

**BOSTON UNIVERSITY MEDICAL CENTER**  
**DEPARTMENT OF MEDICINE**  
**ANNUAL REPORT**  
**SECTION OF Preventive Medicine & Epidemiology**  
**JULY 1, 2007 - JUNE 30, 2008**  
**FISCAL YEAR 2008**

## **Overview of Section**

The Section of Preventive Medicine and Epidemiology is a non-clinical section of the Evans Department of Medicine, with both a research and an educational mission. The research focus of the Section largely comprises the epidemiology and prevention of chronic diseases such as cardiovascular disease, obesity, diabetes or cancer. The study of behavioral and other lifestyle factors in the pathogenesis of these diseases and conditions is of particular interest. Other ongoing work includes studies of biomarkers of chronic diseases in conjunction with various behavioral exposures.

The faculty and staff of the Section have extensive and long-standing expertise in nutritional epidemiology, including the selection and implementation of various nutritional assessment methods (e.g., diet records, 24-hour recalls, food frequency questionnaires), management, use and analysis of large USDA and other nutrient data bases and data sets, and the linkage of food and nutrient information to determine food consumption patterns for individual study participants and to compare those patterns with USDA Food Pyramid Guidelines. This technical expertise is used to guide the study of nutrition-related exposures and various health outcomes. The study of food-based dietary patterns has been a major focus of many of the epidemiologic studies carried out in the Section during the past year. These include studies of dietary patterns such as the “DASH diet” or a Mediterranean-style diet.

The causes and consequences of obesity and body fat distribution throughout the lifespan are other important areas of interest to the Section. During the past year, a large number of analyses have been ongoing with separate longitudinal studies of children, adolescents and adults. These studies are being used to inform our knowledge on the determinants of weight gain and loss, as well as the type and amount of body fat stores. In addition to the examination of nutrition-related exposures, the Section has expertise in the assessment of physical activity using questionnaires for subjects of all ages as well as monitoring with electronic motion sensors.

Another ongoing focus of the Section in the past year has been the study of the health effects of alcohol consumption. These studies include the examination of potential health benefits of light-to-moderate alcohol drinking as well as new studies that are just beginning to address the effects of alcohol use disorders and heavy alcohol intake (in the absence of known use disorders) on health, cognition and psychosocial outcomes. Members of the Section of Preventive Medicine have expertise in the study of various other modifiable risk factors for chronic disease as various psychosocial predictors and outcomes of disease.

The current studies that serve as the basis for the ongoing work of Section members include the Framingham Study cohorts, the Lifetime Health Study, the Family Heart Study and Family Blood Pressure Study, the Framingham Children’s Study, the National Health and Nutrition Examination Surveys, and the National Growth and Health Study. The Section is also involved in the teaching of students, residents, fellows, and faculty at Boston University and supports the Preventive Medicine Residency Program at Boston University Medical Center. During the past year, we have had two fellows in the Section—one Preventive Medicine fellow who will be joining the faculty of BMC in July and one Cardiology fellow in her second year of a three-year fellowship.

## Highlights from the Past Year

In early 2008, our Section Chief, Dr. R. Curtis Ellison, stepped down from this position although he continues as a part-time faculty member in the Section. Dr. Lynn Moore served as Section Chief, ad interim, during the search for a new chief. This period of change has provided us with an important opportunity to re-assess the future direction of the Section.

Dr. Moore plans to expand her work in the areas of nutritional epidemiology, obesity and metabolic disorders. Others at BMC have similar interests and are tackling the problems of obesity and metabolic disorders from different perspectives. This provides us with a unique opportunity to merge the skills and interests of faculty and others across the medical and public health campuses. Dr. Moore is increasingly recognized as an important leader in this field and she is increasingly called upon to lecture not only throughout the U.S., but around the world. She has served as a keynote speaker at numerous recent conferences, such as those in Australia, New Zealand, Ireland, Canada and Germany. Dr. Moore has been an active member of special review panels for the selection and creation of Vanguard Sites and initial study sites for the National Children's Study. She has been asked to provide advice to various scientific advisory committees (e.g., the nationwide Nutrient-Rich Foods Coalition and 2010 Dietary Guidelines).

## Faculty

Lynn L. Moore, DSc, MPH, Ad Interim Chief (Associate Professor of Medicine). Her research includes the following types of studies: (a) obesity, metabolic disorders, diabetes, CVD and other chronic diseases; (b) nutritional exposures, prenatal risk, and behavioral and psychosocial risk factors throughout the lifespan; and (c) pediatric risk assessment for adult chronic diseases.

R. Curtis Ellison, MD, Chief (through March 2008) (Professor of Medicine & Public Health). Dr. Ellison carries out research on the following: (a) lifestyle factors related to the risk of cardiovascular disease and cancer; (b) the interactions of genes and environment on various outcomes; and (c) studies on the relation of the moderate intake of wine and alcohol to health and disease. Included in the Section is the *Institute on Lifestyle & Health* that carries out a surveillance of the scientific literature on alcohol consumption and health. Dr. Ellison directs the Institute and distributes critiques of key papers in this area.

Other scientists who have spent part of their time during 2008 in the Section include the following individuals:

Yuqing Zhang, DSc (Professor of Medicine & Public Health), who carries out research on cancer, arthritis, osteoporosis, moderate alcohol consumption and cardiovascular disease.

Kenneth J. Rothman, DrPH (Professor of Public Health), a leading epidemiologist, teacher, author and the founding editor of the journal, *Epidemiology*. Dr. Rothman mentors many graduate students and is a consultant for many studies at institutions around the world.

Richard H. Meyers, PhD (Professor of Neurology & Medicine) has worked with Dr. Ellison in the conduct of several genetic epidemiology studies.

Jemma B. Wilk, ScD, (Assistant Professor of Neurology & Medicine), who works with Dr. Meyers and has carried out statistical genetic analyses on a number of projects.

In addition, many investigators and scientists from the Framingham Study have adjunct faculty appointments in the Section of Preventive Medicine. These include Philip A. Wolf, MD, a neurologist and epidemiologist, who is PI of the NHLBI Contract supporting the Study and NIH-supported research on stroke and dementia; Daniel Levy, MD, current Director of the Framingham Study; William B. Kannel MD, former Chief of the Section; Emelia Benjamin, MD; Joanne Murabito, MD; Christopher O'Donnell, MD; and Vasan S. Ramachandran, MD. The faculty also includes Pantel S. Vokonas, MD, director of the VA Normative Aging Study.



**BOSTON UNIVERSITY MEDICAL CENTER**  
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**SECTION OF Roger Williams Medical Center**  
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Roger Williams Medical Center is a 256 acute care hospital in Providence, Rhode Island which serves as an important 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 Roger Williams Cancer Center which houses a state of the art radiation oncology facility and a new 7000 square foot outpatient unit for medical oncology, surgical oncology, blood and marrow transplantation and chemotherapy infusions. This is also the site for a hospice unit, nursing home and medical office building for the faculty practice of University Medical Group. In addition, over 20,000 square feet of research space is located on this campus.

The Department of Medicine is comprised of approximately 50 full-time clinical and research faculty. An additional 50 community physicians participate in the Department's teaching programs. There are 43 residents in our internal medicine residency training program and 32 fellows in training programs in pulmonary medicine, infectious diseases, hematology, medical oncology, endocrinology and rheumatology. The Department also serves as a teaching venue for students from the Boston University School of Medicine. Second-year BUSM students participate in a physical diagnosis course and third-year BUSM students complete the ambulatory medicine portion of their clerkship at our outpatient facilities. Housing is provided for the students as well.

The Department is recognized for the quality of its clinical and research programs. The state's only blood and marrow transplantation unit is housed at Roger Williams Medical Center in a 6 bed unit with a stem cell laboratory. Our behavioral medicine division manages the state's only inpatient alcohol and substance abuse detoxification unit as well as a dual diagnosis and geritopsychiatry unit in the hospital. Also recognized in the community are the Department's geriatrics program, endoscopy services, sleep laboratory, endocrinology program including its section of bone and mineral metabolism and rheumatology services.

The research programs of the Department focus on several important areas which are approached in a multidisciplinary manner. Faculty from the Department of Medicine participate in the institutions Center for Stem Cell Research which is funded with a \$15 million grant from the NIH designating this program as a Center of Biologic Research Excellence. Several translational projects involve infectious diseases, complementary medicine and medical/surgical oncology.

Faculty highlights for this academic year include the following:

Dr. Mehrdad Abedi received a grant from the Scleroderma Foundation entitled, "Hematopoietic Origin of Fibroblasts at Sites of Injury."

Dr. Frank Cummings was PI on a randomized study evaluating three treatment regimens for patients with untreated multiple myeloma who were not transplantation candidates.

Dr Richard Junghans, Chief of Surgical Oncology Research and Associate Professor of Medicine, received a major grant from the Department of Defense for \$7.9M to study the use of designer T cells in treating metastatic breast cancer.

Dr. LuGuang Luo published five papers this year in a variety of journals including Diabetes and Biological and Biophysical Research Communications. He also had two abstracts selected for oral presentations at this year's American Diabetes Association Annual Meeting and was invited to present a talk entitled, "Stem cells and Diabetes in Human Therapy."

Dr. Yoram Puius received a grant entitled, "Isolation of circulating, antibody-producing plasma cells against Staphylococcus aureus from colonized, healthy donors."

Dr. Gail Skowron, Chief of Infectious Diseases, was honored by receiving a 2009 Rhode Island Business Women's Award and one of the Jewish Federation of Rhode Island AIDS Task Force Woman of the Year Awards. Dr. Skowron also was chosen to serve as a Stage 1 reviewer for the NIH Challenge Grants in Health and Science Research. She published several papers in Clinical Infectious Diseases and the Journal of AIDS as part of the ACTG 384 Team and was awarded a grant from the Rhode Island Department of Health entitled, "Hospital Clinic-Based Primary & Specialty Health Care." The Rhode Island Department of Health also invited Dr. Skowron to join its Infectious Diseases and Epidemiology Advisory Committee

Dr. Joseph Tucci, Chief of the Division of Endocrinology, received the 2009 Boston University School of Medicine Alumni Award. Dr. Tucci also published an article entitled, "Vitamin D Therapy in Patients with Hyperparathyroidism and Hypovitaminosis D" in the European Journal of Endocrinology. Dr. Tucci received funding as part of a multicenter trial to assess a new oral agent for the treatment of type 2 diabetes mellitus and funding to participate in a trial evaluating the incidence of hypocalcemia post Reclast treatment in patients with Paget's disease.

