Project Title: Dietary calcium and vitamin D on prostate cancer  
Total Direct Cost: \$80,000 3/1/2007 - 3/1/2010  
Direct Cost Current Year: \$80,000

**Michael Holick**

Endocrinology  
Agency: NIAMS  
Project Title: Photobiology of Vitamin D  
Total Direct Cost: \$910,000 4/15/2002 - 3/31/2007  
Direct Cost Current Year: \$235,000

**Michael Holick**

Endocrinology  
Agency: UCB  
Project Title: Phase IIIB multicenter, double blind, placebo controlled, randomized trial to examine the corticosteroid-sparing effects of certolizumab pegol in patients with moderate to severe crohn's disease  
Total Direct Cost: \$5,385 11/1/2006 - 11/5/2008  
Direct Cost Current Year: \$5,385

**Elizabeth Pearce**

Endocrinology  
Agency: NIDDK  
Project Title: Cardiovascular Consequences of Thyroid Dysfunction  
Total Direct Cost: \$587,000 7/1/2003 - 6/30/2008  
Direct Cost Current Year: \$117,400

**Rahul Ray**

Endocrinology  
Agency: National Dairy  
Project Title: Dietary calcium and vitamin D on prostate cancer  
Total Direct Cost: \$375,000 9/30/2005 - 9/29/2008  
Direct Cost Current Year: \$125,000

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**Sayon Roy**

Endocrinology

Agency: NEI

Project Title: Thickening of Basement Membrane in Diabetic Retinopathy

Total Direct Cost: \$490,000 1/1/2004 - 12/31/2007

Direct Cost Current Year: \$125,000

**Neil Ruderman**

Endocrinology

Agency: NIDDK

Project Title: AMPK and Mechanisms of Glucose Toxicity

Total Direct Cost: \$950,000 3/1/2006 - 2/28/2011

Direct Cost Current Year: \$117,458

**Neil Ruderman**

Endocrinology

Agency: NIDDK

Project Title: Nutrient and Hormonal Regulations of AMPK and Malonyl CoA

Total Direct Cost: \$1,035,000 2/15/2006 - 11/30/2010

Direct Cost Current Year: \$174,726

**Neil Ruderman**

Endocrinology

Agency: NHLBI

Project Title: Oxidative Stress, AMPK &amp; Diabetic Cardiovascular Disease

Total Direct Cost: \$4,518,502 5/1/2003 - 4/30/2008

Direct Cost Current Year: \$900,760

**Neil Ruderman**

Endocrinology

Agency: Sanofi

Project Title: AMPK as a mediator of the actions of cannabinoids and rimonabant

Total Direct Cost: \$130,000 9/1/2006 - 2/28/2008

Direct Cost Current Year: \$86,667

**Neil Ruderman**

Endocrinology

Agency: NIDDK

Project Title: Metabolism, Endocrinology and Obesity Training Grant

Total Direct Cost: \$2,708,435 5/15/1998 - 4/30/2008

Direct Cost Current Year: \$310,749

**Michael Holick/Ray Rahul**

Endocrinology

Agency: NCI STTR Grant/IGI

Project Title: PTH (7-34) for Chemotherapy Alopecia in Breast Cancer

Total Direct Cost: \$88,106 11/1/2006 - 10/31/2007

Direct Cost Current Year: \$88,106

**GASTROENTEROLOGY****Francis Farraye**

Gastroenterology

Agency: Aspreva

Project Title: Mycophenolate Mofetil in Systemic Sclerosis

Total Direct Cost: \$21,824 11/1/2006 - 10/31/2007

Direct Cost Current Year: \$21,824

**Francis Farraye**

Gastroenterology

Agency: Actelion

Project Title: Biomarkers of Pulmonary Hypertension in Systemic SCLEROSIS

Total Direct Cost: \$39,423 7/1/2006 - 7/19/2011

Direct Cost Current Year: \$39,423

**Francis Farraye**

Gastroenterology

Agency: Genentech

Project Title: Rituximab in Scleroderma

Total Direct Cost: \$72,915 4/1/2004 - 4/30/2007

Direct Cost Current Year: \$72,915

**Francis Farraye**

Gastroenterology

Agency: Mediquest

Project Title: Phase III in life study of a topical gel formulation of nitroglycerin, MQX-503 and matching placebo gel....

Total Direct Cost: \$10,476 1/1/2007 - 6/30/2007

Direct Cost Current Year: \$10,476

**Francis Farraye**

Gastroenterology

Agency: Scleroderma Foundation

Project Title: The Role Of Anti-Centromere Antibodies In Stimulation Of Toll-Like Receptor 9 In Systemic Sclerosis

Total Direct Cost: \$138,888 1/1/2007 - 12/31/2009

Direct Cost Current Year: \$46,296

**Albena Halpert**

Gastroenterology

Agency: PDL

Project Title: A randomized, double blind, multicenter does exploration study of visilizumab in subjects with intervenous steroid refractory ulcerative colitis

Total Direct Cost: \$7,625 3/29/2006 - 2/28/2011

Direct Cost Current Year: \$7,625

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**Albena Halpert**

Gastroenterology

Agency: PDL

Project Title: An observational follow-up study for subjects receiving salvage therapy after treatment in a visilizumab study for IV steroid refractory ulcerative colitis

Total Direct Cost: \$1,175 2/1/2006 - 2/10/2011

Direct Cost Current Year: \$1,175

**Brian Jacobson**

Gastroenterology

Agency: Intermune PIPF-004

Project Title: IPF Study PIPF 004

Total Direct Cost: \$113,612 8/21/2006 - 12/31/2008

Direct Cost Current Year: \$56,806

**Brian Jacobson**

Gastroenterology

Agency: NIDDK

Project Title: Risk Factors for Barrett's Esophagus

Total Direct Cost: \$593,565 5/1/2005 - 4/30/2010

Direct Cost Current Year: \$105,313

**Thomas Moore**

Gastroenterology

Agency: NIDDK

Project Title: Definition of the Physiological Properties of GIP Supplement

Total Direct Cost: \$210,415 7/1/2004 - 6/30/2008

Direct Cost Current Year: \$58,893

**David Nunes**

Gastroenterology

Agency: Dairy Management, Inc

Project Title: Effects of Early Dairy Intake on Adolescent Bone Density and Content

Total Direct Cost: \$50,000 4/1/2006 - 12/31/2006

Direct Cost Current Year: \$50,000

**David Nunes**

Gastroenterology

Agency: Bristol Myers Squibb

Project Title: A study to describe the safety and antiviral effects of Entecavir (ETV) in blacks/african americans and hispanics with chronic hepatitis b virus who are nucleoside/tide naïve

Total Direct Cost: \$1,538 10/17/2006 - 10/16/2008

Direct Cost Current Year: \$1,538

**David Nunes**

Gastroenterology

Agency: Novelos

Project Title: A Phase IB Trial To Evaluate Safety And Pharmacokinetics Of NOV 205 In Chronic Viral Hepatitis C Subjects, Genotype I, Who Have Failed Treatment With Pegylated Interferon And Ribavirin.

Total Direct Cost: \$2,692 1/1/2007 - 1/11/2008

Direct Cost Current Year: \$2,692

**Gwynneth Offner**

Gastroenterology

Agency: NIDDK

Project Title: Structure and Function of Human Salivary Mucins

Total Direct Cost: \$1,335,265 8/1/1996 - 5/31/2010

Direct Cost Current Year: \$208,727

**Gwynneth Offner**

Gastroenterology

Agency: NIDCR

Project Title: Membrane bound mucins in salivary glands and saliva

Total Direct Cost: \$970,000 4/1/2006 - 3/31/2011

Direct Cost Current Year: \$194,000

**Paul Schroy**

Gastroenterology

Agency: AHRQ

Project Title: Shared Decision Making for Colorectal Cancer Screen

Total Direct Cost: \$1,779,550 9/30/2003 - 9/29/2008

Direct Cost Current Year: \$229,548

**Paul Schroy**

Gastroenterology

Agency: Johnson &amp; Johnson

Project Title: An Open Label, Phase 1/2 Study of Velcade for Injection in Subjects with Light Chain Amyloidosis

Total Direct Cost: \$24,909 5/20/2005 - 3/31/2008

Direct Cost Current Year: \$15,450

**Paul Schroy**

Gastroenterology

Agency: Exact Sciences

Project Title: Effect of Sample Storage Conditions on the Detection of Colorectal Neoplasia by Stool Based DNA Technology Advances

Total Direct Cost: \$24,768 1/1/2004 - 12/31/2007

Direct Cost Current Year: \$24,768

**Satish Singh**

Gastroenterology

Agency: BU Coulter

Project Title: Partnership in Biomedical Engineering: Microfluidic cell lysis and nucleic acid isolation for point of care detection of C. difficile

Total Direct Cost: \$27,918 4/1/2006 - 9/30/2007

Direct Cost Current Year: \$27,918

**Satish Singh**

Gastroenterology

Agency: BU Coulter

Project Title: Partnership in Biomedical Engineering: Optically Guided diagnosis and treatment for colonic and bladder cancers

Total Direct Cost: \$49,800 4/1/2006 - 9/30/2007

Direct Cost Current Year: \$49,800

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**Satish Singh**

Gastroenterology

Agency: BU Coulter

Project Title: Partnership in Biomedical Engineering:  
Flourescence Endomicroscopy with out of focus  
background rejection

Total Direct Cost: \$17,386 4/1/2007 - 3/31/2008

Direct Cost Current Year: \$17,386

**Satish Singh**

Gastroenterology

Agency: BU Coulter

Project Title: Partnership in Biomedical Engineering:  
Development of a biopsy targeting for the surveillance  
of Barrett's esophagus

Total Direct Cost: \$45,024 4/1/2007 - 3/31/2008

Direct Cost Current Year: \$45,024

**Diane Song**

Gastroenterology

Agency: NIDDK

Project Title: Characterization of GIP signaling in  
adipocytes

Total Direct Cost: \$157,476 2/15/2005 - 2/14/2008

Direct Cost Current Year: \$54,352

**H. Christian Weber**

Gastroenterology

Agency: ACG

Project Title: Racial Factors in Symptom Patterns

Total Direct Cost: \$5,000 7/1/2006 - 6/30/2007

Direct Cost Current Year: \$5,000

**Michael Wolfe**

Gastroenterology

Agency: NCI

Project Title: Role of Gastrin in the pathogenesis of  
colorectal cancer

Total Direct Cost: \$753,750 4/5/2006 - 3/31/2009

Direct Cost Current Year: \$157,434

**Michael Wolfe**

Gastroenterology

Agency: NIDDK

Project Title: Def of the Physiological Properties of  
GIP

Total Direct Cost: \$900,000 7/1/2003 - 6/30/2008

Direct Cost Current Year: \$172,108

**GENERAL INTERNAL MEDICINE****Daniel Alford**

Gen'l Internal Med

Agency: SAMHSA

Project Title: Massachusetts Screening and Brief  
Intervention

Total Direct Cost: \$8,464,514 9/15/2006 - 8/14/2011

Direct Cost Current Year: \$1,511,422

**Tracy Battaglia**

Gen'l Internal Med

Agency: Avon Products Fdt.

Project Title: Measuring What Navigators do Task and  
Social Network Analysis

Total Direct Cost: \$472,885 2/1/2007 - 1/31/2009

Direct Cost Current Year: \$144,140

**Tracy Battaglia**

Gen'l Internal Med

Agency: Komen Breast C Fdt.