Dr. Alan Weitberg, Chairman of the Department of Medicine and Assistant Dean for Academic Affairs at the Boston University School of Medicine was named a Castle Connolly Top Doctor in the United States for 2009. He also published a study entitled, "A Phase I/II trial of beta-(1,3)/(1,6) D-glucan in the treatment of patients with advanced malignancies receiving chemotherapy" in the Journal of Experimental and Clinical Cancer Research. Dr. Weitberg also was the PI on a trial entitled, "An Open-Label, Randomized, Phase 2 Study of Efficacy and Tolerability of ABT-869 in Advanced or Metastatic Non-Small Cell Lung Cancer."

BOSTON UNIVERSITY MEDICAL CENTER  
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SECTION OF **Residency Program in Medicine**  
**JULY 1, 2007 - JUNE 30, 2008**  
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**EDUCATION 2008**

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 and 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 two campuses in close proximity to each other, namely the East Newton and the Menino Pavilions. There are eight general medicine teams on Menino, and four general medicine teams on East Newton. In addition, there are three subspecialty services on East Newton, which the house staff rotates: 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 attending 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 master clinicians chosen for their teaching and leadership skills, 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 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 2007-2008 academic year there are 58 PGY-1 interns, 11 of whom are in the preliminary program and 42 of whom (5 primary care trainees and 42 traditional track trainees) are in the categorical program. The PGY2 year has 46 trainees, (five in primary care and 41 traditional); the PGY3 year has 44 trainees (six primary care and 38 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, 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.

### 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, selected by the trainee and complementing the broad representation of clinical experiences. The diverse hands-on clinical training opportunities 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.

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 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. Areas of curricular innovation include: Health Policy and Public Health, Leadership and Advocacy Skills, Mental Health, Addiction Medicine and Health Literacy.

In the **categorical traditional track**, 80% of our residents continue to enter prestigious subspecialty 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 2007-2008 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 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. Students also 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. 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 Coleman, MD	Chair, Department of Medicine Acting 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
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)

### BOSTON UNIVERSITY RESIDENCY PROGRAM IN MEDICINE 2007-2008

#### Chief Residents

Miguel Ariza  
Peter Grays on  
Jeremy Richards

#### Medical School

Boston University  
Medical University of South Carolina  
University of Wisconsin

#### Post Graduate Position

Endocrine Fellowship, Boston University  
Rheumatology Fellowship, BU  
Pulmonary and Critical Care Fellowship  
Massachusetts General Hospital  
Cardiology, University of Illinois-Chicago  
Gastroenterology Fellowship, BU  
Cardiology, Cleveland Clinic

David Schopfer  
Hillary Tompkins  
Edwin Zishiri

Rush University  
Boston University  
University of Zimbabwe

#### Senior Residents

#### Medical School

#### Post-Graduate Position

Renata Aguiar	Universidade Federal Do Rio de Janeiro	Endocrine Fellowship, Yale University
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Anthony Annese	Boston University School of Medicine	Amyloid Fellowship, Boston University
Ogheneruona Apoe	Tufts University School of Medicine	Hospitalist Fellowship Johns Hopkins University
Daniel Arnold	Tulane University School of Medicine	Chief Resident BMC
Donette Campbell	State University of New York Stony Brook School of Medicine	Hematology/Oncology Fellowship BMC
Philip Cefalo	University of Massachusetts Medical School	Medical Consult Spaulding Rehabilitation Hospital
Jorge Chaves	University of Texas Medical School at Houston	Hematology/Oncology Fellowship Yale University
Eddy Chen	Keck School of Medicine of the University of Southern California	Chief Resident BMC
Regine Cherazard	Temple University School of Medicine	Hospitalist, Weatherby Locum Fort Lauderdale, FL
Warren Chuang	Boston University School of Medicine	Hospitalist Massachusetts General Hospital
William Cooney	Boston University School of Medicine	Hospitalist Cape Cod Hospital, Hyannis, MA
Damian Crawford	University of Maryland School of Medicine	Hospitalist Caritas-Good Samaritan Hospital, Brockton, MA
Carrie Daniel	University of Kansas School of Medicine	Hospitalist BMC
David Denmark	New York Medical College	Cardiology Fellowship North Shore/LIJ
Mustali Dohadwala	Medical College of Wisconsin	Cardiology Research Boston Medical Center
Peter Everett	Boston University School of Medicine	Hematology/Oncology Research Beth Israel Deaconess Medical Center, Boston, MA
Celia Garner	University of Minnesota-Minneapolis School of Medicine	Chief Resident BMC
Geoffrey Gibney	University of Connecticut School of Medicine	Hematology/Oncology Fellowship Yale University
Rejane Guerrier	University of Medicine & Dentistry of New Jersey/ New Jersey Medical School	Hospitalist Florida Medical Center
Eiman Jahangir	University of Tennessee College of Medicine	Cardiology Fellowship Vanderbilt University
Jaime Jenkins	University of North Carolina School of Medicine	Primary Care Physician High Point, NC
Aarti Kakkar	Emory University School of Medicine	Gastroenterology Fellowship BMC
Andrew Kim	Boston University School of Medicine	Hospitalist Lawrence Memorial Hospital
Jeffrey King	University of Massachusetts Medical School	Chief Resident BMC
Myung Lee	New York Medical College	Hospitalist BMC
Janette Lin	Brown Medical School	Primary Care Dorchester House Multi-Service Center
Yann-Bor Lin	Boston University School of Medicine	Pulmonary/Critical Care Fellowship BMC
Christine Liu	Temple University School of Medicine	Gerontology Fellowship BMC
Sezmin Noorani	Medical College of Georgia	Primary Care Physician University of North Carolina, Chapel Hill, NC
Nitin Patel	University of Medicine & Dentistry of New Jersey/R.W. Johnson Med School	Gastroenterology Fellowship UNMDNJ
William Rabitaille	New York Medical College	Primary Care University of Connecticut
Alan Rosen	Boston University School of Medicine	Chief Resident BMC
John Ryan	University College Cork	Chief Resident BMC

Jennifer Sinclair	Boston University School of Medicine	Hospitalist Lahey Clinic
Amulya Siram	Boston University School of Medicine	Endocrine Fellowship Mt. Sinai School of Medicine
David Solarz	University of Cincinnati College of Medicine	Chief Resident BMC
Lesley Stead	New York Medical College	Hematology/Oncology Fellowship Montefiore Medical Center
Sohera Syeda	Rush Medical College	Chief Resident BMC
Sara-Maiz Thomas	State University of New York at Buffalo	Hospitalist Gaston Medical Center, Gaston, NC
Megan Titas	Emory University School of Medicine	Attending Physician United States Navy
Tonslyn Toure	Brown Medical School	Endocrine Fellowship University of Pittsburgh
Pantila Vanichakarn	University of Chicago Pritzker School of Medicine	Cardiology Fellowship Dartmouth/Hitchcock Medical Center

## JUNIORS

Tobin Abraham	University of Massachusetts Medical School
Dominique Bayard	Mount Sinai School of Medicine
Priti Bijipuria	University of Maryland School of Medicine
Patrick Boland	Jefferson Medical College of Thomas Jefferson University
Stephanie Christenson	Medical College of Wisconsin
Amy Clark	Milton S. Hershey Medical Centre
Jason Craft	Brown Medical School
Mircea-Cristian Dobre	University of Minnesota-Minneapolis School of Medicine
Maureen Dubreuil	University of Connecticut School of Medicine
João Daniel Fontes	Universidade Federal Do Rio de Janeiro
Mark Franciosa	Boston University School of Medicine
Neel Gandhi	University of Tennessee College of Medicine
Anthony Garcia	Tufts University School of Medicine
Sandeep Ghai	Wayne State University School of Medicine
Saulius Girnius	University of Cincinnati College of Medicine
Vu Ho	Temple University School of Medicine
Jason Homsy	University of Rochester School of Medicine and Dentistry
Tinatin Khizanishvili	Medical College of Virginia of Virginia Commonwealth University
Woojin Kim	Brown Medical School
Joann Kwah	Drexel University College of Medicine
John Lee	Dartmouth Medical School
Suru Lin	Northwestern University - The Feinberg School of Medicine
Maria Lopez	University of Puerto Rico School of Medicine
Jason Luke	Rosalind Franklin University of Medicine and Science/Chicago
Hector Marquez	University of Medicine & Dentistry of New Jersey
Jana Montgomery	Boston University School of Medicine
Cassandra Pierre	SUNY at Buffalo
Ava Port	University of Medicine & Dentistry of New Jersey
Rajeev Prabakaran	University of Miami School of Medicine
Sujata Ramamurthy	Northeastern Ohio Universities College of Medicine

## MEDICAL SCHOOL

Anjana Ranganathan	University of Pittsburgh School of Medicine
Judith Richards	SUNY Downstate College of Medicine
Belinda Rivera	Universidad Central Del Caribe
Daniel Roseman	Rush Medical College
Alefiya Shakir	Boston University School of Medicine
Torfay Sharifnia	Tulane University School of Medicine
Rohit Sharma	University of Texas Medical School at Dallas
Rebecca Summers	Tufts 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
Megan Young	University of Chicago Pritzker School of Medicine

### INTERNS

Yazan Alderazi  
 Mir Alikhan  
 Dominic Amirtharaj  
 Mekdelawit Aschenaki  
 Keren Bakal  
 Vikram Brahmanadam  
 Tony Chow  
 Benjamin Chu  
 Richard Chung  
 Jason DeLong  
 Silpa Dhoma  
 Scott Dresden  
 Jessica Eng  
 Mary Evans  
 Joseph Feuerstein  
 Robert Fuller  
 Joanna Ghobrial  
 Lalitha Gudipaty  
 Astrid Gutierrez  
 Farah Hameed  
 Christine Hsu  
 Nadia Huancahuari  
 Arooj Hyat  
 Vinu Ipe  
 Elizabeth Jalkut  
 Robert Jungman  
 Neelima Karipineni  
 Maya Kommineni  
 Jennifer Ku  
 Nicole LaRue

### MEDICAL SCHOOL

Royal College of Surgeons of Ireland  
 University of Texas Medical School at San Antonio  
 University of Massachusetts Medical School  
 Rush Medical College  
 University of Medicine & Dentistry of New Jersey/ New Jersey Medical School  
 University of Pittsburgh School of Medicine  
 Temple University School of Medicine  
 Texas Tech University School of Medicine  
 State University of New York Stony Brook School of Medicine  
 Eastern Virginia Medical School  
 University of Texas Medical School at San Antonio  
 Loyola University of Chicago Stritch School of Medicine  
 Boston University School of Medicine  
 Uniformed Services University of Health Sciences  
 Boston University School of Medicine  
 University of Medicine & Dentistry of New Jersey/ New Jersey Medical School  
 Wayne State University School of Medicine  
 Case Western Reserve University School of Medicine  
 Ponce School of Medicine Puerto Rico  
 University of Texas Medical Branch  
 Jefferson Medical College of Thomas Jefferson University  
 University of California at Davis School of Medicine  
 University of Vermont College of Medicine  
 University of Texas Southwestern Medical School at Dallas  
 Tufts University School of Medicine  
 Tulane University School of Medicine  
 George Washington University School of Medicine  
 University of North Carolina School of Medicine  
 University of Virginia School of Medicine  
 Boston University School of Medicine

Sun Lee	University of Medicine & Dentistry of New Jersey/ New Jersey Medical School
Elaine Lin	New York University School of Medicine
Lyndonna Marrast	State University of New York Stony Brook School of Medicine
Roderick McCoy	Washington University School of Medicine
Matthew Mendlik	Ohio State University College of Medicine
Amit Nanavati	Texas A & M University System HSC College of Medicine
Najlla Nassery	Tufts University School of Medicine
Judy Nee	Brown Medical School
Kelly O'Hara	Northwestern University - The Feinberg School of Medicine
Felicia Patch	Baylor College of Medicine
Neepta Patel	Wayne State University School of Medicine
David Popoli	Tulane University School of Medicine
Eric Pound	Boston University School of Medicine
Ido Preis	Brown Medical School
Shilpa Ravella	University of Pittsburgh School of Medicine
Rebecca Sandfort	Boston University School of Medicine
Peter Shaw	Case Western Reserve University School of Medicine
Joshua Sheehan	Boston University School of Medicine
Andrea Stanton	Albert Einstein College of Medicine/Yeshiva University
Elizabeth Sutton	McGill University Faculty of Medicine
Corey Tabit	Jefferson Medical College of Thomas Jefferson University
Katrina Traber	New York University School of Medicine
Jaime Vasquez	Brown Medical School
Jessica Viola	University of Massachusetts Medical School
Xiaohui Wang	China Medical University
Bradley Yamanaka	Rosalind Franklin University of Medicine and Science/Chicago Medical School
Leah Zallman	New York University School of Medicine
James Zimmerman	Brown Medical School
Ryan Zitnay	Loyola University of Chicago Stritch School of Medicine

**BOSTON UNIVERSITY MEDICAL CENTER**  
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**ANNUAL REPORT**  
**SECTION OF Rheumatology**  
**JULY 1, 2007 - JUNE 30, 2008**  
**FISCAL YEAR 2008**

The Rheumatology Section includes nine full-time M.D. faculty, four full-time Ph.D. faculty and four part-time clinical faculty. Dr. Simms assumed the role of Rheumatology Section Head, after three years as Interim Section Head and Center Director. Dr. Kissin assumed the role of Clinical Director and Dr. Monach became Associate Fellowship Program Director. Dr. Hyon Choi, Professor of Medicine (pending) joined the faculty of the Section this past academic year. Dr. Choi is an internationally recognized epidemiologist in the area of gout and rheumatoid arthritis and adds these areas to existing research and clinical expertise. During the past academic year, there were five rheumatology fellows. We also have on staff nine clinical trial coordinators.

Center faculty have continued to achieve widespread national recognition for both their research programs and their clinical expertise. They serve on national and international committees for the American College of Rheumatology, the National Institutes of Health, the Arthritis Foundation, the Scleroderma Foundation, the International Scleroderma Network, and the Scleroderma Clinical Trials Consortium and on advisory boards for a number of biotechnology and pharmaceutical companies. They have continued to play pivotal and leading roles in studies of scleroderma, osteoarthritis and vasculitis. The faculty of Section of Rheumatology, the Clinical Epidemiology Section and the Vasculitis Center work together collaboratively in many teaching, research and clinical programs.

Teaching:

Medical school: The faculty of the Rheumatology Section teaches the Musculoskeletal component of the Biology of Disease course. An important feature of this course is bringing patients into small group sessions to bridge didactic work with clinical contact. In addition to approximately 19 hours of formal lectures in the Biology of Disease course, the Center contributed over 600 hours of teaching time in the outpatient department and inpatient services for medical students, residents and fellows. Our faculty have been active in continuing medical education and have given many Department of Medicine Grand Rounds, Rheumatology Grand Rounds, and invited to lectures at national meetings, including the American College of Rheumatology.

Residents: Our rheumatology rotation teaches a large number of medical residents from Primary Care, General Internal Medicine, Dermatology, Rehabilitation Medicine and Orthopedics. Residents gain exposure to outpatient medicine in rheumatology, which is not achieved unless they rotate through the specialty.

Fellows: The fellowship program, headed by Dr. Simms, with Dr. Monach as Associate Program Director and Dr. Felson as PI, continues to be funded by an NIH T32 grant. Our fellowship program had a large number of outstanding candidates this year and our two positions for July 2009 were filled with two highly ranked applicants in the rheumatology match. Three fellows were successful in obtaining foundation grants to support their research and all three fellows graduating in 2008, assumed full-time faculty positions at prestigious institutions. Dr. Kissin has successfully integrated musculoskeletal ultrasound into the rheumatology fellowship curriculum which now serves as a sought-after model for other rheumatology training programs.

#### Laboratory and Clinical Research Programs:

The laboratory research efforts of the Section relate to basic biologic mechanisms in the pathogenesis of scleroderma, arthritis, and systemic lupus erythematosus. There is a concordant research effort in clinical investigation of these disorders, including the testing of novel therapies.

#### Affiliated Rheumatology Section Research Programs:

The Scleroderma Laboratory Research Program, directed by Dr. Robert Lafyatis, Professor of Medicine includes Dr. Michael York (Assistant Professor) and visiting scholar, Dr. Alessandra Farina. The focus of this group has been on understanding the interactions between the three key pathogenic events in systemic sclerosis: autoimmunity, fibrosis and vascular biology. The traditional base of research in the group is in fibrosis and matrix biology is led by Dr. Lafyatis on understanding the pathogenesis of fibrosis in the tight skin (Tsk) mouse with several key observations over the past year, most notably observations about the role of Wnt regulation in Tsk mice and systemic sclerosis, and CCN3 regulation of elastogenesis. A second axis of scleroderma research in the laboratory is being spearheaded by Dr. York, Dr. Lafyatis and Dr. Farina, and two Rheumatology Research fellows, Dr. John McCahan and Dr. Fabienne Denhez, working closely with Dr. Marshak-Rothstein (Professor of Immunology). The goals of these closely related projects are to further explore innate immunity in scleroderma. Dr. York has obtained important results showing 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. Dr. Farina and Dr. York are carrying out pivotal work on understanding the roles on TLRs on fibroblasts and endothelial cells.

Dr. McCahan and Dr. Denhez working with Dr. Marshak-Rothstein are developing several new models of autoimmunity, one of which promises to become an exciting model for systemic sclerosis. Work in vascular disease has also seen significant progress over the past years, which is due to a strong collaboration between the laboratories of Drs. Lafyatis and Farber (BUMC) and Dr. Whitfield (Dartmouth Medical Center). These groups identified several intriguing microarray biomarkers of pulmonary hypertension in scleroderma patients. Our success over the last year has been manifest by important publications ranging from basic science to translational medicine to clinical trials. In addition, there is successful funding through NIH U01 and R01 grants (Dr. Lafyatis, PI), grants for biomarker studies from Actelion and BiogenIdec (Dr.

Lafyatis), grants for studies on innate immunity in systemic sclerosis from the Scleroderma Foundation and the American College of Rheumatology (Dr. York) and grants for Dr. Marshak-Rothstein for closely collaborative work on animal models of scleroderma from the NIH (R01) and the Scleroderma Research Foundation. These highly collaborative research efforts continue to position the section well to make further advances in understanding this devastating disease.

The Scleroderma Clinical Trial Program continues to grow with many active clinical trials in scleroderma. Dr. Robert Simms, Section Head and Professor of Medicine, is the regional PI for a pivotal NIH-funded, 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 of the Scleroderma Program include those involving an innovative topical therapy for Raynaud's phenomenon, mycophenolate mofetil (an anti-rejection therapy for transplantation) and imatinib for diffuse scleroderma. The Scleroderma Program is also one of five national sites conducting a trial of a novel antifibrotic therapy, anti-interleukin 13 for pulmonary fibrosis associated with scleroderma. The Program is also conducting several therapeutic trials of vasodilators for pulmonary hypertension, a common and severe complication of scleroderma. Scleroderma Program faculty including Drs. Lafyatis, Simms, Farber, Kissin and York are actively conducting prospective translational longitudinal studies to link biomarkers of scleroderma to clinical outcomes such as the development of pulmonary hypertension, worsening skin disease, pulmonary fibrosis and renal crisis. Program faculty including Drs. Simms, Merkel and Lafyatis are also working to develop improved outcomes of disease activity and involvement.

#### Clinical activities:

The clinical program in rheumatology is a major referral center for autoimmune and rheumatic diseases. Patients with scleroderma and vasculitis are seen from throughout the Northeast and in substantial numbers from throughout the United States and even abroad. Center faculty serve as identified expert clinicians broadly in the field of rheumatology as well within their research interest area. Dr. Kissin, Assistant Professor of Medicine, assumed the role of Clinical Director as the expanding clinical program continues to meet the needs of patients and referring physicians. Total clinical volume has continued to grow with over 8000 annual outpatient visits in addition to several hundred inpatient consultations each year. Many of referred patients have complex medical problems and their referral to the institution contributes substantially to the reputation of the Medical Center and further enhances clinical collaborative efforts with colleagues in multiple specialties, including in Cardiology, Pulmonary Diseases, Radiology and other medical specialties. Both Drs. Simms and Merkel were recognized among Boston Magazine's "Top Doctors".

In summary, the Rheumatology Section remains a key player in research, clinical activity, clinical investigation, and educational programs nationally and internationally. We anticipate continued growth on all these fronts.

**BOSTON UNIVERSITY MEDICAL CENTER**  
**DEPARTMENT OF MEDICINE**  
**ANNUAL REPORT**  
**SECTION OF Pulmonary, Allergy, Critical Care and Sleep Medicine**  
**JULY 1, 2007 - JUNE 30, 2008**  
**FISCAL YEAR 2008**

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

**SECTION SUMMARY REPORT**

**Introduction:**

The Pulmonary Section is a multi-disciplinary integrated clinical and scientific division. Research Faculty are members of the BUSM Pulmonary Center. The Section provides In- and Out-patient services to Boston Medical Center, The Boston Veterans Administration Medical Center, and the Neighborhood Health Centers. There are 40 full time faculty members and 3 part time or adjunct faculty including: 31 MDs, 11 PhDs, 1 MSN with 11 Professors and 10 Associate Professors. We are pleased to have recruited two new MD faculty James Murphy, M.D. and Karin Sloan, MD as Assistant Professors of Medicine, both former B.U. fellows whose research interests are in gene therapy, rehabilitation medicine and airway genomics, respectively; and 5 new PhD faculty, Susan Doctrow, PhD, Joseph Mizgerd, D.Sc, Matthew Jones, PhD and Lee Quinton, PhD who joined our pulmonary immunology research group; and Xin-bin Ai, PhD who joined our developmental biology research group.