Project Title: Improving Mammography Follow-up at  
an Inner City Community Health

Total Direct Cost: \$210,560 5/1/2005 - 4/30/2008

Direct Cost Current Year: \$50,313

**Chava Chapman**

Gen'l Internal Med

Agency: Mass DPH

Project Title: WHN Breast &amp; cervical Cancer Screening

Total Direct Cost: \$270,746 7/1/2001 - 6/30/2006

Direct Cost Current Year: \$63,158

**Chava Chapman**

Gen'l Internal Med

Agency: Susan Komen Breast Cancer Fdt.

Project Title: Reach Out

Total Direct Cost: \$111,089 3/1/1999 - 3/31/2008

Direct Cost Current Year: \$13,636

**Haakon Chevalier**

Gen'l Internal Med

Agency: VA

Project Title: Telehealth Intervention to Promote  
Diabetes Prevention

Total Direct Cost: \$93,081 8/1/2006 - 9/30/2008

Direct Cost Current Year: \$23,696

**Michele David**

Gen'l Internal Med

Agency: Columbia University

Project Title: Physician Advocacy Fellowship

Total Direct Cost: \$164,581 7/1/2006 - 6/30/2008

Direct Cost Current Year: \$81,104

**Michele David**

Gen'l Internal Med

Agency: Johnson &amp; Johnson

Project Title: Fostering Excellence in Women's Health  
through Academic-Community Partnership

Total Direct Cost: \$175,135 7/1/2006 - 6/30/2009

Direct Cost Current Year: \$32,365

**Leyda Delgado**

Gen'l Internal Med

Agency: Sub C, NEMC

Project Title: Explaining Disparities in Care of Older  
Patients

Total Direct Cost: \$32,588 7/14/2004 - 6/30/2007

Direct Cost Current Year: \$14,056



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**Ramesh Farzanfar**

Gen'l Internal Med

Agency: CDC

Project Title: Automated Assessment of Mental Health in the Work Place

Total Direct Cost: \$891,902 9/30/2004 - 9/29/2007

Direct Cost Current Year: \$258,095

**Ramesh Farzanfar**

Gen'l Internal Med

Agency: NIMH Sub-C Harvard Pilgrim Health Care

Project Title: A System for Management of Depression in Medical Illness

Total Direct Cost: \$291,867 9/1/2004 - 5/31/2009

Direct Cost Current Year: \$62,906

**Karen Freund**

Gen'l Internal Med

Agency: Dimagi, Inc.

Project Title: A System to Coordinate and Track Home Based Chronic Care in Patients with Cancer

Total Direct Cost: \$4,550 11/15/2006 - 5/14/2007

Direct Cost Current Year: \$4,550

**Karen Freund**

Gen'l Internal Med

Agency: Avon Products Fdt.

Project Title: Patient Navigation and Coordination: The BMC AVON Initiative

Total Direct Cost: \$2,377,819 4/1/2001 - 3/31/2009

Direct Cost Current Year: \$270,000

**Karen Freund**

Gen'l Internal Med

Agency: NCI

Project Title: Patient Navigation in the Safety

Net:CONNECTeDD

Total Direct Cost: \$2,754,356 9/30/2005 - 8/31/2010

Direct Cost Current Year: \$464,603

**Karen Freund**

Gen'l Internal Med

Agency: DHHS

Project Title: CoE/CCOE--Ambassadors for Change Program

Total Direct Cost: \$15,385 9/1/2006 - 8/31/2007

Direct Cost Current Year: \$15,385

**Karen Freund**

Gen'l Internal Med

Agency: FDA

Project Title: Use and Outcomes of Coronary Stents in Women

Total Direct Cost: \$105,655 9/30/2004 - 9/29/2008

Direct Cost Current Year: \$31,075

**Robert Friedman**

Gen'l Internal Med

Agency: NLM

Project Title: Biomedical and Health Informatics

Research Training

Total Direct Cost: \$761,816 7/1/2002 - 6/30/2007

Direct Cost Current Year: \$154,224

**Robert Friedman**

Gen'l Internal Med

Agency: NIAAA

Project Title: Telecom & Bibliography Programs for Problem Drinkers

Total Direct Cost: \$913,391 9/1/2005 - 5/31/2008

Direct Cost Current Year: \$316,209

**Robert Friedman**

Gen'l Internal Med

Agency: NIA

Project Title: Telecom Tech to Improve Adherence to Medication

Total Direct Cost: \$2,426,289 7/15/2002 - 6/30/2007

Direct Cost Current Year: \$449,506

**Robert Friedman**

Gen'l Internal Med

Agency: NCI

Project Title: Trial of 2 TeleComputer Diet Change Maintenance Programs

Total Direct Cost: \$2,021,181 9/1/2004 - 8/31/2009

Direct Cost Current Year: \$216,756

**Robert Friedman**

Gen'l Internal Med

Agency: NCI

Project Title: Trial of 2 TeleComputer Diet Change Maintenance Programs-Minority Supplement

Total Direct Cost: \$185,698 9/1/2005 - 6/30/2007

Direct Cost Current Year: \$91,723

**Robert Friedman**

Gen'l Internal Med

Agency: NHLBI

Project Title: Improving Dietary Behavior Through Tailored Messages

Total Direct Cost: \$2,478,193 7/1/2006 - 4/30/2010

Direct Cost Current Year: \$362,092

**Robert Friedman**

Gen'l Internal Med

Agency: HRSA

Project Title: National Research Service Award for Research Training in Primary Medical Care

Total Direct Cost: \$2,985,298 7/1/1998 - 6/30/2008

Direct Cost Current Year: \$425,910

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**Angela Jackson**

Gen'l Internal Med

Agency: HRSA

Project Title: Primary Care Training Program for Residents

Total Direct Cost: \$422,137 9/1/2004 - 6/30/2007

Direct Cost Current Year: \$115,567

**Nancy Kressin**

Gen'l Internal Med

Agency: NIDCR Sub-C NYU

Project Title: Center for Research to Reduce Oral Health Disparities

Total Direct Cost: \$18,275 8/1/2006 - 7/31/2007

Direct Cost Current Year: \$18,275

**Nancy Kressin**

Gen'l Internal Med

Agency: NHLBI

Project Title: Hypertension Control & Therapy Adherence

Total Direct Cost: \$684,870 2/1/2006 - 1/31/2008

Direct Cost Current Year: \$298,034

**Jane Liebschutz**

Gen'l Internal Med

Agency: American Cancer Society

Project Title: BU Preventive Medicine Residency Program

Total Direct Cost: \$300,000 1/1/2005 - 12/31/2008

Direct Cost Current Year: \$100,000

**Jane Liebschutz**

Gen'l Internal Med

Agency: NIDA

Project Title: Substance Abuse, Post-Traumatic Stress, Chronic Pain in Primary Care Setting

Total Direct Cost: \$866,120 7/25/2004 - 6/30/2009

Direct Cost Current Year: \$205,113

**Kevin Ludena**

Gen'l Internal Med

Agency: VA

Project Title: Telehealth Intervention to Promote Diabetes Prevention

Total Direct Cost: \$93,081 8/1/2006 - 9/30/2006

Direct Cost Current Year: \$44,461

**Frank Perna**

Gen'l Internal Med

Agency: NIDA Sub-C Harvard Dental School

Project Title: Exercise and Nicotine Replacement for Female Smokers

Total Direct Cost: \$179,145 4/1/2006 - 3/31/2008

Direct Cost Current Year: \$101,126

**Richard Saitz**

Gen'l Internal Med

Agency: NIAAA

Project Title: Linkage of Alcohol Abusers to Primary Care

Total Direct Cost: \$2,882,672 9/30/2005 - 8/31/2010

Direct Cost Current Year: \$575,761

**Richard Saitz**

Gen'l Internal Med

Agency: Sub C, U. of Pittsburgh

Project Title: Patient and Societal Utilities for Alcohol Problems

Total Direct Cost: \$29,296 9/28/2004 - 8/31/2008

Direct Cost Current Year: \$7,361

**Jeffrey Samet**

Gen'l Internal Med

Agency: NIDA

Project Title: Enhanced Linkage of Drug Abusers to Primary Medical Care

Total Direct Cost: \$2,125,975 4/20/2006 - 3/31/2011

Direct Cost Current Year: \$440,047

**Jeffrey Samet**

Gen'l Internal Med

Agency: NIAAA

Project Title: Impact of Alcohol Use on HIV Infection- In the United States and Russia

Total Direct Cost: \$699,655 9/30/2006 - 8/31/2011

Direct Cost Current Year: \$140,264

**Jeffrey Samet**

Gen'l Internal Med

Agency: NIDA Sub-C University of Alabama

Project Title: Homeless Persons Use of Addiction Treatment Services

Total Direct Cost: \$63,676 12/3/2002 - 8/31/2007

Direct Cost Current Year: \$13,277

**Jeffrey Samet**

Gen'l Internal Med

Agency: NIDA

Project Title: Clinical Addiction Research and Education (CARE) Program

Total Direct Cost: \$1,562,423 9/20/2006 - 4/30/2011

Direct Cost Current Year: \$594,904

**Jeffrey Samet**

Gen'l Internal Med

Agency: NIAAA

Project Title: Maximizing Opportunity-HIV Prevention in Hospitalized Russian Drinkers

Total Direct Cost: \$2,599,711 9/30/2006 - 8/31/2011

Direct Cost Current Year: \$226,662

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**Jeffrey Samet**

Gen'l Internal Med  
Agency: BPHC  
Project Title: Office Based Methadone  
Total Direct Cost: \$1,335,285 12/1/2002 - 6/30/2007  
Direct Cost Current Year: \$455,827

**Jeffrey Samet**

Gen'l Internal Med  
Agency: BPHC  
Project Title: Methadone Program-Res Nurse  
Total Direct Cost: \$274,391 7/1/2002 - 6/30/2007  
Direct Cost Current Year: \$61,058

**Jeffrey Samet**

Gen'l Internal Med  
Agency: BPHC  
Project Title: Substance Abuse Program  
Total Direct Cost: \$290,970 7/1/2004 - 6/30/2007  
Direct Cost Current Year: \$137,536

**Julie Wright**

Gen'l Internal Med  
Agency: NCI  
Project Title: Pediatric Behavioral Informatics to Prevent Cancer  
Total Direct Cost: \$606,093 9/1/2006 - 8/31/2011  
Direct Cost Current Year: \$116,898

**Julie Wright**

Gen'l Internal Med  
Agency: Robert Wood Johnson Fdt.  
Project Title: Improving Health Behaviors through Linked Telephone Care  
Total Direct Cost: \$102,941 7/1/2005 - 6/30/2007  
Direct Cost Current Year: \$21,958

**GERIATRICS****James Kirkland**

Geriatrics  
Agency: NIA  
Project Title: Regional Differences in Preadipocyte Development  
Total Direct Cost: \$1,238,250 9/30/2003 - 8/31/2008  
Direct Cost Current Year: \$244,125

**James Kirkland**

Geriatrics  
Agency: NIA  
Project Title: Regional Differences in Preadipocyte Development Supplement  
Total Direct Cost: \$186,336 9/15/2006 - 8/31/2008  
Direct Cost Current Year: \$93,168

**Sharon Levine**

Geriatrics  
Agency: Donald W. Reynolds Foundation  
Project Title: BUMC Comprehensive Geriatric Education Project  
Total Direct Cost: \$1,677,611 11/1/2003 - 10/31/2007  
Direct Cost Current Year: \$396,066

**Thomas Perls**

Geriatrics  
Agency: NIA  
Project Title: Exceptional survival and longevity in New England  
Total Direct Cost: \$2,720,350 9/1/2004 - 5/31/2009  
Direct Cost Current Year: \$488,285

**Thomas Perls**

Geriatrics  
Agency: NIH  
Project Title: Characterizing Human Exceptional Longevity  
Total Direct Cost: \$634,180 3/1/2006 - 1/31/2011  
Direct Cost Current Year: \$123,015

**Rebecca Silliman**

Geriatrics  
Agency: NCI  
Project Title: Cancer Control in Older Adults  
Total Direct Cost: \$1,286,792 7/5/2001 - 6/30/2011  
Direct Cost Current Year: \$137,563

**Rebecca Silliman**

Geriatrics  
Agency: NIH  
Project Title: Impact of Breast Cancer on Older Survivors  
Total Direct Cost: \$931,970 9/1/2004 - 6/30/2009  
Direct Cost Current Year: \$180,164

**Rebecca Silliman**

Geriatrics  
Agency: NICHD  
Project Title: BU Interdisciplinary Research Careers in Women's Health  
Total Direct Cost: \$2,318,558 9/26/2002 - 7/31/2007  
Direct Cost Current Year: \$453,692

**Rebecca Silliman**

Geriatrics  
Agency: John A. Hartford, Fnd.  
Project Title: Center of Excellence in Geriatrics  
Total Direct Cost: \$272,727 4/1/2004 - 3/31/2007  
Direct Cost Current Year: \$49,915

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**Rebecca Silliman**

Geriatrics

Agency: John A. Hartford, Fnd.