The faculty published over 80 peer reviewed original papers, invited reviews, editorials, and book chapters this year. Faculty members were invited as visiting Professors at Institutions in Asia, Europe, South America the United States delivering over 60 invited lectures. In addition, the faculty served as Officers, Chairs, or committee members for key committees for the NHLBI, American Thoracic Society, American Heart Association and Massachusetts Thoracic Society and as peer reviewers or editorial staff members for over 20 international journals.

This year marked the 34th year of our Institutional Training Grant providing support for pre-doctoral and post-doctoral trainees. David Center is the Principal Investigator of the program. He succeeded Jerome S. Brody, who piloted the training program for the first 20 years. During its existence, the program has trained over 65 doctoral students and 135 post-doctoral fellows in multiple disciplines related to the lung. Our graduates include nine Academic Chiefs of Pulmonary Medicine, two Chairs of Medicine, 1 Dean and national and international leaders in virtually every field of pulmonary science, as well as a number of PhD graduates who are now leaders in academia and in industry.

**Noted Events:**

On September 12, 2008 we hosted the seventh Sue Kim Hanson memorial lecture. Sue was a beloved immunology student enrolled in our training program. She had worked and studied in the Pulmonary Center with her mentor Hardy Kornfeld for over ten years before her untimely death with her husband and daughter as passengers in one of the aircraft which crashed into the World Trade Center. The lectureship is now generously endowed by BU campus members and a

number of local philanthropies. This year's lecture was delivered by Laurie Glimcher, M.D. from Harvard Medical School. Prior lectures were delivered by Jonathan Yewdel, Nobel laureate Peter Doherty, PhD, Arthur Weiss, MD, William Paul, MD, a former Boston University house officer and now Director of the Laboratory for Immunology in the NIAID of the NIH and Brian Seed, Ph.D. of Harvard. The lectureship will be held annually on or around September 11.

#### **A. Research Programs:**

Our Pulmonary Research Center is divided into six major groups. Dr. Wellington Cardoso heads the research program in developmental biology of the lung. Among its funding, the nine MD and PhD faculty in this group are supported by a recently renewed Program Project Grant from the National Heart, Lung, and Blood Institute of the National Institutes of Health of which Dr. Cardoso is principal investigator and three R01 awards. Faculty member Maria Ramirez is supported by a P01 and an R01. Dr. Jining Lu recently received a new R01 to study the contribution of microRNAs in lung development.

David Center, Chief of the Pulmonary Section, heads a second research subdivision in Pulmonary Immunology and Inflammation. The nine MD and PhD faculty members in this group are supported by four R01 awards, a U01, 1 K99/R00 award, 2 K08 awards, and numerous foundation grants. Additionally, the group participates in a multi-center study of immune responses in children (URECA). Senior faculty include David Center, MD and William Cruikshank, PhD who study the role of Interleukin-16 in modulation of asthmatic inflammation; Jay Mizgerd who studies innate immune responses to bacterial pneumonia with Lee Quinton and Matt Jones, and George O'Connor, MD whose interests are in genetic polymorphisms that predict asthma severity. Junior faculty members Fred Little, and Michael Jeong are supported by K08 faculty research training awards from the NHLBI whose interests are in asthma proteomics and innate immunity. Dr. Little is also supported by a U01 in collaboration with the school of dentistry to study proteomics of saliva in allergic exacerbations. Ross Summer, recipient of a K08 award studies the role of adiponectin in the innate immune response to infections in the lung. In addition, other senior members of the group John Bernardo and Jussi Saukkonen are supported by funding from the CDC to study the treatment of tuberculosis and Jeffrey Berman is part of a multicenter trial to study the use of infliximab in pulmonary sarcoidosis. Drs. Cruikshank and O'Connor are also part of the multi-center URECA study involved in determining mechanisms of childhood asthma.

The Epidemiology and Genetics research group is headed by Dr. George O'Connor. This group has several major interests: to determine the 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 Framingham Heart Study and the Veterans Administration Normative Aging Study, in addition to the NHLBI-sponsored study on the Effects of Retinoids in Emphysema. Dr. Daniel Gottlieb of the group serves as Assistant Director of the GCRC. Dr. Robert Walter is funded by the Flight Attendants Medical Research Institute to study the epidemiology of smoking related effects on the airways.

Dr. Harrison Farber heads a fourth group, which studies the patho-biology of the Pulmonary vasculature. In addition to his research interests, he heads the clinical pulmonary hypertension service at BMC. Dr. Elizabeth Klings is a junior faculty member supported by the American Heart Association and a K23 award from the NHLBI. In addition to their studies on stress responses of the endothelium to low and high oxygen tensions, the group has nationally recognized experience treating patients with pulmonary hypertension and acute chest syndrome associated with Sickle Cell anemia.

The fifth group focuses on the genetic changes that occur in the airways that are predispose to the development of lung cancer and COPD. Jerome Brody, MD, the Director of the Pulmonary Center; along with Avi Spira, MD, Assistant Professor of Engineering and Medicine, and new faculty member, Frank Schembri, heads this group. They have established a bio-informatics program in collaboration with the School of

Engineering and have recently published groundbreaking work describing the gene profiles in the airways present in cigarette smokers who develop lung cancer. Hasmeena Kathuria, MD, has developed a clinical referral pathway for lung cancer patients and her research focuses on the role of caveolin-1 in lung cancer funded by a new grant from the American Lung Association. Dr. Spira is supported by a faculty development award from the Doris Duke Society, an NIH R21 and just received new R01 and U01 support.

The last group, headed by Darrell Kotton and Alan Fine, MD is devoted to the study of the contribution of stem cells to repair of the lung following injury supported by a grant from the Department of Defense. They have substantial interactions with the development group, looking at normal and abnormal repair processes as extensions of normal the developmental process. Darrell Kotton, MD and Andrew Wilson, MD study gene delivery targeted by stem cells, and Dr. Kotton is the leader of a University wide consortium of scientists pursuing ways to develop clinical grade iPS cells for use in organ repair.

In addition, the Pulmonary Center sponsors a number of clinical trials. Including Arthur Theodore, MD is PI of a multi-center trial of cyclophosphamide in the treatment of systemic sclerosis lung disease, Helen Hollingsworth directs several trials related to treatment of pulmonary fibrosis and Jeffrey Berman, MD, coordinates a trial of infliximab for Sarcoidosis. New trials on mechanical non-invasive lung reduction in emphysema are being overseen by Karin Sloan, MD, Martin Joyce-Brady, MD and Ronald Goldstein, MD.

## **B. Clinical Activities:**

The clinical programs of the Section are extensive and diverse. Jeffrey Berman, MD leads our clinical programs. Our faculty provides all the staffing for the Medical Intensive Care Units at BMC and the BVAMC and run active consultation services in each institution. The volume of intensive care patients at BMC has increased steadily and we are now preparing to increase from three separate staff ICU teams to a fourth. There were 12,000 in-patient daily visits, 7,000 outpatient visits in addition to 1,000 procedures performed. Additional clinical activities include staffing the public health clinic in Tuberculosis and Dr. John Bernardo serves as state Tuberculosis control officer. Out-patient services, include subspecialty clinics in asthma and allergy (Helen Hollingsworth, George O'Connor, Fred Little, John Bernardo, and David Center) and large referral practices in Pulmonary Fibrosis (Helen Hollingsworth, Ronald Goldstein), Sarcoidosis (Jeffrey Berman), Scleroderma (Arthur Theodore), Amyloidosis (John Berk), Pulmonary Hypertension and Sickle Cell Anemia Chest Diseases (Harrison Farber and Elizabeth Klings), COPD (Ronald Goldstein and Arthur Theodore) and lung cancer (Christine Reardon and Hasmeena Kathuria). The clinical volume of the Section saw an 8 % rise this past year. We provide satellite consultation and care at Quincy Medical Center, Sturdy Memorial Hospital, East Boston Neighborhood Health Center, South End Health Unit, South Boston Neighborhood Health Center, the Massachusetts Hospital School, and direct pulmonary rehabilitation at the Radius facilities in Roxbury and Quincy. We provide key administrative support to BMC in a number of venues. Arthur Theodore, MD is director of the Medical Intensive Care Unit and Respiratory Therapy, Michael Jeong, MD is director of the Pulmonary Function Laboratory, and Karin Sloan, MD became director of our pulmonary rehabilitation program.

## **C. Education:**

The Section has many major educational efforts. We present a full block to the second year students in the Biology of Disease course, supervise students on clinical and research electives, and 8 faculty participate in the department of medicine morning report and deliver multiple lectures to house officers. The pulmonary fellows established the L. Jack Faling annual teaching award in honor of Jack Faling in 2003. The award is given each year to a pulmonary faculty member who best exemplifies Jack's devotion to teaching and clinical practice. The awardees are chosen by the pulmonary fellows. Anthony O'Regan, MD was honored as the first teacher of the year in 2004; Ross Summer, MD received the 2005 award, Michael Jeong, MD received the 2006 award; in 2007 the recipient was Darrell Kotton, MD and in 2008 it was Christine Reardon, M.D.

The flagship of our Section is our post-doctoral training program in pulmonary, allergy and critical care medicine. It is one of the most highly regarded training programs in the country, having trained over 160 MD clinicians and scientists over the past 30 years. In addition, our research laboratories are a magnet for visiting scientists and PhD post-doctoral fellows seeking training in disciplines associated with lung diseases. In that regard we have hosted 14 visiting scientists in the past 15 years from Japan, France, Italy, China, Israel, South America and other institutions in the United States. Christine Reardon, MD is the new director of our clinical training program assuming the role from Jeffrey Berman, MD who served in that capacity for the past 20 years. Dr. David Center heads the allergy training program and the pulmonary research component of the newly accredited Sleep Medicine Program is headed by Daniel Gottlieb, MD

#### **D. Honors and achievements:**

The faculty were visiting professors at 14 institutions in the United States, Europe, Asia and South America and gave over 50 invited grand rounds presentations, research presentations, and lectureships in the United States, Europe, Asia, and South America. They received 8 new grants from NIH and private sources along with over 25 existing awards representing over \$9.5 million dollars per year in total support.

Alan Fine, MD was promoted to Professor of Medicine.

Avrum Spira and Darrell Kotton were promoted to Associate Professor.

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

Drs. David Center and Helen Hollingsworth were listed in America's Best Doctors and Dr. Hollingsworth was also listed in Boston Consumer's Checkbook.

Dr. Center received the Chadwick Medal from the Massachusetts Thoracic Society for his contributions to research and education in Pulmonary Medicine.

#### **E. Selected Pulmonary Center Publications, July 2006 – June 2007**

1: Ai X, Kitazawa T, Do AT, Kusche-Gullberg M, Labosky PA, Emerson CP Jr. SULF1 and SULF2 regulate heparan sulfate-mediated GDNF signaling for esophageal innervation. *Development*. 2007 Sep;134(18):3327-38. PubMed PMID: 17720696.

2: Ambasta RK, Ai X, Emerson CP Jr. Quail Sulf1 function requires asparagine-linked glycosylation. *J Biol Chem*. 2007 Nov 23;282(47):34492-9. Epub 2007 Sep 12. PubMed PMID: 17855356.

3: Beane J, Sebastiani P, Whitfield TH, Steiling K, Dumas YM, Lenburg ME, Spira A. A prediction model for lung cancer diagnosis that integrates genomic and clinical features. *Cancer Prev Res (Phila Pa)*. 2008 Jun;1(1):56-64. Epub 2008 Mar 31. PubMed PMID: 19138936.

4: Chami HA, Devereux RB, Gottdiener JS, Mehra R, Roman MJ, Benjamin EJ, Gottlieb DJ. Left ventricular morphology and systolic function in sleep-disordered breathing: the Sleep Heart Health Study. *Circulation*. 2008 May 20;117(20):2599-607. Epub 2008 May 5. PubMed PMID: 18458174.

- 5: Chen F, Desai TJ, Qian J, Niederreither K, Lü J, Cardoso WV. Inhibition of Tgf beta signaling by endogenous retinoic acid is essential for primary lung bud induction. *Development*. 2007 Aug;134(16):2969-79. Epub 2007 Jul 18. PubMed PMID: 17634193.
- 6: Farber HW. The status of pulmonary arterial hypertension in 2008. *Circulation*. 2008 Jun 10;117(23):2966-8. PubMed PMID: 18541751.
- 7: Gaposchkin DP, Farber HW, Zoeller RA. On the importance of plasmalogen status in stimulated arachidonic acid release in the macrophage cell line RAW 264.7. *Biochim Biophys Acta*. 2008 Apr;1781(4):213-9. Epub 2008 Feb 20. PubMed PMID: 18328831.
- 8: Herrmann JM, Bernardo J, Long HJ, Seetoo K, McMenamin ME, Batista EL Jr, Van Dyke TE, Simons ER. Sequential chemotactic and phagocytic activation of human polymorphonuclear neutrophils. *Infect Immun*. 2007 Aug;75(8):3989-98. Epub 2007 May 25. PubMed PMID: 17526745; PubMed Central PMCID: PMC1952002.
- 9: Izvolsky KI, Lu J, Martin G, Albrecht KH, Cardoso WV. Systemic inactivation of Hs6st1 in mice is associated with late postnatal mortality without major defects in organogenesis. *Genesis*. 2008 Jan;46(1):8-18. PubMed PMID: 18196599.
- 10: Jean JC, Lü J, Joyce-Brady M, Cardoso WV. Regulation of Fgf10 gene expression in murine mesenchymal cells. *J Cell Biochem*. 2008 Apr 15;103(6):1886-94. PubMed PMID: 18022820.
- 11: Kathuria H, Cao Y, Hinds A, Ramirez MI, Williams MC. ERM is expressed by alveolar epithelial cells in adult mouse lung and regulates caveolin-1 transcription in mouse lung epithelial cell lines. *J Cell Biochem*. 2007 Sep 1;102(1):13-27. PubMed PMID: 17390339.
- 12: Klings ES. Pulmonary hypertension of sickle cell disease: more than just another lung disease. *Am J Hematol*. 2008 Jan;83(1):4-5. PubMed PMID: 17924550.
- 13: Kotton DN, Fine A. Lung stem cells. *Cell Tissue Res*. 2008 Jan;331(1):145-56. Epub 2007 Sep 6. Review. PubMed PMID: 17805578.
- 14: Lang JE, Williams ES, Mizgerd JP, Shore SA. Effect of obesity on pulmonary inflammation induced by acute ozone exposure: role of interleukin-6. *Am J Physiol Lung Cell Mol Physiol*. 2008 May;294(5):L1013-20. Epub 2008 Mar 21. PubMed PMID: 18359888.
- 15: Langsdorf A, Do AT, Kusche-Gullberg M, Emerson CP Jr, Ai X. Sulfs are regulators of growth factor signaling for satellite cell differentiation and muscle regeneration. *Dev Biol*. 2007 Nov 15;311(2):464-77. Epub 2007 Sep 7. PubMed PMID: 17920055.
- 16: Little F, Cruikshank W. Interleukin-16: The Ins and Outs of Regulating T-Cell

Activation. *Crit Rev Immunol*. 2008;28(6):467-83. PubMed PMID: 19265505.

17: Liu P, Lu J, Cardoso WV, Vaziri C. The SPARC-related factor SMOC-2 promotes growth factor-induced cyclin D1 expression and DNA synthesis via integrin-linked kinase. *Mol Biol Cell*. 2008 Jan;19(1):248-61. Epub 2007 Nov 7. PubMed PMID: 17989364; PubMed Central PMCID: PMC2174189.

18: Lowry MH, McAllister BP, Jean JC, Brown LA, Hughey RP, Cruikshank WW, Amar S, Lucey EC, Braun K, Johnson P, Wight TN, Joyce-Brady M. Lung lining fluid glutathione attenuates IL-13-induced asthma. *Am J Respir Cell Mol Biol*. 2008 May;38(5):509-16. Epub 2007 Dec 6. PubMed PMID: 18063838; PubMed Central PMCID: PMC2335334.

19: Lü J, Qian J, Keppler D, Cardoso WV. Cathespin H is an Fgf10 target involved in Bmp4 degradation during lung branching morphogenesis. *J Biol Chem*. 2007 Jul 27;282(30):22176-84. Epub 2007 May 11. PubMed PMID: 17500053.

20: Marshall J, Finn CA, Theodore AC. Impact of a clinical pharmacist-enforced intensive care unit sedation protocol on duration of mechanical ventilation and hospital stay. *Crit Care Med*. 2008 Feb;36(2):427-33. PubMed PMID: 18091554.

21: Mazurek GH, Weis SE, Moonan PK, Daley CL, Bernardo J, Lardizabal AA, Reves RR, Toney SR, Daniels LJ, LoBue PA. Prospective comparison of the tuberculin skin test and 2 whole-blood interferon-gamma release assays in persons with suspected tuberculosis. *Clin Infect Dis*. 2007 Oct 1;45(7):837-45. Epub 2007 Aug 24. PubMed PMID: 17806047.

22: McFadden C, Morgan R, Rahangdale S, Green D, Yamasaki H, Center D, Cruikshank W. Preferential migration of T regulatory cells induced by IL-16. *J Immunol*. 2007 Nov 15;179(10):6439-45. PubMed PMID: 17982032.

23: Millien G, Beane J, Lenburg M, Tsao PN, Lu J, Spira A, Ramirez MI. Characterization of the mid-foregut transcriptome identifies genes regulated during lung bud induction. *Gene Expr Patterns*. 2008 Jan;8(2):124-39. Epub 2007 Sep 26. PubMed PMID: 18023262; PubMed Central PMCID: PMC2440337.

24: Mizgerd JP, Skerrett SJ. Animal models of human pneumonia. *Am J Physiol Lung Cell Mol Physiol*. 2008 Mar;294(3):L387-98. Epub 2007 Dec 27. Review. PubMed PMID: 18162603.

25: Mizgerd JP. Acute lower respiratory tract infection. *N Engl J Med*. 2008 Feb 14;358(7):716-27. Review. PubMed PMID: 18272895.

26: Morris CR, Suh JH, Hagar W, Larkin S, Bland DA, Steinberg MH, Vichinsky EP, Shigenaga M, Ames B, Kuypers FA, Klings ES. Erythrocyte glutamine depletion, altered redox environment, and pulmonary hypertension in sickle cell disease. *Blood*. 2008 Jan 1;111(1):402-10. Epub 2007 Sep 11. PubMed PMID: 17848621; PubMed Central PMCID: PMC2200820.

27: Murphy J, Summer R, Wilson AA, Kotton DN, Fine A. The prolonged life-span of alveolar macrophages. *Am J Respir Cell Mol Biol*. 2008 Apr;38(4):380-5. Epub 2008 Jan 10. PubMed PMID: 18192503; PubMed Central PMCID: PMC2274942.

28: Murphy J, Summer R, Fine A. Stem cells in airway smooth muscle: state of the art. *Proc Am Thorac Soc*. 2008 Jan 1;5(1):11-4. Review. PubMed PMID: 18094079; PubMed Central PMCID: PMC2645296.

29: Nicol MQ, Mathys JM, Pereira A, Ollington K, Jeong MH, Skolnik PR. Human immunodeficiency virus infection alters tumor necrosis factor alpha production via Toll-like receptor-dependent pathways in alveolar macrophages and U1 cells. *J Virol*. 2008 Aug;82(16):7790-8. Epub 2008 Jun 4. PubMed PMID: 18524817; PubMed Central PMCID: PMC2519548.

30: Pan H, Mostoslavsky G, Eruslanov E, Kotton DN, Kramnik I. Dual-promoter lentiviral system allows inducible expression of noxious proteins in macrophages. *J Immunol Methods*. 2008 Jan 1;329(1-2):31-44. Epub 2007 Oct 18. PubMed PMID: 17967462; PubMed Central PMCID: PMC2244810.

31: Patel NR, Zhu J, Tachado SD, Zhang J, Wan Z, Saukkonen J, Koziel H. HIV impairs TNF-alpha mediated macrophage apoptotic response to *Mycobacterium tuberculosis*. *J Immunol*. 2007 Nov 15;179(10):6973-80. PubMed PMID: 17982088.

32: Quinton LJ, Jones MR, Robson BE, Simms BT, Whitsett JA, Mizgerd JP. Alveolar epithelial STAT3, IL-6 family cytokines, and host defense during *Escherichia coli* pneumonia. *Am J Respir Cell Mol Biol*. 2008 Jun;38(6):699-706. Epub 2008 Jan 10. PubMed PMID: 18192501; PubMed Central PMCID: PMC2396249.