Project Title: Redesigning Long-Term Care Services for Urban Vulnerable Elders

Total Direct Cost: \$140,909 1/3/2006 - 12/31/2007

Direct Cost Current Year: \$84,004

**Rebecca Silliman**

Geriatrics

Agency: NIA

Project Title: Summer Institute in Geriatric Medicine

Total Direct Cost: \$190,000 5/1/2006 - 4/30/2011

Direct Cost Current Year: \$36,317

**Dellara Terry**

Geriatrics

Agency: NIA

Project Title: Centenarian Offspring and Vascular Disease Resistance

Total Direct Cost: \$600,000 9/1/2005 - 7/31/2008

Direct Cost Current Year: \$200,000

**HEMATOLOGY AND MEDICAL ONCOLOGY****Karen Antman**

Hem/Oncology

Agency: NCRR GCRC

Project Title: General Clinical Research Center

Total Direct Cost: \$2,800,000 11/6/1997 - 11/30/2011

Direct Cost Current Year: \$2,205,400

**David Chui**

Hem/Oncology

Agency: NHLBI

Project Title: Genetic Modulation of HbF in Beta

Thalassemia

Total Direct Cost: \$1,857,167 9/30/2005 - 8/31/2010

Direct Cost Current Year: \$28,423

**Rita Blanchard**

Hem/Oncology

Agency: Industry

Project Title: Educational funds

Total Direct Cost: \$212,589 7/1/2006 - 6/30/2007

Direct Cost Current Year: \$212,589

**Katherine Gere**

Hem/Oncology

Agency: Boston Foundation

Project Title: Patient Navigation Services at BMC's Medical Oncology Clinic

Total Direct Cost: \$100,000 4/1/2005 - 3/31/2007

Direct Cost Current Year: \$50,000

**Kevan Hartshorn**

Hem/Oncology

Agency: NHLBI

Project Title: Novel Genetically Targeted Antibodies

Total Direct Cost: \$140,000 7/1/2006 - 6/30/2008

Direct Cost Current Year: \$70,000

**Kevan Hartshorn**

Hem/Oncology

Agency: NHLBI

Project Title: Enhancing Collectin-Mediated Defense Against Influenza

Total Direct Cost: \$1,293,300 4/1/2006 - 3/31/2011

Direct Cost Current Year: \$220,410

**Adam Lerner**

Hem/Oncology

Agency: Logica Foundation

Project Title: Tamoxifen Resistance in Breast Cancer

Total Direct Cost: \$484,500 1/1/2007 - 12/31/2010

Direct Cost Current Year: \$90,909

**Adam Lerner**

Hem/Oncology

Agency: NCI

Project Title: C-AMP Mediated Apoptosis in Lymphoid Malignancies

Total Direct Cost: \$768,783 7/1/2005 - 6/30/2010

Direct Cost Current Year: \$154,287

**Adam Lerner**

Hem/Oncology

Agency: IMPROVIT

Project Title: IMPROVE IT

Total Direct Cost: \$65,450 1/20/2006 - 1/20/2010

Direct Cost Current Year: \$2,768

**Adam Lerner**

Hem/Oncology

Agency: Genmab

Project Title: Double Blind, Randomized, 2 Dose parallel Group, MultiCenter Clinical Trial of HuMax-CD4, a Fully Human Monoclonal Anti-CD4 Antibody, in Patients with Mycosis Fungoides type CTCL who are Refractory or Intolerant to Targretin and one other Standard Therapy.

Total Direct Cost: \$16,108 7/1/2006 - 6/30/2008

Direct Cost Current Year: \$11,151

**Adam Lerner**

Hem/Oncology

Agency: Gloucester

Project Title: A Single Agent Phase II Study of Depsipeptide (FK228) in the Treatment of CTCL

Total Direct Cost: \$63,685 4/1/2006 - 12/31/2008

Direct Cost Current Year: \$63,695

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**Adam Lerner**

Hem/Oncology  
Agency: NHLBI  
Project Title: Research Training in Blood Diseases and Resources  
Total Direct Cost: \$1,942,970 7/1/2003 - 6/30/2008  
Direct Cost Current Year: \$394,378

**Adam Lerner**

Hem/Oncology  
Agency: NCI  
Project Title: Analysis of AND-34 in Human Breast Cancer  
Total Direct Cost: \$745,554 7/1/2005 - 6/30/2009  
Direct Cost Current Year: \$146,963

**Qiangzhong Ma**

Hematology/Oncology  
Agency: -- Prostate Cancer Foundation  
Project Title: 2005 Prostate Cancer Foundation Award  
Total Direct Cost: \$25,000 3/3/2006 - 3/2/2007  
Direct Cost Current Year: \$25,000

**Lillian McMahon**

Hem/Oncology  
Agency: NHLBI  
Project Title: Boston Sickle Cell Research Consortium Clinical Research Network Grant  
Total Direct Cost: \$573,078 4/1/2006 - 3/31/2011  
Direct Cost Current Year: \$71,799

**Carol Rosenberg**

Hem/Oncology  
Agency: NIH  
Project Title: Genetic Signatures of Preinvasive  
Total Direct Cost: \$230,000 1/1/2007 - 12/31/2009  
Direct Cost Current Year: \$60,000

**Carol Rosenberg**

Hem/Oncology  
Agency: Department of Defense  
Project Title: Allele Imbalance or loss of heterozygosity  
Total Direct Cost: \$300,000 7/1/2006 - 6/30/2009  
Direct Cost Current Year: \$100,000

**Carol Rosenberg**

Hem/Oncology  
Agency: Department of Defense  
Project Title: Quantitative DNA Fingerprinting to Distinguish New Primary Breast Cancers from Recurrent Disease  
Total Direct Cost: \$413,970 6/1/2006 - 5/31/2008  
Direct Cost Current Year: \$206,985

**Vaishali Sanchorawala**

Hem/Oncology  
Agency: Hoffmann-La Roche, Inc.  
Project Title: Randomized, Multicenter, double blinded, phase IV study comparing the safety and efficacy of PEGASYS 180 ug plus COPEGUS 1000 or 1200  
Total Direct Cost: \$15,160 6/16/2006 - 4/30/2009  
Direct Cost Current Year: \$15,160

**David Seldin**

Hem/Oncology  
Agency: NHLBI  
Project Title: Multistep Lymphomagenesis Tumorigenesis in Transgenic Mice  
Total Direct Cost: \$957,000 5/1/2006 - 4/30/2011  
Direct Cost Current Year: \$159,500

**David Seldin**

Hem/Oncology  
Agency: NHLBI  
Project Title: Multistep Lymphomagenesis Tumorigenesis in Transgenic Mice  
Total Direct Cost: \$198,080 5/1/2006 - 4/30/2007  
Direct Cost Current Year: \$198,080

**David Seldin**

Hem/Oncology  
Agency: Avon Foundation  
Project Title: Protein Kinase CK2: Identification of Regulatory Signaling Pathways & Development of CK2 inhibitors with Potential for Therapeutic use  
Total Direct Cost: \$295,454 6/1/2007 - 6/30/2009  
Direct Cost Current Year: \$113,636

**Martin H Steinberg**

Hem/Oncology  
Agency: NHLBI  
Project Title: Comprehensive Sickle Cell Center  
Total Direct Cost: \$6,781,351 4/1/2003 - 3/31/2008  
Direct Cost Current Year: \$482,067

**Martin H Steinberg**

Hem/Oncology  
Agency: NHLBI  
Project Title: Comprehensive Sickle Cell Center  
Total Direct Cost: \$6,781,351 4/1/2008 - 3/31/2013  
Direct Cost Current Year: \$160,689

**Martin H Steinberg**

Hem/Oncology  
Agency: NHLBI  
Project Title: Genetic Modulation of Sickle Cell Anemia  
Total Direct Cost: \$2,628,593 9/30/2001 - 7/31/2006  
Direct Cost Current Year: \$499,975

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**Xuemei Zhong**

Hem/Oncology

Agency: American Heart Association

Project Title: Probing the Role of Inflammatory

Total Direct Cost: \$183,512 1/1/2006 - 12/31/2011

Direct Cost Current Year: \$36,702

**HYPERTENSION****Haralambos Gavras**

Hypertension

Agency: NHLBI

Project Title: Mouse models of heart, lung, and blood disease

Total Direct Cost: \$36,272 8/1/2006 - 7/31/2007

Direct Cost Current Year: \$36,272

**Haralambos Gavras**

Hypertension

Agency: Apotex Inc

Project Title: Protocols for Testing Ace

Total Direct Cost: \$78,700 3/15/2007 -

Direct Cost Current Year: \$78,700

**Haralambos Gavras**

Hypertension

Agency: Boehringer Ingelheim

Project Title: Effects of Telmisaran on Cardiac ...

Total Direct Cost: \$45,727 11/1/2006 - 12/31/2007

Direct Cost Current Year: \$45,727

**INFECTIOUS DISEASES****Frank Gibson**

Infectious Diseases

Agency: NIDCR

Project Title: The Role of P. gingivalis Capsule in Cell Inflammation

Total Direct Cost: \$750,000 5/1/2003 - 1/31/2008

Direct Cost Current Year: \$146,475

**Frank Gibson**

Infectious Diseases

Agency: NIDCR

Project Title: Infections-Elicited Oral Bone Loss: TLR2, Ontogeny and Porphyromonas Gingivalis

Total Direct Cost: \$1,000,000 4/1/2007 - 3/31/2011

Direct Cost Current Year: \$200,000

**Andrew Henderson**

Infectious Diseases

Agency: NIAID

Project Title: Regulation of HIV by T-Cell Signal Transduction

Total Direct Cost: \$351,041 5/1/2005 - 1/31/2009

Direct Cost Current Year: \$82,512

**Robin Ingalls**

Infectious Diseases

Agency: NIAID

Project Title: Innate Immune Receptors in Host Responses to Neisseria

Total Direct Cost: \$1,096,240 1/15/2000 - 1/31/2010

Direct Cost Current Year: \$171,468

**Robin Ingalls**

Infectious Diseases

Agency: NIAID

Project Title: Interaction of Chlamydia with Innate Immune Receptors

Total Direct Cost: \$1,000,000 3/15/2005 - 2/28/2010

Direct Cost Current Year: \$189,636

**Mark Klempner**

Infectious Diseases

Agency: NIAID

Project Title: National center for emerging infectious diseases and biodefense (construction)

Total Direct Cost: \$141,020,930 9/30/2003 - 6/30/2008

Direct Cost Current Year: \$58,082,598

**Mark Klempner**

Infectious Diseases

Agency: NIAID

Project Title: National Emerging Infectious Diseases Laboratories Operations

Total Direct Cost: \$32,053,956 7/1/2006 - 4/30/2011

Direct Cost Current Year: \$3,922,186

**Monty Montano**

Infectious Diseases

Agency: NIAID

Project Title: Molecular Analysis of HIV-1C Transmission Co-factors

Total Direct Cost: \$750,000 4/1/2003 - 3/31/2007

Direct Cost Current Year: \$232,221

**John Murphy**

Infectious Diseases

Agency: NIAID

Project Title: Immuno - Prophylaxis Therapy and Diagnosis of Tularemia

Total Direct Cost: \$8,143,620 9/15/2003 - 2/29/2008

Direct Cost Current Year: \$751,358

**Li Shen**

Infectious Diseases

Agency: NIAID

Project Title: Analysis of Sigma Factor 28 of C. trachomatis

Total Direct Cost: \$1,000,000 12/1/2004 - 11/30/2009

Direct Cost Current Year: \$156,240



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**Paul Skolnik**

Infectious Diseases

Agency: HRSA

Project Title: Ryan White Care Act Title IV Adolescent Initiative

Total Direct Cost: \$208,213 12/15/2003 - 8/31/2007

Direct Cost Current Year: \$90,909

**Paul Skolnik**

Infectious Diseases

Agency: NIAID

Project Title: Partners Health Care Systems / Harvard Medical School / Boston Medical Center AIDS CTU

Total Direct Cost: \$1,715,319 2/1/2007 - 11/30/2013

Direct Cost Current Year: \$310,867

**Paul Skolnik**

Infectious Diseases

Agency: NIAID

Project Title: Training Program in Host Pathogen Interactions

Total Direct Cost: \$1,094,512 7/1/2002 - 6/30/2008

Direct Cost Current Year: \$234,009

**Paul Skolnik**

Infectious Diseases

Agency: CDC

Project Title: HIV Prevention Projects for CBOs

Total Direct Cost: \$2,076,470 7/1/2004 - 6/30/2009

Direct Cost Current Year: \$423,850

**Paul Skolnik**

Infectious Diseases

Agency: NIDA

Project Title: Understanding and Improving Adherence in HIV Disease

Total Direct Cost: \$92,121 4/1/2003 - 3/31/2007

Direct Cost Current Year: \$30,707

**Paul Skolnik**

Infectious Diseases

Agency: NIDA

Project Title: Natural History of Hepatitis C Infection in HIV Disease

Total Direct Cost: \$1,304,473 7/1/2005 - 6/30/2009

Direct Cost Current Year: \$313,937

**Paul Skolnik**

Infectious Diseases

Agency: NHLBI

Project Title: Modeling of Lung HIV Cytokine/Chemokine Networks

Total Direct Cost: \$1,426,886 9/26/2003 - 8/31/2008

Direct Cost Current Year: \$197,316

**Paul Skolnik**

Infectious Diseases

Agency: MDPH

Project Title: HIV Counseling, Testing, and Support Services

Total Direct Cost: \$1,615,000 7/1/2003 - 6/30/2008

Direct Cost Current Year: \$330,434

**Paul Skolnik**

Infectious Diseases

Agency: MDPH

Project Title: Enhanced Medical Management System Supplemental Services

Total Direct Cost: \$176,227 7/1/2005 - 6/30/2010

Direct Cost Current Year: \$30,435

**Paul Skolnik**

Infectious Diseases

Agency: MDPH

Project Title: Enhanced Medical Management Services

Total Direct Cost: \$2,973,354 7/1/2005 - 6/30/2010

Direct Cost Current Year: \$679,379

**Paul Skolnik**

Infectious Diseases

Agency: MDPH

Project Title: Comprehensive Home-Based Medical Care

Total Direct Cost: \$827,817 7/1/2005 - 6/30/2010

Direct Cost Current Year: \$170,781

**Paul Skolnik**

Infectious Diseases

Agency: MDPH

Project Title: STD Preventive Clinical Services

Total Direct Cost: \$1,771,204 7/1/2006 - 6/30/2009

Direct Cost Current Year: \$198,879

**Paul Skolnik**

Infectious Diseases

Agency: MDPH

Project Title: AIDS Prevention and Ed. Services for Haitians in Boston

Total Direct Cost: \$195,652 1/1/2007 - 6/30/2008

Direct Cost Current Year: \$65,217

**Paul Skolnik**

Infectious Diseases

Agency: Merck

Project Title: A Multicenter, Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Safety and Antiretroviral Activity of MK-0518 in Combination with an Optimized Background Therapy (OBT), Versus Optimized Background Therapy Alone, in HIV-Infected Patients with Documented Resistance to At Least 1 Drug in Each of the 3 Classes of Licensed Oral Antiretroviral Therapies

Total Direct Cost: \$21,248 3/10/2006 - 3/9/2009

Direct Cost Current Year: \$21,248

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**Paul Skolnik**

Infectious Diseases

Agency: Pfizer

Project Title: A Multicenter, Randomized, Double-Blind, Comparative Trial of a Novel CCR5 Antagonist, UK-427,857, in Combination with Zidovudine/Lamivudine Versus Efavirenz in Combination with Zidovudine/Lamivudine for the Treatment of Antiretroviral-Naïve HIV-1 Infected Subjects

Total Direct Cost: \$13,675 4/15/2005 - 6/30/2007

Direct Cost Current Year: \$13,675

**Paul Skolnik**

Infectious Diseases

Agency: Pfizer

Project Title: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial of a Novel CCR5 Antagonist, UK-427,857, in Combination with Optimized Background Therapy Versus Optimized Background Therapy Alone for the Treatment of Antiretroviral-Experienced HIV-1-Infected Subjects

Total Direct Cost: \$9,072 4/15/2005 - 4/14/2008

Direct Cost Current Year: \$9,072

**Paul Skolnik**

Infectious Diseases

Agency: Pfizer

Project Title: A Multicenter, Open-Label, Expanded Access Trial of Maraviroc

Total Direct Cost: \$5,575 4/17/2007 - 4/16/2009

Direct Cost Current Year: \$5,575

**Paul Skolnik**

Infectious Diseases

Agency: Gilead Sciences

Project Title: A Phase 3, Randomized, Open-Label, Multicenter Study of the Treatment of Antiretroviral-Naïve HIV-1-Infected Subjects Comparing Tenofovir Disoproxil Fumarate and Emtricitabine in Combination with Efavirenz Versus Combivir

(lamivudine/zidovudine) and Efavirenz

Total Direct Cost: \$3,555 7/29/2003 - 2/28/2007

Direct Cost Current Year: \$3,555

**Paul Skolnik**

Infectious Diseases

Agency: Gilead Sciences

Project Title: A Phase 2, Randomized Study of the Treatment of Antiretroviral Treatment-Experienced, HIV-1 Infected Subjects Comparing Ritonavir Boosted GS-9137 (GS-9137/r) Versus a Comparator Ritonavir Boosted Protease Inhibitor (CPI/r) in Combination with a Background Antiretroviral Therapy

Total Direct Cost: \$1,550 4/18/2006 - 8/30/2006

Direct Cost Current Year: \$1,550

**Paul Skolnik**

Infectious Diseases

Agency: GlaxoSmithKline

Project Title: A Phase IIB, Randomized, Multicenter, Parallel Group Study to Evaluate the Short-Term Safety, Pharmacokinetics and Antiretroviral Activity of Four Blinded Dosing Regimens of GW640385/Ritonavir Therapy Compared to Open-Label Current Protease Inhibitor Therapy in HIV-1 Infected, Protease Inhibitor-Experienced Adults for 2 weeks with Long-Term Evaluation (>48 weeks) of Safety, Pharmacokinetics and Antiretroviral Activity of Selected GW640385/Ritonavir Dosing Regimen(s) vs. A Ritonavir-Boosted, Protease Inhibitor Containing Regimen

Total Direct Cost: \$4,528 12/16/2005 - 4/30/2007

Direct Cost Current Year: \$4,528

**Paul Skolnik**

Infectious Diseases

Agency: Abbott

Project Title: A Phase 3, Randomized, Open-Label Study of Lopinavir/Ritonavir Tablets 800/200 mg Once-Daily Versus 400/100 mg Twice-Daily When Co-Administered with Nucleoside/Nucleotide Reverse Transcriptase Inhibitors in Antiretroviral Experienced HIV-1 Subjects

Total Direct Cost: \$2,225 6/9/2006 - 6/8/2008

Direct Cost Current Year: \$2,225

**Paul Skolnik**

Infectious Diseases

Agency: Schering Plough

Project Title: Vicriviroc in Combination Therapy with Optimized Antiretroviral Regimen in Experienced Subjects (VICTOR-E1)

Total Direct Cost: \$4,700 1/17/2006 - 10/31/2006

Direct Cost Current Year: \$4,700

**Paul Skolnik**

Infectious Diseases

Agency: Schering Plough

Project Title: Vicriviroc (SCH417690) Treatment Protocol in HIV-Infected Subjects: A Rollover Study for ACTG Protocol A5211

Total Direct Cost: \$1,255 11/23/2005 - 11/22/2008

Direct Cost Current Year: \$1,255

**Paul Skolnik**

Infectious Diseases

Agency: Schering Plough

Project Title: Vicriviroc in Combination Therapy with Optimized Antiretroviral Regimen in Experienced Subjects (VICTOR-E2)

Total Direct Cost: \$4,700 1/17/2006 - 10/31/2006

Direct Cost Current Year: \$4,700

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**Paul Skolnik**

Infectious Diseases

Agency: Tibotec

Project Title: A Randomized, Controlled, Open-Label Trial to Compare Efficacy, Safety and Tolerability of TMC114/ritonavir versus lopinavir/ritonavir in treatment-naïve HIV-1 Infected Subjects

Total Direct Cost: \$9,556 3/1/2006 - 2/29/2010

Direct Cost Current Year: \$9,556

**Paul Skolnik**

Infectious Diseases

Agency: Tibotec

Project Title: Early Access of TMC114 in Combination with Low-Dose ritonavir (RTV) and Other Antiretrovirals (ARVs) in Highly Treatment Experienced HIV-1 Infected Subjects with Limited to No Treatment Options

Total Direct Cost: \$8,350 3/31/2006 - 3/30/2007

Direct Cost Current Year: \$8,350

**Paul Skolnik**

Infectious Diseases

Agency: Tibotec

Project Title: An Open-Label, Multicenter Trial to Compare the Efficacy, Safety, and Tolerability of PREZISTA/r by Gender and Race, When Administered in Combination with an Individually Optimized Background Regimen Over a 48-Week Treatment Period

Total Direct Cost: \$13,535 1/16/2007 - 1/15/2009

Direct Cost Current Year: \$13,535

**Paul Skolnik**

Infectious Diseases

Agency: Tibotec

Project Title: Early Access of TMC125 in Combination with Other Antiretrovirals in Treatment-Experienced HIV-1 Infected Subjects with Limited Treatment Options