33: Sancherawala V, Wright DG, Quillen K, Finn KT, Dember LM, Berk JL, Doros G, Fisher C, Skinner M, Seldin DC. Tandem cycles of high-dose melphalan and autologous stem cell transplantation increases the response rate in AL amyloidosis. *Bone Marrow Transplant*. 2007 Sep;40(6):557-62. Epub 2007 Jun 25. Erratum in: *Bone Marrow Transplant*. 2007 Sep;40(6):607. PubMed PMID: 17589534.

34: Sridhar S, Schembri F, Zeskind J, Shah V, Gustafson AM, Steiling K, Liu G, Dumas YM, Zhang X, Brody JS, Lenburg ME, Spira A. Smoking-induced gene expression changes in the bronchial airway are reflected in nasal and buccal epithelium. *BMC Genomics*. 2008 May 30;9:259. PubMed PMID: 18513428; PubMed Central PMCID: PMC2435556.

35: Summer R, Fitzsimmons K, Dwyer D, Murphy J, Fine A. Isolation of an adult mouse lung mesenchymal progenitor cell population. *Am J Respir Cell Mol Biol*. 2007 Aug;37(2):152-9. Epub 2007 Mar 29. PubMed PMID: 17395889; PubMed Central PMCID: PMC1976547.

36: Tzianabos AO, Holsti MA, Zheng XX, Stucchi AF, Kuchroo VK, Strom TB, Glimcher LH, Cruikshank WW. Functional Th1 cells are required for surgical adhesion

formation in a murine model. *J Immunol.* 2008 May 15;180(10):6970-6. PubMed PMID: 18453619.

37: Wiener RS, Cao YX, Hinds A, Ramirez MI, Williams MC. Angiotensin converting enzyme 2 is primarily epithelial and is developmentally regulated in the mouse lung. *J Cell Biochem.* 2007 Aug 1;101(5):1278-91. PubMed PMID: 17340620.

38: Wilson AA, Kwok LW, Hovav AH, Ohle SJ, Little FF, Fine A, Kotton DN. Sustained expression of alpha 1-antitrypsin after transplantation of manipulated hematopoietic stem cells. *Am J Respir Cell Mol Biol.* 2008 Aug;39(2):133-41. Epub 2008 Mar 6. PubMed PMID: 18323534; PubMed Central PMCID: PMC2542452.

39: Wilson AA, Kotton DN. Another notch in stem cell biology: *Drosophila* intestinal stem cells and the specification of cell fates. *Bioessays.* 2008 Feb;30(2):107-9. Review. PubMed PMID: 18200564.

40: Zhang Y, Tuzova M, Xiao ZX, Cruikshank WW, Center DM. Pro-IL-16 recruits histone deacetylase 3 to the Skp2 core promoter through interaction with transcription factor GABP. *J Immunol.* 2008 Jan 1;180(1):402-8. PubMed PMID: 18097041.



BOSTON UNIVERSITY MEDICAL CENTER  
DEPARTMENT OF MEDICINE  
ANNUAL REPORT  
SECTION OF Section of Endocrinology, Diabetes, Nutrition and Weight Management  
JULY 1, 2007 - JUNE 30, 2008  
FISCAL YEAR 2008



## RESEARCH ACTIVITIES

The past year witnessed substantial growth in research awards and clinical activity in the Section of Endocrinology, Diabetes, Nutrition and Weight Management, under the leadership of Shalender Bhasin, M.D., Professor of Medicine.

During this period, the level of federal and private funding increased, in spite of 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 and a new multidisciplinary Grant from the Claude Pepper Ageing Center. Currently the Section has more than \$36 million in total project dollars. Several research initiatives are active and productive, including 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.

Over the past year, the **Androgen Clinical Research Unit (ACRU)** staff has continued to grow and includes Dr. Bhasin, Dr. Barsaria and Dr. Bachman. The unit 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 Joanne Krasnoff, Ph.D., Assistant Professor of Medicine) and drug supplies 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 mechanisms by which androgens regulate mesenchymal stem cell differentiation. These investigations are being led by Section faculty members Ravi Jasuja, Ph.D., Assistant Professor of Medicine; and Wen Guo, Ph.D., Assistant Professor of Medicine.

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. Under Dr. Holick's direction, 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.

The **Biophotonics Laboratory**, under Dr. Jasuja's direction, 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 receptor 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., at Ohio State, Chris Yengo, Ph.D. at University of North Carolina and James Head, Ph.D., Professor of Physiology at Boston University. 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 Drs. Storer and Krasnoff. 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 health and disease; Dr. Bhasin is the Principal Investigator. These research protocols include: the Role of 5-Alpha Reductase in Mediating Testosterone Actions (NIH/National Institute of Child Health & Human Development, 1R01HD43348-02); Testosterone Dose Response in Surgically Menopausal Women (NIH/National Institute of Diabetes & Digestive & Kidney Diseases, R01); Effects of Testosterone Replacement on Muscle Performance and Physical Function in Older Men (NIH/National Institute of Aging, 2R01AG014369-06); and Testosterone Effects on Atherosclerosis Progression in Older Men. In addition to forging collaborations with other Sections within the Department, 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).

Dr. Wen Guo's investigations, supported by an RO1 grant, focus on the role of free fatty acids in inducing insulin resistance. Dr. Guo's research has also 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.

**Diabetes Research Unit.** The Diabetes Research Unit under the direction of **Neil Ruderman, M.D., D.Phil.**, has continued to focus its research on the AMPK / malonyl CoA fuel sensing and signaling mechanism and its role in regulating cell metabolism and disease prevention. Over the past year the laboratory has 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, we have 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 (pre-doc), Yasuo Ido, Asst. Prof. of Medicine). We 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 though to initiate atherogenesis.

Dr. Ido, together with Lan Fan, 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 studies, Marie-Soleil Gauthier, a post-doctoral fellow working in part with Dr. Asish Saha (Asst. 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 we did in the endothelial cell, she found that failure to activate AMPK in this situation causes a substantial increase in oxidative stress. Other projects are examining the mechanism for glucose-induced downregulation of AMPK and the induction of insulin resistance in skeletal muscle (Dr. Saha) and cultured HepG2 cells (G. Suchankova, post-doctoral fellow); the inhibition of keratinocyte growth by AMPK and Vitamin D (joint effort of the Diabetes Unit and the Holick laboratory); and 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 (M. Kelly, post-doc). All of these studies are supported by grants from the NIH and many have been done in collaboration with other laboratories in U.S. and overseas.

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

**Vitamin D, Skin and Bone Research Laboratory.** Michael F. Holick, PhD, MD, Professor of Medicine, Physiology and Biophysics, Program Director for General Clinical Research Center and Director of the Bone Healthcare Clinic and his team of physicians and researchers continue to be leaders in the field of

vitamin D, osteoporosis, metabolic bone disease, psoriasis and hair research. Dr. Holick and his colleagues, Dr. Ray, Dr. Chen have been investigating the important role of sunlight and artificial ultraviolet B radiation devices in providing elders and patients with fat malabsorption with their 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 of identifying one for clinical trials. Progress has been made in formulating a parathyroid hormone related peptide receptor antagonist for the mitigation of chemotherapy induced alopecia. Dr. Holick recently received the Eli Lilly Lecturer Award from the Canadian Society of Endocrinology and Metabolism.

**Center for Nutrition and Weight Management.** In the Center for Nutrition and Weight Management, Dr. Apovian and her colleagues 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 R-01 grants from the NIH are funding this project; Dr. Gokce is the Principal Investigator and Dr. Apovian is the Co-investigator. In addition, Center 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 in the Center. It is funded by the Boston Obesity Nutrition Research Center (BONRC), which receives funding from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

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 in treatment of Type 2 diabetes with exenatide; participants are currently being recruited. Pfizer is funding a 14-month weight maintenance following low-calorie-diet study. This is crucial during this time of obesity research as there is very little research on effective means for weight maintenance.

The **BMC Thyroid Nodule and Cancer Center** is a newly established comprehensive multidisciplinary center for the evaluation and treatment of patients with thyroid nodules and cancer and to promote translational research targeted to improve diagnosis and management of patients with thyroid disease. The research team of Dr. Lee and Dr. Rosen of Surgical Oncology was recently awarded a pilot project grant by the Genome Science Institute to encourage new collaborations between groups with diverse expertise to address an important scientific question in genetics and genomics research. The pilot project will examine if there is a relationship between specific miRNAs and papillary thyroid carcinoma resulting in tumorigenesis and influencing extent of disease and prognosis. Future collaborations will be multidisciplinary with the participation of pathology, Dr. De Las Morenas and Dr. Factor, nuclear medicine in Radiology, Dr. Subramaniam, and Radiation Physics, Dr. Rick Behrman.

## CLINICAL ACTIVITIES

The consolidated clinic 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 has expanded in the last year by the addition of 4 large exam rooms, a patient intake room, a medication room, a nurses station, an administration area and additional patient waiting room. The current clinical space on the second floor of the Preston Building includes 17 spacious examining rooms, 2 patient intake areas, three thyroid ultrasound instruments, two procedure rooms, three bone densitometry instruments, a patient education and conference room, a phlebotomy room, and rooms for dietary and diabetes teaching dietitians and nurses. The clinic census has increased steadily at an annualized rate of 10% over the past five years; the past year witnessed an even more impressive 20% increase in patient visits. The wait time to first appointment decreased by 50% during the past 2 years and is expected to fall further with additional faculty recruitment and 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 clinical expertise of our physicians has been recognized by five of our faculty listed at Best Doctors in Boston Magazine and participating in national treatment guideline:

- Bhasin: Chair, Endocrine Society's Androgen Panel
- Lee: Member, American Thyroid Association's Evidence based Guidelines for Thyroid Nodules and Thyroid Cancer
- Holick: Chair: Endocrine Society's Vitamin D Deficiency Panel
- Apovian: Member, American Association of Clinical Endocrinology's Bariatric Surgery Panel
- Rosenzweig: Chair: Endocrine Society's CV Risk Reduction in Diabetes; Chair, Endocrine Society's Committee on Performance Metrics

Our faculty are editors or associate editors of four premier endocrine and nutrition journals: Journal of Clinical Endocrinology and Metabolism, Endocrine Practice, Thyroid and Obesity Research. The section recently added three new physicians, Dr. James Rosenzweig, a specialist in diabetes mellitus, Dr. Pietras, a specialist in diabetes mellitus, Dr. Shehzad Basaria, a specialist in androgen and 2 nurse practitioners specializing in Diabetes Mellitus, Deb Urquhart and Roberta Capelson. Housed within the clinic is the Center for Weight Management and Nutrition. The Center includes three physician nutrition specialists, two bariatric surgeons, four registered dietitians, a behaviorist, and an exercise specialist. Drs. Apovian, Istfan and Khaodhiar provide medical consultation in the area of obesity and nutritional disorders. Drs. Hess and Burch consult on gastric bypass surgery, and Dr. Ruderman, Dr. Sternthal, Dr. Rosenzweig and Dr. McDonnell provide expertise on the management of diabetes mellitus. The clinic has a comprehensive, multidisciplinary approach to diabetes with a patient management coordinated by a physician, four nurse practitioners, three certified Diabetes Nurse Educators (CDE) and dietitians.