Total Direct Cost: \$4,200 2/8/2007 - 2/7/2009

Direct Cost Current Year: \$4,200

**Paul Skolnik**

Infectious Diseases

Agency: MDPH

Project Title: STD Prevention Training Center

Total Direct Cost: \$30,906 8/1/1999 - 7/31/2008

Direct Cost Current Year: \$9,906

**Lee Wetzler**

Infectious Diseases

Agency: NIAID

Project Title: Neisserial Porins and Antigen Presenting Cells

Total Direct Cost: \$1,350,000 4/1/1997 - 8/31/2010

Direct Cost Current Year: \$270,000

**Lee Wetzler**

Infectious Diseases

Agency: NIAID

Project Title: Effect of Neisserial Porin in Immune Cell Apoptosis

Total Direct Cost: \$1,125,000 7/1/2002 - 6/30/2007

Direct Cost Current Year: \$175,093

**MOLECULAR MEDICINE****Kenneth Albrecht**

Molecular Medicine

Agency: NICHD

Project Title: Genetic Mechanisms of Mammalian Sex Determination

Total Direct Cost: \$900,000 7/7/2003 - 4/30/2008

Direct Cost Current Year: \$180,000

**Kenneth Albrecht**

Molecular Medicine

Agency: ACS

Project Title: Genetic and genomic analysis of ovarian granulosa cell differentiation

Total Direct Cost: \$720,000 1/1/2006 - 12/31/2009

Direct Cost Current Year: \$150,000

**Ajit Bharti**

Molecular Medicine

Agency: NHLBI

Project Title: Role of Neuroregulin/erbB Signaling

Total Direct Cost: \$50,837 7/1/2006 - 6/30/2007

Direct Cost Current Year: \$50,837

**Victoria Bolotina**

Molecular Medicine

Agency: NHLBI

Project Title: Ion channels and Ca regulation in vascular SMC function

Total Direct Cost: 8/5/1996 - 7/31/2009

Direct Cost Current Year: \$244,125

**Victoria Bolotina**

Molecular Medicine

Agency: NHLBI

Project Title: Store-operated Ca<sup>2+</sup> influx 7 iPLA2 in vascular SMC

Total Direct Cost: 6/13/2003 - 5/31/2008

Direct Cost Current Year: \$366,189

**Barbara Corkey**

Molecular Medicine

Agency: NIDDK

Project Title: Mitochondrial Dynamics in Beta Cell Function and Dysfunction

Total Direct Cost: \$60,798 2/1/2007 - 11/30/2007

Direct Cost Current Year: \$60,798

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**Barbara Corkey**

Molecular Medicine

Agency: NIDDK

Project Title: Metabolic Regulation of Insulin Secretion

Total Direct Cost: \$820,000 6/1/2005 - 3/31/2009

Direct Cost Current Year: \$200,182

**Barbara Corkey**

Molecular Medicine

Agency: ASGE

Project Title: Validation of a novel bowel prep rating scale

Total Direct Cost: \$25,000 1/1/2007 - 12/31/2007

Direct Cost Current Year: \$25,000

**Barbara Corkey**

Molecular Medicine

Agency: NIDDK

Project Title: Metabolic Regulation of Insulin Secretion

Total Direct Cost: \$141,546 6/1/2005 - 3/31/2007

Direct Cost Current Year: \$70,621

**Barbara Corkey**

Molecular Medicine

Agency: NIDDK

Project Title: Boston Obesity Nutrition Research Center (BONRC)

Total Direct Cost: \$4,966,460 5/20/2003 - 3/31/2008

Direct Cost Current Year: \$244,202

**Barbara Corkey**

Molecular Medicine

Agency: NIDDK

Project Title: Metabolic Signal Transduction in Adipocytes

Total Direct Cost: \$1,367,440 3/1/2006 - 1/31/2011

Direct Cost Current Year: \$172,772

**Karen T.Cuenco**

Molecular Medicine

Agency: NICHD Brigham & Women's

Project Title: Finding Genes for Uterine Fibroids

(Subcontract via Brigham and Women's Hospital )

Total Direct Cost: \$189,263 9/26/2003 - 7/31/2008

Direct Cost Current Year: \$46,011

**Lina Moitoso de Vargas**

Molecular Medicine

Agency: NIDDK

Project Title: Lipid modulation of beta-cell calcium channels

Total Direct Cost: \$700,000 7/1/2003 - 4/30/2007

Direct Cost Current Year: \$95,888

**Lindsay Farrer**

Molecular Medicine

Agency: American College Of Rheum

Project Title: Stimulation Of Plasmactoid Dendritic

Cells With Nucleic-Acid Containing Immune

Complexes From Scleroderma Patients With Ant-Centromere A

Total Direct Cost: \$150,000 3/1/2007 - 6/30/2010

Direct Cost Current Year: \$50,000

**Lindsay Farrer**

Molecular Medicine

Agency:

Project Title: Multi-ethnic Genome-wide Alzheimers Association

Total Direct Cost: \$1,681,062 9/15/2006 - 8/31/2011

Direct Cost Current Year: \$262,160

**Lindsay Farrer**

Molecular Medicine

Agency: NIDA

Project Title: The Genetics of Cocaine Dependence

Total Direct Cost: \$474,577 9/1/2004 - 8/31/2009

Direct Cost Current Year: \$234,991

**Lindsay Farrer**

Molecular Medicine

Agency: NIA

Project Title: Genetic Epidemiological Studies of Alzheimers Disease

Total Direct Cost: \$9,714,494 9/15/2002 - 6/30/2007

Direct Cost Current Year: \$1,130,870

**Lindsay Farrer**

Molecular Medicine

Agency: NIA

Project Title: Genetics of Alzheimer Disease in Israeli-Arabs

Total Direct Cost: \$646,230 9/30/2000 - 3/31/2010

Direct Cost Current Year: \$28,571

**Lindsay Farrer**

Molecular Medicine

Agency: NIDA

Project Title: Genetics of Opioid Dependence (Subcontract via Yale University)

Total Direct Cost: \$459,717 8/10/2005 - 6/30/2010

Direct Cost Current Year: \$50,219

**Lindsay Farrer**

Molecular Medicine

Agency: NIEHS Mayo Clinic

Project Title: Genetics of Macular Degeneration

Total Direct Cost: \$238,414 9/2/2003 - 8/31/2007

Direct Cost Current Year: \$46,793

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**Lindsay Farrer**

Molecular Medicine

Agency: Fidelity

Project Title: Multi-Ethnic Genome Wide Alzheimers Association

Total Direct Cost: \$500,000 2/1/2007 - 2/7/2009

Direct Cost Current Year: \$250,000

**Lindsay Farrer**

Molecular Medicine

Agency: Telik, Inc.

Project Title: Phase III Randomized Study of TLK286 versus Doxil/Caelyx or Hycamptin as Third Line Therapy in Platinum Refractory or Resistant Ovarian Cancer

Total Direct Cost: \$31,469 6/15/2004 - 12/31/2008

Direct Cost Current Year: \$5,000

**Caroline Genco**

Molecular Medicine

Agency: NHLBI

Project Title: Invasive Bacteria Accelerate Atherosclerosis Through TLRs

Total Direct Cost: \$971,000 2/1/2006 - 1/31/2010

Direct Cost Current Year: \$242,750

**Caroline Genco**

Molecular Medicine

Agency: NHLBI

Project Title: Invasive Bacteria Accelerate Atherosclerosis Through TLRs

Total Direct Cost: \$26,060 2/1/2006 - 1/31/2010

Direct Cost Current Year: \$10,858

**Jianlin Gong**

Molecular Medicine

Agency: Susan G. Komen Breast Cancer Foundation

Project Title: Role of Telomerase and Telomeres in the Tumorigenesis of Breast Cancer

Total Direct Cost: \$200,000 5/1/2005 - 4/30/2007

Direct Cost Current Year: \$100,000

**Jianlin Gong**

Molecular Medicine

Agency: Ellison Foundation

Project Title: Development of HSP70-based Vaccine from Fusion Cells for Clinical Use

Total Direct Cost: \$156,000 1/1/2007 - 12/31/2007

Direct Cost Current Year: \$156,000

**Jianlin Gong**

Molecular Medicine

Agency: Leukemia & Lymphoma Society

Project Title: Dendritic/Leukemic Fusion Cell Vaccine Therapy for AML Patients in First Remission: A Phase I Clinical Trial

Total Direct Cost: \$240,740 12/31/2003 - 12/30/2006

Direct Cost Current Year: \$120,370

**Jianlin Gong**

Molecular Medicine

Agency: Department of Defense-Army

Project Title: Combined telomerase inhibition and immunotherapy in the prevention and treatment of mammary carcinomas

Total Direct Cost: \$300,000 1/15/2006 - 1/14/2009

Direct Cost Current Year: \$100,000

**Victoria Herrera**

Molecular Medicine

Agency: NIAG

Project Title: Prenatal Malnutrition and the Aging Brain

Total Direct Cost: \$100,548 9/1/2006 - 8/31/2008

Direct Cost Current Year: \$100,548

**Victoria Herrera**

Molecular Medicine

Agency: NIEHS

Project Title: Environmental Toxicants: Fetal Basis, Adult-onset Stroke

Total Direct Cost: \$271,375 1/1/2006 - 12/31/2007

Direct Cost Current Year: \$135,688

**Kyriakos Kypreos**

Molecular Medicine

Agency: American Heart Association

Project Title: Domains of ApoCIII contributing to hypertriglyceridemia

Total Direct Cost: \$477,750 1/1/2005 - 12/31/2008

Direct Cost Current Year: \$159,250

**John Murphy**

Molecular Medicine

Agency: NIAID

Project Title: New England Regional Center of Excellence for Biodefense

Total Direct Cost: \$428,484 9/4/2003 - 2/29/2008

Direct Cost Current Year: \$96,723

**John Murphy**

Molecular Medicine

Agency: NIAID

Project Title: Peptide Activators of Diphtheria Toxin Repressor (DtxR)

Total Direct Cost: \$2,050,756 2/1/2005 - 1/31/2010

Direct Cost Current Year: \$211,014

**John Murphy**

Molecular Medicine

Agency: NIAID

Project Title: Diphtheria & Anthrax Toxins: Mechanisms of Cell Entry

Total Direct Cost: \$1,359,003 7/1/2003 - 12/31/2007

Direct Cost Current Year: \$296,224

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**John Murphy**

Molecular Medicine

Agency: NCI

Project Title: Novel Targeted Reagents that Modify  
Oncogene Expression

Total Direct Cost: \$200,000 4/1/2005 - 3/31/2008

Direct Cost Current Year: \$97,650

**Faina Schwartz**

Molecular Medicine

Agency: NIA

Project Title: The Role of Mitochondrial Genes in  
Hypertension

Total Direct Cost: \$662,237 5/15/2001 - 4/30/2005

Direct Cost Current Year: \$71,211

**Sam Thiagalingam**

Molecular Medicine

Agency: NCI

Project Title: The Role of hBub1-p53 Pathway in  
Genomic Stability

Total Direct Cost: \$912,250 8/1/2003 - 7/31/2008

Direct Cost Current Year: \$173,817

**Sam Thiagalingam**

Molecular Medicine

Agency: NARSAD

Project Title: EpiGenetic Modulation of Serotonin  
Signaling in the Pathogenesis of Schizophrenia and  
Bipolar Disorder

Total Direct Cost: 9/15/2006 - 9/14/2008

Direct Cost Current Year: \$46,296

**Gordon Yaney**

Molecular Medicine

Agency: American Diabetes Association

Project Title: Incretin action of fatty acids in glucose-  
stimulated insulin secretion

Total Direct Cost: \$351,033 7/1/2005 - 6/30/2008

Direct Cost Current Year: \$119,276

**Vassilis Zannis**

Molecular Medicine

Agency: NHLBI

Project Title: Functions of apoE in Cholesterol and  
triglyceride

Total Direct Cost: \$1,125,000 9/1/2006 - 4/30/2011

Direct Cost Current Year: \$225,000

**Agustin Yip**

Molecular Medicine

Agency: Alzheimer's Association

Project Title: Genetic Basis of Cerebrovascular  
Mechanisms in Alzheimer's Disease

Total Direct Cost: \$90,910 9/1/2003 - 8/31/2006

Direct Cost Current Year: \$57,572

**NEPHROLOGY****Steven Borkan**

Nephrology

Agency: NIDDK

Project Title: Cytoprotective Role of HSP72 in Renal  
Cell Injury

Total Direct Cost: \$1,097,450 7/1/1999 - 6/30/2008

Direct Cost Current Year: \$214,332

**Herbert Cohen**

Nephrology

Agency: NCI

Project Title: VHL, Jade-41 and Protein Stability in  
Renal Cancer

Total Direct Cost: \$1,000,000 4/1/1999 - 6/30/2008

Direct Cost Current Year: \$195,300

**Herbert Cohen**

Nephrology

Agency: NIDDK

Project Title: Jade-1 Cystic Renal Disease

Total Direct Cost: \$990,000 4/1/2004 - 3/31/2009

Direct Cost Current Year: \$193,347

**Laura Dember**

Nephrology

Agency: NIDDK

Project Title: Dialysis access consortium clinical trials

Total Direct Cost: \$1,032,070 9/30/2000 - 5/31/2008

Direct Cost Current Year: \$216,595

**David Salant**

Nephrology

Agency: NIDDK

Project Title: Research Training in Nephrology

Total Direct Cost: \$814,415 7/1/2005 - 6/30/2010

Direct Cost Current Year: \$154,097

**David Salant**

Nephrology

Agency: NIDDK

Project Title: Antibody Mediated Glomerular Injury

Total Direct Cost: \$1,025,000 3/1/2006 - 12/31/2010

Direct Cost Current Year: \$205,000

**John Schwartz**

Nephrology

Agency: NIDDK

Project Title: Mechanism of Renal Tubular

Total Direct Cost: \$820,003 7/1/2002 - 5/31/2007

Direct Cost Current Year: \$56,427

**John Schwartz**

Nephrology

Agency: NIDDK

Project Title: Snare's in the Trafficking of IMCD H+-  
Atpase AQP2

Total Direct Cost: \$1,100,000 3/1/2002 - 12/31/2006



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Direct Cost Current Year: \$209,337

**Andrea Havasi**

Nephrology  
Agency: NKF  
Project Title: HSP70 As a Cytoprotective  
Total Direct Cost: \$120,000 7/1/2005 - 6/30/2008  
Direct Cost Current Year: \$40,000

**Weining Lu**

Nephrology  
Agency: NKF  
Project Title: Molecular Pathology of Vesicoureteral  
Total Direct Cost: \$100,000 7/1/2005 - 6/30/2007  
Direct Cost Current Year: \$50,000

**Maria Panchenko**

Nephrology  
Agency: AHA  
Project Title: Jade-1 in Hypoxic Injury of Renal  
Epithelial Cells  
Total Direct Cost: \$180,000 7/1/2005 - 6/30/2008  
Direct Cost Current Year: \$60,000

**Ian Rifkin**

Nephrology  
Agency: NIAMS  
Project Title: TLR-Dependent Dendritic Cell Activation  
in SLE  
Total Direct Cost: \$820,000 9/1/2004 - 8/31/2009  
Direct Cost Current Year: \$164,000

**James Kaufman**

Nephrology  
Agency: Don Joy, Inc.  
Project Title: A Randomized Trial of Realignment  
Therapy for Treatment of Medial Knee OA - Don Joy  
Total Direct Cost: \$58,963 4/1/2005 - 10/31/2007  
Direct Cost Current Year: \$29,482

**James Kaufman**

Nephrology  
Agency: Pfizer Inc.  
Project Title: A Longitudinal Study of Osteoarthritis -  
Pfizer  
Total Direct Cost: \$678,837 11/1/2004 - 9/30/2007  
Direct Cost Current Year: \$132,647

**James Kaufman**

Nephrology  
Agency: VA Dept.  
Project Title: Homocysteinemia in Kidney and End  
Stage Renal  
Total Direct Cost: \$7,944,412 10/1/2001 - 9/30/2007  
Direct Cost Current Year: \$1,847,307

**PREVENTIVE MEDICINE AND  
EPIDEMIOLOGY**

**R. Curtis Ellison**

Prev Med & Epi  
Agency: NIAAA  
Project Title: Net Lifetime Health Effects of Alcohol  
Use & Abuse  
Total Direct Cost: \$2,252,249 5/16/2003 - 4/30/2008  
Direct Cost Current Year: \$438,579

**R. Curtis Ellison**

Prev Med & Epi  
Agency: NHLBI  
Project Title: GENCAC - Framingham Field Center  
Total Direct Cost: \$767,446 9/17/2001 - 8/31/2007  
Direct Cost Current Year: \$92,303

**Lynn Moore**

Prev Med & Epi  
Agency: NIDDK  
Project Title: Dietary Patterns, Obesity, and Associated  
Metabolic Outcomes in Adolescents  
Total Direct Cost: \$288,145 4/1/2007 - 3/31/2009  
Direct Cost Current Year: \$156,853

**Richard Myers**

Prev Med & Epi  
Agency: NHLBI  
Project Title: HYPERGEN-Boston  
University/Framingham Field Center  
Total Direct Cost: \$32,166 9/30/2005 - 8/31/2007  
Direct Cost Current Year: \$32,166

**Lynn Moore**

Prev Med & Epi  
Agency: Guidant Corp  
Project Title: MENDMI  
Total Direct Cost: \$39,590 1/1/2006 - 12/30/2008  
Direct Cost Current Year: \$17,541

**PULMONARY**

**John Bernardo**

Pulmonary  
Agency: CDC  
Project Title: TB Trials Consortium  
Total Direct Cost: \$1,452,409 9/30/1999 - 8/29/2009  
Direct Cost Current Year: \$139,694

**Jerome Brody**

Pulmonary  
Agency: NIDCR  
Project Title: Microsensor Arrays for Saliva Diagnostics  
Total Direct Cost: \$1,326,337 9/1/2006 - 6/30/2011  
Direct Cost Current Year: \$180,059

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**Jerome Brody**

Pulmonary  
Agency: Inst Rech Intl Servi  
Project Title: Search For New Therapeutic Targets By  
Further Understanding Pathophysiology Of Arterial  
And Venous Vascular Disease  
Total Direct Cost: \$529,167 12/1/2005 - 12/31/2008  
Direct Cost Current Year: \$158,750

**John Berk**

Pulmonary  
Agency: FDA  
Project Title: Effect of Diflunisal on Familial  
Amyloidosis  
Total Direct Cost: \$577,322 9/30/2004 - 9/29/2007  
Direct Cost Current Year: \$147,465

**John Berk**

Pulmonary  
Agency: NINDS  
Project Title: Effect of Diflunisal (IND68092) on  
Familial Amyloidosis  
Total Direct Cost: \$4,615,345 9/15/2005 - 5/31/2010  
Direct Cost Current Year: \$418,452

**Jeffrey Berman**

Pulmonary  
Agency: NHLBI  
Project Title: Immunopathology of the Nasal Mucosa in  
Sarcoidosis  
Total Direct Cost: \$275,000 9/15/2004 - 6/30/2007  
Direct Cost Current Year: \$150,000

**John Bernardo**

Pulmonary  
Agency: CDC  
Project Title: Regional Training and Medical  
Consultation Center  
Total Direct Cost: \$48,692 9/1/2005 - 12/31/2007  
Direct Cost Current Year: \$18,740

**Jerome Brody**

Pulmonary  
Agency: BU OIT  
Project Title: A New Diagnostic Tool for Diseases of  
the Lung: Nasal Epithelial Cell Gene Expression  
Total Direct Cost: \$50,150 06/05/06- -  
Direct Cost Current Year: \$50,150

**Wellington Cardoso**

Pulmonary  
Agency: NHLBI  
Project Title: Retinoic Acid Signaling in Lung  
Morphogenesis  
Total Direct Cost: \$978,250 5/1/2006 - 3/31/2010  
Direct Cost Current Year: \$242,750

**David Center**

Pulmonary  
Agency: NIAID  
Project Title: Modulation of airway inflammation in  
asthma models  
Total Direct Cost: \$2,829,899 9/24/2001 - 6/30/2007  
Direct Cost Current Year: \$609,779

**David Center**

Pulmonary  
Agency: NIAID  
Project Title: Role of Interleukin 16 in Asthma  
Total Direct Cost: \$1,189,000 4/15/2005 - 12/31/2009  
Direct Cost Current Year: \$244,125

**David Center**

Pulmonary  
Agency: NHLBI  
Project Title: Biology of the Lung: A Multidisciplinary  
Program  
Total Direct Cost: \$5,009,630 7/1/2006 - 6/30/2011  
Direct Cost Current Year: \$1,001,926

**William Cruikshank**

Pulmonary  
Agency: NIDDK  
Project Title: Immunoglobulin Activation of Fibroblasts  
Total Direct Cost: \$262,792 7/1/2004 - 5/31/2009  
Direct Cost Current Year: \$52,512

**Harrison Farber**

Pulmonary  
Agency: NHLBI  
Project Title: A Comprehensive Sickle Cell Center  
(Subcontract via Boston Medical Center)  
Total Direct Cost: \$771,894 4/1/2003 - 3/31/2008  
Direct Cost Current Year: \$155,268

**Harrison Farber**

Pulmonary  
Agency: NHLBI  
Project Title: Endothelial Cell Hypoxia Tolerance: Role  
of Plasmalogens  
Total Direct Cost: \$994,125 7/1/2003 - 6/30/2007  
Direct Cost Current Year: \$244,125

**Harrison Farber**

Pulmonary  
Agency: NIAMS  
Project Title: International Workshop For Scleroderma  
Research  
Total Direct Cost: \$20,572 8/1/2006 - 11/30/2007  
Direct Cost Current Year: \$20,527

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**Alan Fine**

Pulmonary  
Agency: NHLBI  
Project Title: Characterization of a Lung Mesenchymal Progenitor Cell  
Total Direct Cost: \$275,000 8/1/2006 - 6/30/2008  
Direct Cost Current Year: \$150,000

**Alan Fine**

Pulmonary  
Agency: NHLBI  
Project Title: Bone Marrow Cells as Precursors of Alveolar Epithelium  
Total Direct Cost: \$1,000,000 7/1/2002 - 6/30/2007  
Direct Cost Current Year: \$244,125

**Ronald Goldstein**

Pulmonary  
Agency: NHLBI  
Project Title: Lung Connective Tissue - Response to Injury and Repair  
Total Direct Cost: \$917,731 12/20/2001 - 11/30/2006  
Direct Cost Current Year: \$190,933

**Ronald Goldstein**

Pulmonary  
Agency: NHLBI  
Project Title: Regulation of Collagen Formation in Pulmonary Fibrosis  
Total Direct Cost: \$900,000 8/1/2002 - 7/31/2007  
Direct Cost Current Year: \$225,000

**Ronald Goldstein**

Pulmonary  
Agency: VA  
Project Title: A multi-disciplinary study of COPD & its treatment  
Total Direct Cost: \$1,000,000 10/1/1998 - 6/30/2007  
Direct Cost Current Year: \$200,000