***Thyroid Nodule and Cancer Center*** Drs. Braverman, Lee, Farwell, Safer, and Pearce offer nationally and internationally recognized expertise in diseases of the thyroid in the Thyroid Nodule and Cancer Center. The Thyroid Center offers comprehensive medical evaluation and medical and surgical therapies of diseases of the thyroid. Specialized services offered at the Thyroid Center include:

- Thyroid ultrasound
- Neck ultrasound for adenopathy
- Parathyroid ultrasound
- US guided biopsy of thyroid nodules
- US guided biopsy of parathyroid masses
- US guided biopsy of cervical neck adenopathy
- Radioactive iodine ablation of hyperthyroidism
- Radioactive iodine ablation of thyroid cancer
- Dosimetry for maximal dose radioactive iodine therapy

With eighty years of combined experience with radioactive iodine therapies, Drs. Braverman and Lee offer special expertise in the treatment of hyperthyroidism and thyroid cancer. Drs. Lee and Braverman 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 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 endocrinologists and surgeons (David McAneny, M.D., Jennifer Rosen, M.D., and Michael Stone, M.D. of Surgical Oncology and Gregory Grillone, M.D, Sharukh Jalisi, M.D., and Dr. Pieter Noordzij, M.D. of Otolaryngology-Head and Neck Surgery) work closely to ensure excellent coordinated care of patients who require surgical treatment of their thyroid disease.

***General Endocrinology*** 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.

***Male and Female Sexual Health Disorders Clinic*** Dr. Bhasin, Dr. Coviello, Dr. Safer and Dr. Basaria have initiated a sexual health program at BMC 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. Dr. Andrea Coviello is a nationally-recognized expert in polycystic ovary disease and other androgen-related disorders in women. The breadth of clinical conditions

seen in this clinic is wide including. Dr. Safer has special expertise in the hormonal management of trans-sexual patients.

- Androgen deficiency in men
- Sexual dysfunction in men and women
- Male infertility
- Gynecomastia
- Hirsutism
- Acne
- Polycystic ovary syndrome
- Disorders of puberty
- Hormonal treatment of trans-sexual patients

***Center for Nutrition and Weight Management*** The Center for Nutrition and Weight Management is a multidisciplinary clinic with 3 Nutrition physicians, Dr. Apovian, Dr. Istfan and Dr. Khaodhair, 6 Registered Dietitians, Stephanie Spaide, Jena Carr, Wendy Anderson, Karen Chalmers, Kelly Karlstad Smallcomb, Zong Liu, and Anette Vehus, 1 social work counselor, Kelly Fornier, and 2 bariatric surgeons, Dr. Hess and Dr. Burch. In addition to weight management, this team also will see patient with nutritional deficiencies and eating disorders. This is a medical nutrition program that is integrated with one of the largest Bariatric Surgery programs in New England to provide pre- and post-operative care of bariatric surgery patients.

***Diabetes Clinical Service*** The Diabetes Clinical Service has greatly expanded in the last year under new physician leadership by Dr. Jamie Rosenzweig. Under the leadership of Barbara Jarvis, R.N., C.D.E., the service's Clinical Diabetes Education Program, accredited by the American Diabetes Association, successfully completed a re-evaluation and certification. The service has expanded to accommodate and increase in both outpatient and inpatient referrals for diabetes care. In the past year, the service has welcomed one R.D. CDE, Karen Chalmers and a NP/Nurse manager, Deb Urquhart. Dr. Rosenzweig is completely revamping the Diabetes Services to build a team with the referring primary care doctor as the center with a diabetes nurse manager for triage and care coordination to assure appointments within 2 weeks for new diabetes referrals for coordinated care in the Endocrine, Nutrition and Diabetes center to include a physician evaluation, dietary education by a RD and diabetes management education by a CDE all within the center. Dr. Rosenzweig's vision is to support the BMD community primary care providers at BMC or at an affiliated community health care center with multi-language educational patient materials and provider education for process improvement measures of diabetes care. The Diabetes center will integrate new technology into routine practice including:

- Continuous Glucose Monitoring (CGM)

- Intensive insulin therapy, including pumps
- Non-mydriatic camera
- Point of Care A1C

Since 2005, a team of diabetes experts including, Dr. McDonnell, Dr. Pietras Dr. Sternthal and NPs Hanrahan, Donahue and White has successfully initiated a comprehensive Inpatient Diabetes Management Service and guidelines for intensive management of diabetes in BMC's surgical and medical intensive care units. The Adult Inpatient Diabetes Program 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, Dr. Pietras, and Dr. Sternthal, the 3 NPs and an Endocrine fellow 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 Diabetes Management Program is the education of nurses, physicians and patients. A multidisciplinary endocrine subcommittee, comprised of representatives from Pharmacy, Nursing, 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 intensive care units (medical and surgical) and will assist the transition to the floors to improve medical outcomes.

***Bone Clinic*** Dr. Michael Holick, an international expert in both clinical and research aspects of vitamin D, with 3 additional providers , Dr. Knapp, Dr. Coviello and Dr. Khadohiar, read more than 3,000 axial and peripheral DPX bone mineral density exams annually. The bone clinic provides expert consultation on all aspects of common metabolic bone diseases including osteoporosis and Paget's disease, as well as, rare conditions such as hypophosphataemic rickets and pseudo-hypoparathyroidism.

***Neuroendocrine/Pituitary Clinic:*** Dr. Sonia Ananthakrishnan is director of a new clinical program in Endocrinology. She has created a multidisciplinary program that coordinates and streamlines the evaluation and care of patients with neuroendocrine/pituitary conditions with close collaboration with the Departments of Neurological Surgery, Otolaryngology and Radiation Oncology.

## **EDUCATION**

The Section's fellowship training program is accredited by the Accreditation Council for Graduate Medical Education (ACGME) for five years with the next site visit planned for late 2009. Joshua Safer, Associate Professor of Medicine, is the Endocrine fellowship training program director. The fellowship program remains

highly competitive and received over 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 in Pennsylvania, Beverly Hospital, Penn State University Medical School, and Boston University Medical Center. Dr. Apovian in the last year has created a new stand alone fellowship in Nutrition with the first graduate completing the fellowship requirements in June 2009. Selected Endocrinology fellow applicants are being considered for a 3 year program to include 2 years of Endocrinology and 1 year of Medical Nutrition training. This has become a highly competitive and attractive component of our Endocrine Fellowship program which has lead to increase applicants to our fellowship program.

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 continued funding**. The Training Grant has had only two principal investigators over this long period: Dr. James Melby from inception to 1985 and Dr. Neil 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 one or two times weekly. The conferences include core topics, case discussion, pathology review, and a journal club. Also, the fellows run a weekly board review luncheon. In addition, the Androgen Research Group 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. Joshua Safer, Associate Professor of Medicine, oversees the Section's participation, which continues to garner excellent reviews from students. Section members participate in "Introduction to Clinical Medicine," offered to first- and second-year BUSM students. Section members participate in the ambulatory portion of the Medicine clinical 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, Caroline Apovian, Associate Professor of Medicine, and Carine Lenders, M.D., Assistant Professor of Pediatrics, are collaborating with BUSM faculty directors to meet this need.

## **MAJOR ACCOMPLISHMENTS**

Section faculty's research productivity continued to ace and awards.

Dr. Lewis Braverman was the recipient of the Robert Williams Distinguished Service Award of the Endocrine Society. He was also appointed the Editor-in-Chief of the Endocrine Practice, the flagship journal of the American College 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.

Dr. Shalender 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. Caroline Apovian co-directs the Harvard Obesity Course on a yearly basis, spoke about the Obesity crisis to the Republican and Democratic National Conventions.

Dr. Stephanie is the Robert Dawson Evans Clinician for 2007-2009

Dr. Sonia Ananthkrishnan was named as an Evans Educator 2009.

## **Endocrine, Nutrition and Diabetes Staff:**

SHALENDER BHASIN, MD- SECTION CHIEF



**Professor of Medicine at Boston University School of Medicine;  
Section Chief, Division of Endocrinology, Diabetes & Nutrition**

**Medical School:** All India Institute of Medical Sciences

**Residency:** Northwestern University School of Medicine

**Fellowship/Post-residency:** Fellowship in Endocrinology and Metabolism at Harbor-UCLA Medical Center

**Areas of Interest:** Male and female reproductive endocrinology, sexual dysfunction

in men and women; testosterone deficiency; erectile dysfunction

**Awards received:**

• Institute Gold Medal for the Graduate of the Year, 1976, AIIMS

• Fellow of the Year Award, Harbor-UCLA Medical Center, 1984

• Richard Weitzman Memorial Young Investigator Award, Harbor-

UCLA Medical Center, 1990

• Distinguished Teaching Award of Harbor-UCLA Medical Center, 1990

• JCEM Pharmacia Award for the Finalist Research Paper in JCEM, 2003

• UT Southwestern Medical School, GCRC Award for Excellence in Patient-Oriented Research, 2000

• Best Doctors in Boston, 2006

**Reviewer/editor of journals:**

• Associate Editor, Journal of Clinical Endocrinology and Metabolism

• Chair, Endocrine Society's Expert Panel on Androgen Deficiency Syndromes in Men

CAROLINE M. APOVIAN, M.D., FACP, FACN



**Associate Professor of Medicine and Pediatrics at Boston University School of Medicine;**  
**Director, Nutrition and Weight Management Center at Boston Medical Center;**  
**Director, Clinical Research at the Obesity Research Center of Boston Medical Center**  
**Medical School:** University of Medicine and Dentistry of New Jersey  
**Residency:** New England Deaconess Hospital  
**Fellowship/Post Residency:** Fellowship in Nutrition Support at New England Deaconess Hospital  
**Areas of Interest:** Novel medical treatments for obesity, monitoring type 2 diabetes, endothelial cell dysfunction and obesity and cytokine expression of

adipose cells after weight loss treatment in humans

**Accomplishments:**

- Physician certification in Obesity Medicine and Nutrition
- Dr. Apovian is an Associate Editor of the Obesity Journal and is co-editor of the Obesity and Nutrition Section of Current Opinion in Endocrinology and Diabetes
- Dr. Apovian serves on the Betsy Lehman Center for Patient Safety and Medical Error Reduction
- Expert Panel on Weight Loss Surgery for the Massachusetts Department of Public Health
- Heads an unique Nutrition fellowship programs at the Boston University School of Medicine



SONIA ANANTHAKRISHNAN, M.D.