**Daniel Gottlieb**

Pulmonary  
Agency: VA  
Project Title: RCT of a Telecommunications System in Sleep Apnea  
Total Direct Cost: \$9,367 4/1/2004 - 9/30/2007  
Direct Cost Current Year: \$5,800

**Helen Hollingsworth**

Pulmonary  
Agency: Abbott  
Project Title: Open-label treatment of human anti-TNF monoclonal antibody Adalimumab in patients with moderate to severe Crohn's disease with previous exposure to Infliximab  
Total Direct Cost: \$1,243 12/8/2006 - 6/7/2007  
Direct Cost Current Year: \$1,243

**Helen Hollingsworth**

Pulmonary  
Agency: Eisai  
Project Title: Multi-Institutional Research in Alzheimers Genetic Epidemiology  
Total Direct Cost: \$218,953 8/11/2006 - 8/10/2007  
Direct Cost Current Year: \$218,953

**Helen Hollingsworth**

Pulmonary  
Agency: Glaxo-Wellcome, Inc  
Project Title: Genetic Epidemiology Center  
Total Direct Cost: \$2,700,351 1/1/1999 - 6/30/2004  
Direct Cost Current Year: \$349,496

**Michael Jeong**

Pulmonary  
Agency: NHLBI  
Project Title: Redox Regulated HIV Expression in Alveolar Macrophages  
Total Direct Cost: \$591,125 8/15/2003 - 5/31/2008  
Direct Cost Current Year: \$118,225

**Konstantin Izvolsky**

Pulmonary  
Agency: Parker B. Francis Fdn  
Project Title: Heparan sulfate-Fgf10 Interactions in Lung Morphogenesis  
Total Direct Cost: \$132,000 7/1/2005 - 6/30/2008  
Direct Cost Current Year: \$44,000

**Hasmeena Kathuria**

Pulmonary  
Agency: ALA  
Project Title: Molecular Regulation of Caveolin-1 Lung Cancer  
Total Direct Cost: \$80,000 7/1/2006 - 6/30/2008  
Direct Cost Current Year: \$40,000

**Elizabeth Klings**

Pulmonary  
Agency: NHLBI  
Project Title: Gene Polymorphisms in Chronic Sickle Cell Lung Disease  
Total Direct Cost: \$589,625 1/1/2005 - 12/31/2009  
Direct Cost Current Year: \$117,925

**Elizabeth Klings**

Pulmonary  
Agency: Actelion Pharm.  
Project Title: ASSET 1 & 2  
Total Direct Cost: \$46,154 12/1/2005 - 12/31/2006  
Direct Cost Current Year: \$46,154

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**Darrell Kotton**

Pulmonary  
Agency: NHLBI  
Project Title: Cell-specific Delivery of RNAi to  
Pulmonary Alveolar Macrophages in vivo  
Total Direct Cost: \$275,000 9/30/2006 - 7/31/2008  
Direct Cost Current Year: \$150,000

**Darrell Kotton**

Pulmonary  
Agency: ATS  
Project Title: Stem Cell-Based Therapy for Alpha-1  
Antitrypsin Deficiency  
Total Direct Cost: \$100,000 1/1/2006 - 12/31/2007  
Direct Cost Current Year: \$50,000

**Darrell Kotton**

Pulmonary  
Agency: NHLBI  
Project Title: Derivation of Lung Epithelium from  
Bone Marrow  
Total Direct Cost: \$587,000 2/4/2003 - 1/31/2008  
Direct Cost Current Year: \$117,400

**Frederick Little**

Pulmonary  
Agency: NHLBI  
Project Title: Effect of IL-16 on the Murine Allergic  
Airway Response  
Total Direct Cost: \$587,000 7/1/2003 - 6/30/2008  
Direct Cost Current Year: \$117,400

**Jining Lu**

Pulmonary  
Agency: NHLBI  
Project Title: MicroRNA-mediated Gene Regulation in  
Lung Development  
Total Direct Cost: \$1,098,900 5/1/2006 - 2/28/2011  
Direct Cost Current Year: \$218,475

**George O'Connor**

Pulmonary  
Agency: ICATA  
Project Title: ICATA  
Total Direct Cost: \$227,856 7/1/2006 - 9/30/2008  
Direct Cost Current Year: \$227,858

**George O'Connor**

Pulmonary  
Agency: NIAID  
Project Title: Inner-City Asthma Consortium  
Total Direct Cost: \$776,994 9/30/2002 - 9/29/2008  
Direct Cost Current Year: \$144,985

**George O'Connor**

Pulmonary  
Agency: NIAID  
Project Title: URECA  
Total Direct Cost: \$1,890,282 9/30/2002 - 9/29/2009  
Direct Cost Current Year: \$476,450

**George O'Connor**

Pulmonary  
Agency: NHLBI  
Project Title: Cardiovascular risk in sleep apnea: the  
Framingham Study  
Total Direct Cost: \$1,177,843 9/1/2004 - 8/31/2008  
Direct Cost Current Year: \$72,555

**Marisa Ramirez**

Pulmonary  
Agency: NIH  
Project Title: Lung Alveolar Type I Cell Morphogenesis  
Total Direct Cost: \$1,250,000 7/1/2006 - 6/30/2011  
Direct Cost Current Year: \$250,000

**Avrum Spira**

Pulmonary  
Agency: NCI  
Project Title: The Airway Transcriptome as A Biomarker  
for Lung Cancer  
Total Direct Cost: \$172,000 8/9/2005 - 7/31/2007  
Direct Cost Current Year: \$83,979

**Avrum Spira**

Pulmonary  
Agency: NCI  
Project Title: Airway Gene Expression in Smokers: An  
Early Diagnostic Biomarker for Lung Cancer  
Total Direct Cost: \$950,000 5/1/2007 - 2/29/2012  
Direct Cost Current Year: \$190,000

**Avrum Spira**

Pulmonary  
Agency: Doris Duke Foundation  
Project Title: Tobacco, Cancer and Epithelial Gen  
Expression  
Total Direct Cost: \$200,000 7/1/2005 - 6/30/2007  
Direct Cost Current Year: \$100,000

**Ross Summer**

Pulmonary  
Agency: NHLBI  
Project Title: Characterization of Embryonic Lung Side  
Population Cells  
Total Direct Cost: \$594,030 4/1/2006 - 3/31/2011  
Direct Cost Current Year: \$118,806

**Robert Walter**

Pulmonary  
Agency: Flight Attendant Medical Research Institute,  
Inc.  
Project Title: Biomarkers of Chronic Obstructive  
Pulmonary Disease  
Total Direct Cost: \$500,000 7/1/2003 - 6/30/2008  
Direct Cost Current Year: \$100,000

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**Mary Williams**

Pulmonary  
Agency: NHLBI  
Project Title: Regulation of alveolar epithelial cell differentiation  
Total Direct Cost: \$7,116,131 7/1/2002 - 6/30/2007  
Direct Cost Current Year: \$1,445,963

**Andrew Wilson**

Pulmonary  
Agency: ALA  
Project Title: Stem Cell-Based Therapy for Alpha-1 Antitrypsin Deficiency  
Total Direct Cost: \$32,500 7/1/2006 - 6/30/2007  
Direct Cost Current Year: \$32,500

**Yujun Zhang**

Pulmonary  
Agency: NHLBI  
Project Title: Role of P80 pro-IL-16 in T Cell Malignancy  
Total Direct Cost: \$738,000 1/1/2005 - 12/31/2008  
Direct Cost Current Year: \$180,164

**RHEUMATOLOGY****Robert Lafyatis**

Rheumatology  
Agency: NIAMS  
Project Title: Altered Elastogenesis by Tsk Fibrillin-1 and in SSc  
Total Direct Cost: \$750,000 8/20/2005 - 7/31/2010  
Direct Cost Current Year: \$260,898

**Peter Merkel**

Rheumatology  
Agency: NCRR  
Project Title: Vasculitis Clinical Research Network  
Total Direct Cost: \$4,704,256 9/30/2003 - 8/31/2008  
Direct Cost Current Year: \$937,419

**Peter Merkel**

Rheumatology/Vasculitis Center  
Agency: NIH/NIAID 3324SC  
Project Title: Rituximab Therapy for the Induction of Remission and Tolerance in ANCA-Associated Vasculitis (RAVE) Rituximab for ANCA-Associated Vasculitis (RAVE) Study –  
Total Direct Cost: \$183,524  
Direct Cost Current Year: \$118,566

**Peter Merkel**

Rheumatology/Vasculitis Center  
Agency: NIH NIAMS/ R01 AR051874  
Project Title: Vasculitis Outcome Measures: Development and Validation  
Total Direct Cost: \$99,579  
Direct Cost Current Year: \$32,403

**Peter Merkel**

Rheumatology/Vasculitis Center  
Agency: NIH NIAMS/ 2P60 2P60 AR047785-06  
Project Title: The Interplay of Thrombosis and Vasculitis  
Total Direct Costs: \$126,515  
Direct Costs Current Year: \$621,527

**Peter Merkel**

Rheumatology/Vasculitis Center  
Agency: NIH-NCRR  
Project Title: Clinical Research for Rare Diseases: Opportunities, Challenges, and Solutions 2007-2008  
Total Direct Costs: \$93,938  
Direct Costs Current Year: \$93,938

**Martha Skinner**

Rheumatology  
Agency: NIDDK  
Project Title: Xith International Symposium On Amyloidosis  
Total Direct Cost: \$19,700 9/30/2006 - 8/31/2007  
Direct Cost Current Year: \$19,700

**Robert Lafyatis**

Rheumatology  
Agency: AstraZeneca  
Project Title: Molecular and Histological Characterization of Bone Marrow Lesions in Knee Osteoarthritis  
Total Direct Cost: \$26,379 11/1/2005 - 10/31/2006  
Direct Cost Current Year: \$23,884

**Robert Lafyatis**

Rheumatology  
Agency: Merck & Co.  
Project Title: a 2-week Pilot Study to Assess Recruitment of Patients with Osteoarthritis of the Knee for a Disease Modification Trial Using Magnetic Resonance Imaging  
Total Direct Cost: \$23,125 10/14/2005 - 4/13/2006  
Direct Cost Current Year: \$7,753

**Robert Lafyatis**

Rheumatology  
Agency: Stryker  
Project Title: A Phase I, Double-Blind, Randomized, Single Dose Escalation Safety Study of Intra-Articular Osteogenic Protein-1 (OP-1) in Subjects  
Total Direct Cost: \$223,230 5/7/2007 - 5/6/2008  
Direct Cost Current Year: \$31,728

**Robert Lafyatis**

Rheumatology  
Agency: Cordis  
Project Title: DEScover Registry  
Total Direct Cost: \$6,300 4/1/2005 - 12/31/2008  
Direct Cost Current Year: \$385

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**Robert Simms**

Rheumatology  
Agency: Ambergen  
Project Title: Molecular Diagnostic Assay for Colorectal Cancer  
Total Direct Cost: \$1,950 6/1/2003 - 12/31/2007  
Direct Cost Current Year: \$1,950

**Michael York**

Rheumatology  
Agency: TAP Pharmaceutical  
Project Title: An Online Case-Crossover Study of Risk Factors Triggering Acute Gout Flares  
Total Direct Cost: \$66,770 7/15/2004 - 3/31/2006  
Direct Cost Current Year: \$65,292

**Michael York**

Rheumatology  
Agency: TAP Pharmaceutical  
Project Title: Low Dose Aspirin Use and the Risk of Recurrent Gout Attacks  
Total Direct Cost: \$33,306 3/7/2007 - 3/6/2008  
Direct Cost Current Year: \$8,007

**VASCULAR BIOLOGY****Richard Cohen**

Vascular Biology  
Agency: NHLBI  
Project Title: Project 3--Oxidative Stress, AMPK, and Diabetic Cardiovascular Disease  
Total Direct Cost: \$1,315,266 5/1/2003 - 4/30/2008  
Direct Cost Current Year: \$261,960

**Richard Cohen**

Vascular Biology  
Agency: sanofi-aventis U.S. Inc.  
Project Title: Beta cElls and CB1: A Protective Role for CB1 Antagonisms in Lipotoxicity  
Total Direct Cost: \$205,968 6/5/2006 - 10/31/2007  
Direct Cost Current Year: \$205,968

**Richard Cohen**

Vascular Biology  
Agency: NIA  
Project Title: Angiotensin-induced Oxidants and Vascular Cell Phenotype  
Total Direct Cost: \$1,000,000 3/1/2005 - 2/28/2010  
Direct Cost Current Year: \$189,636

**Richard Cohen**

Vascular Biology  
Agency: NHLBI  
Project Title: Project #4--Insulin resistance, endothelial oxidants, and Ras  
Total Direct Cost: \$1,250,000 9/30/2005 - 8/31/2010  
Direct Cost Current Year: \$257,500

**Richard Cohen**

Vascular Biology  
Agency: NHLBI  
Project Title: No, Serca And Oxidative Stress In Atherosclerosis  
Total Direct Cost: \$1,131,000 5/1/2004 - 6/30/2009  
Direct Cost Current Year: \$216,026

**Bingbing Jiang**

Vascular Biology  
Agency: American Heart Assoc  
Project Title: Bimodal modulation of interleukin 1B induced signaling  
Total Direct Cost: \$236,364 7/1/2004 - 6/30/2008  
Direct Cost Current Year: \$59,091

**ROGER WILLIAMS MEDICAL CENTER****Mehrdad Abedi**

Agency: -- RI Foundation  
Project Title: Origin of Marrow-Derived Fibroblasts in the Skin Sclerotic Process  
Total Direct Cost: \$10,000 1/13/2006 - 1/13/2007  
Direct Cost Current Year: \$10,000

**Mehrdad Abedi**

Agency: NHLBI  
Project Title: Cell Cycle Related Transdifferentiation Plasticity  
Total Direct Cost: \$561,500 7/14/2003 - 6/30/2008  
Direct Cost Current Year: \$112,300

**Mehrdad Abedi**

Agency: Mayne Pharmaceuticals  
Project Title: Radiation for HLA-Matched Sibling and Matched Unrelated Donor Transplantation in Patients with Hematologic Malignancies  
Total Direct Cost: \$10,750 4/17/06 - 4/17/08  
Direct Cost Current Year: \$10,750

**EVANGELOS BADIIVAS, MD**

Agency: NIA  
Project Title: Bone Marrow Stem Cells and the Microenvironment of Chronic Wounds  
Total Direct Cost: \$205,000 5/15/07 - 2/29/08  
Direct Cost Current Year: \$205,000

**Gerald Colvin**

Agency: NIDDK  
Project Title: Stem/Progenitor Cell Inversions with Cell Cycle  
Total Direct Cost: \$464,500 8/1/2003 - 6/30/2007  
Direct Cost Current Year: \$116,125



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**Gerald Colvin**

Agency: ABT Associates  
Project Title: Dose Registry  
9/20/04 – 12/31/06  
Total Direct Cost: \$6,208 9/20/04 – 12/31/06  
Direct Cost Current Year: \$6,208

**ALAN EPSTEIN**

Agency: Schering-Plough  
Project Title: Comparison of PEG-Intron 1.5 mcg/kg/wk lusREBETOL vs. Previously Untreated Adult Subjects with Chronic Hepatitis C Infected Genotype 1  
Total Direct Cost: \$8,900 10/11/05 – 10/10/07  
Direct Cost Current Year: \$8,900

**VINCENT FALANGA**

Agency: Scleroderma Foundation  
Project Title: Autologous Bone Marrow-Derived Mesenchymal Stem Cells and Bioengineered Skin  
Total Direct Cost: \$138,890 1/30/06 – 1/30/08  
Direct Cost Current Year: \$138,890

**VINCENT FALANGA**

Agency: Intercytex  
Project Title: Topical II: A Prospective, Multi-Center, Double-Blind Randomized Placebo Controlled Study to Evaluate the Safety and Efficacy of ICZP007 in Phase III Trial with four-Layer Therapeutic Compression for the Treatment of Non-Infected Skin Leg Ulcers, due to Venous-Insufficiency  
Total Direct Cost: \$24,160 6/1/05 – 6/30/07  
Direct Cost Current Year: \$24,160

**VINCENT FALANGA**

Agency: Genentech  
Project Title: A Phase II, Double-Blind, Randomized, Placebo Controlled Study to Asses the Effect of Topical Recombinant Human Vascular endothelium growth Factor for Induction of Healing Diabetic Foot Ulcers  
Total Direct Cost: \$4,000 1/3/07 – 11/7/07  
Direct Cost Current Year: \$4,000

**VINCENT FALANGA**

Agency: Healthpoint, LTD  
Project Title: Extend of Scarring in a Full-Thickness Wound Model in the Mouse Trial: Effect of Collagenase

Total Direct Cost: \$15,928 4/17/07 – 4/16/08  
Direct Cost Current Year: \$15,928

**RAKESH GUPTA**

Agency: IM Systems  
Project Title: OxiTrac Trial  
Total Direct Cost: \$1,900 11/14/05 – 11/14/06  
Direct Cost Current Year: \$1,900

Agency: NIAID

Project Title: Designer T Cell Therapy for PML  
Total Direct Cost: \$595,300 5/1/2004 - 4/30/2008  
Direct Cost Current Year: \$195,300

**Richard Junghans**

Agency: DOD  
Project Title: Phase I Trial of Anti-PSMA Designer T cells in Advanced Prostate Cancer  
Total Direct Cost: \$749,999 6/24/2005 - 6/23/2008  
Direct Cost Current Year: \$250,000

**Richard Junghans**

Agency: FDA  
Project Title: Anti-CEA Designer T cells in GastricCancer, Phase I Trial  
Total Direct Cost: \$450,000 2/1/06 – 1/31/09  
Direct Cost Current Year: \$150,000

**Richard Junghans**

Agency: Prostate Cancer Foundation  
Project Title: 2005 Prostate Cancer Foundation Award  
Total Direct Cost: \$100,000 2/23/06 - ongoing  
Direct Cost Current Year: \$100,000

**Richard Junghans**

Agency: -- Association Francaise Contre Les Myopathies  
Project Title: Transcription factor distrupction in Myotonic Dystrophy  
Total Direct Cost: \$17,962 7/24/2006 - 7/23/2008  
Direct Cost Current Year: \$8,961

**Lawrence Lum**

Agency: NCI  
Project Title: Breast Cancer Treatment with Antibody Targeted T cells  
Total Direct Cost: \$1,824,179 4/1/2002 - 3/31/2007  
Direct Cost Current Year: \$524,210

**Lawrence Lum**

Agency: NCRR  
Project Title: COBRE – The New Stem Cell Biology  
Total Direct Cost: \$8,690,054 9/30/03 – 4/30/08  
Direct Cost Current Year: \$2,483,377

**Lawrence Lum**

Agency: Leukemia & Lymphoma Society  
Project Title: Circumventing Rituximab Resistance in Patients with B Cell Malignancies  
Total Direct Cost: \$360,966 12/1/04 – 11/30/07  
Direct Cost Current Year: \$360,966

**Richard Junghans**

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**LUGUANG LUO**

Agency: Juvenile Diabetes Research Foundation  
Project Title: A New Strategy for Improving Human Islet Longevity  
Project Period:  
Total Direct Cost: \$145,448 5/1/07 – 4/30/08  
Direct Cost Current Year: \$145,448

**ANITA PEDVIS**

Agency: Omnicare  
Project Title: Observational post-Marketing Safety Surveillance Registry of Enbrel for the treatment of Psoriasis  
Project Period:  
Total Direct Cost: \$9,000 8/2/06 – 8/2/11  
Direct Cost Current Year: \$9,000

**Peter Quesenberry**

Agency: NHLBI  
Project Title: GABP Transcription Factor in Myeloid Differentiation  
Total Direct Cost: \$4,947 8/1/2005 - 9/30/2006  
Direct Cost Current Year: \$4,947

**Peter Quesenberry**

Agency: NHLBI  
Project Title: Cell Cycle Related Transdifferentiation into Lung Cells  
Total Direct Cost: \$1,034,047 8/15/2003 - 7/31/2007  
Direct Cost Current Year: \$259,430

**Peter Quesenberry**

Agency: NHLBI --  
Project Title: Cell Cycle Related Transdifferentiation into Lung Cells  
Total Direct Cost: \$1,034,047 8/15/2003 - 7/31/2007  
Direct Cost Current Year: \$259,430

**GAIL SKOWRON**

Agency: AMFAR  
Project Title: Res. Det. of HIV Vir. Res.  
Total Direct Cost: \$30,000 6/1/00 – ongoing  
Direct Cost Current Year: \$30,000

**GAIL SKOWRON**

Agency: BioAlliance  
Project Title: A Comparative, Randomized, Double-Blind, Double-Dummy, Multi-Center Study of the Efficacy and Safety of Miconazole Laurid 50 mg Administered Once a Day and Nyceles Troches Administered Five Times a Day in the Treatment of Oropharyngeal candidiasis in Immunocompromised Patients  
Total Direct Cost: \$2,755 8/18/06 – 8/17/07  
Direct Cost Current Year: \$2,755

**Gail Skowron**

Agency: GlaxoSmithKline  
Project Title: Antiviral Effect of GW873140 in Combination with COMBIVIR  
Project Period:  
Total Direct Cost: \$12,138 1/26/05 – 6/5/08  
Direct Cost Current Year: \$12,138

**Gail Skowron**

Agency: Kendle NC Inc.  
Project Title: A Multi-Center Randomized, Double-Blind, Controlled Study of NGX-4010 for Treatment of Painful HIV-Associated Neutropathy  
Total Direct Cost: \$2,000 1/29/07 – 1/29/08  
Direct Cost Current Year: \$2,000

**JOSEPH TUCCI**

Agency: Novartis  
Project Title: Project ZOL446H-2304  
Total Direct Cost: \$33,815 5/10/02 – 11/30/06  
Direct Cost Current Year: \$33,815

**JOSEPH TUCCI**

Agency: Amgen/Quintiles  
Project Title: A randomized, Double-Blind Study to Compare the Efficacy of Treatment with Denosumab vs. Alendronate Sodium in Postmenopausal Women with Low Bone Mineral Density  
Total Direct Cost: \$25,720 3/20/06 – 3/20/07  
Direct Cost Current Year: \$25,720

**Wen Yang**

Agency: RI Foundation  
Project Title: A Pilot Test of Co-overexpressing Bcl-xL and FLIP for its potential in promoting Tcell survival  
Total Direct Cost: \$10,000 1/13/2006 - 1/12/2007  
Direct Cost Current Year: \$10,000

**Wen Yang**

Agency: -- The Campbell Foundation  
Project Title: Enhancing Potency of Anti-HIV Chimeric Immune Receptors (CIRS)  
Total Direct Cost: \$73,636 6/1/2007 - 5/31/2008  
Direct Cost Current Year: \$73,636