**Instructor of Medicine at Boston University School of Medicine**  
**Medical School:** Northwestern University School of Medicine  
**Residency:** Hospital of the University of Pennsylvania  
**Fellowship/Post Residency:** Fellowship in Endocrinology, Boston Medical Center  
**Areas of Interest:** General Endocrinology, Pituitary disorders, Thyroid disorders  
**Accomplishments:** Involved in teaching medical students, Evans Educator

**Shehzad Bararia, M.D.**

**Associate Professor of Medicine Boston University School of Medicine**

**Medical School:** The Aga Khan University, Karachi, Pakistan

**Residency:** The University of Texas Health Sciences Center at Houston

**Fellowship/Post Residency:** The Johns Hopkins University School of Medicine

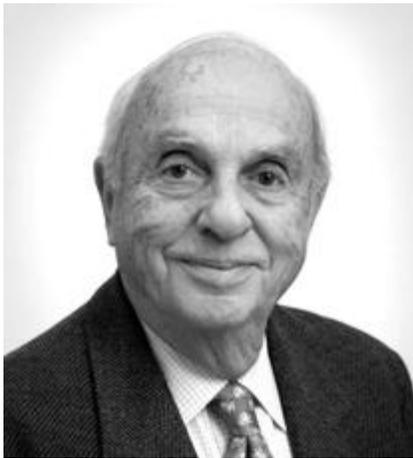
**Areas of Interest:** Testosterone and Fertility Disorders in Men

**Accomplishments:**

- Dr. Basaria has done important research showing that men undergoing castration for prostate cancer are at risk for diabetes and metabolic syndrome

Dr. Basaria is on the editorial board of The Journal of Clinical Endocrinology & Metabolism, which is the main clinical journal of The Endocrine Society

- Dr. Basaria is the founding Associate Editor of the journal, Advances in Pharmacological Sciences
- Dr. Basaria has received the “Most Outstanding Teacher” award from the Johns Hopkins University
- Dr. Basaria also has special clinical interest in seeing men with low testosterone levels related to opioid (narcotics) pain medications and in men undergoing castration for prostate cancer



LEWIS BRAVERMAN, MD

**Professor of Medicine at Boston University School of Medicine**

**Medical School:** Johns Hopkins School of Medicine; Honorary Doctorate in Medicine from University of Parma

**Residency:** Internal Medicine Residency on the II-IV Medical Services (Harvard) and Thorndike Memorial Laboratory (Harvard), Boston City Hospital

**Fellowship/Post Residency:** Fellowship in Endocrinology at the Thorndike Memorial Laboratory (Harvard), Boston City Hospital

**Areas of Interest:** Research and clinical interest have focused on the physiology and pathophysiology of the thyroid

**Accomplishments:**

- Recipient of Robert H Williams Distinguished Leadership Award from Society in 2007

Endocrine

- Currently is Editor in Chief of Current Opinion in Endocrinology, Diabetes and Obesity; and is Editor in Chief of Endocrine Practice, the journal of the American Association of Clinical Endocrinologists



ROBERTA CAPELSON, MS, ANP

**Certified Nurse Practitioner in the Department of Medicine at Boston Medical Center**

**Graduate School:** Master of Science from Boston College

Certificate of Advanced Graduate Study in Primary Care from MGH Institute of Health Professions

**Areas of interest:** Diabetes in the older adult, Weight management in patients with Diabetes, Web based systems for diabetes management, Diabetes in the community health setting, Inpatient management of Diabetes

**Accomplishments:**

- ANCC certification - Adult Nurse Practitioner
- Clinical associate at BUSM
- Currently working in both the outpatient and inpatient setting at BMC.
- Program manager for diabetes outreach efforts



TAI CHEN, PHD

**Professor of Medicine at Boston University School of Medicine**

**Grad school/PhD training:** University of Wisconsin, Madison (Ph.D.)

**Areas of interest:** Vitamin D metabolism, Cytochrome P-450 enzymes, cancers, biomarker and hormone and analyses

**Accomplishments:** Reviewer of scientific manuscripts and grants



ANDREA COVIELLO, M.D., MSE, FACE

**Assistant Professor of Medicine at Boston University School of Medicine**

**Medical School:** Duke University School of Medicine, 1995.

Master of Science in Epidemiology, University of Washington, 2003

**Residency:** Duke University Medical Center, 1998

**Fellowship/Post Residency:** Fellowship in Endocrinology, Diabetes and Metabolism, University of Washington School of Medicine, 2003

**Areas of interest:** Reproductive Disorders, Polycystic Ovary Syndrome, Insulin Resistance and Diabetes, Neuroendocrine Disorders

**Accomplishments:**

- Fellow in the American College of Endocrinology, 2006
- Editorial Board, Journal of Clinical Endocrinology and Metabolism, 2006



MARINA DONAHUE, R.N., M.S., FNP, CDE

**Certified Family Nurse Practitioner in the Department of Medicine at Boston Medical Center**

**Graduate School:** Masters of Science in Nursing from the University of Massachusetts of Boston

**Areas of Interest:** Passionate about educating both patients and clinic staff to understand the link between diabetes, heart disease and stroke. Aspiring to attain certification as a Clinical Lipid Specialist.

**Accomplishments:**

- Certified in diabetes since 1995, Certified as a Family Nurse Practitioner through American Academy of Nurse Practitioners since 2005.
- Served on several professional committees, recently awarded Excellence in Nursing Practice through the Honor Society of Nursing Theta Alpha Chapter



ALAN P. FARWELL, M.D.

**Associate Professor of Medicine at Boston University School of Medicine;**

**Director of Endocrine Clinics**

**Medical School:** University of Massachusetts Medical School

**Residency:** Internal Medicine Residency at Medical Center Hospital of Vermont

**Fellowship/Post Residency:** Academic Fellowship in Endocrinology at the University of Massachusetts Medical Center

**Areas of Interest:** Clinical and research interest in the etiology and treatment

of thyroid disorders including thyroid ultrasonography and ultrasound-guided thyroid biopsies. Particular interest educating the public and patients about the management of thyroid disorders

**Accomplishments:**

- Currently serves as Associate Editor of the journal *Thyroid*, the scientific flagship of the American Thyroid Association
- Director of Patient Education for the American Thyroid Association



MICHAEL F. HOLICK, PH.D., M.D.

**Professor of Medicine, Physiology and Biophysics at Boston University School of Medicine**

**Medical School:** University of Wisconsin, Madison

**Residency:** Massachusetts General Hospital

**Fellowship/Post-residency:** Massachusetts General Hospital

**Areas of Interest:** Vitamin D, Calcium, Bone Metabolism, Photobiology of Vitamin D, Osteoporosis

**Accomplishments:**

• Increased awareness in the pediatric and medical communities regarding vitamin D deficiency pandemic, and its role in causing not only metabolic bone disease, and osteoporosis in adults, but increasing risk of children and adults developing common deadly cancers, autoimmune diseases, including type 1 diabetes and multiple sclerosis and heart disease.

- Recipient of numerous awards and honors, including the American Skin Associations Psoriasis Research Achievement Award, the American College of Nutrition Award, the Robert H Herman Memorial Award in Clinical Nutrition from the American Society for Clinical Nutrition, the Annual General Clinical Research

Centers Program Award for Excellence in Clinical Research and the Linus Pauling Functional Medicine Award from the Institute for Functional Medicine



PATRICIA HANRAHAN, R.N., ANP, CDE

**Certified Nurse Practitioner in the Department of Medicine, Diabetes Nurse Educator**

**Graduate School:** Masters in Nursing at Boston College

**Areas of Interest:** Focus has been diabetes management and education for hospitalized people with diabetes.

**Accomplishments:**

- Certified Adult Nurse Practitioner, Certified Diabetes Educator (CDE) and Insulin pump trainer

- Currently works in the clinic and inpatient units at BMC providing diabetes management and education



NAWFAL W. ISTFAN, M.D., PH.D.

**Associate Professor of Medicine at Boston University School of Medicine**

**Medical School:** American University of Beirut

**Residency:** Internal Medicine at the American University of Beirut

**Post Graduate School:** PhD in Human and Clinical Nutrition, Massachusetts Institute of Technology

**Fellowship:** Clinical Nutrition at New England Deaconess Hospital

**Areas of Interest:** Nutrition and cancer; regulation of cell proliferation and the effects of polyunsaturated fatty acids on cancer; insulin resistance in obesity; cardiovascular disease in obesity.

**Accomplishments:** Best Doctors in America list



*Lalita Khaodhjar, M.D.*

**Assistant Professor of Medicine at Boston University School of Medicine**

**Medical School:** Siriraj Hospital, Mahidol University, Thailand

**Residency:** University of Hawaii, Honolulu, Hawaii

**Fellowship/Post-residency:** Fellowship in Endocrinology at University of Massachusetts Medical Center

**Fellowship in Clinical Nutrition at Beth Israel Deaconess Medical Center**

**Areas of interest:** Obesity, diabetes

**Accomplishments:** Reviewer: obesity, metabolism



***Philip Knapp, M.D., M.S.***

**Assistant Professor of Medicine at Boston University School of Medicine**

**Medical School:** University of Massachusetts Medical School, Boston  
University School of Public Health

**Residency:** Boston Medical Center

**Fellowship/Post Residency:** Fellowship in Endocrinology at Boston Medical Center

**Areas of Interest:** Adrenal disorders



***Stephanie L. Lee, Ph.D., M.D., FACE***

**Associate Professor of Medicine at Boston University School of Medicine;  
Associate Chief of Faculty Development in the Section of Endocrinology,  
Diabetes and Nutrition; Director of the Thyroid Nodule and Cancer  
Center at Boston Medical Center**

**Medical School:** University of California, San Diego School of Medicine.  
Ph.D. in Physiology and Pharmacology, University of California, San Diego

**Residency:** University of California, San Diego Medical Center

**Fellowship/Post Residency:** Clinical Fellowship in Endocrinology and a  
Research Fellowship in Molecular Medicine at the New England Medical  
Center

**Areas of Interest:** Clinical and Research Interest in the Etiology and

Treatment of Thyroid Disease.

**Accomplishments:**

- Recently participated in writing the 2009 American Thyroid Association Evidence-based Guidelines for the diagnosis and management of thyroid nodules and cancer
- Robert Dawson Evans Clinician Award
- Named in Boston Magazine's "Boston's Top Doctors" and the "Guide to America's Top Physicians"



**ROBERT M. LEVIN, M.D.**

**Professor of Medicine at Boston University School of Medicine**

**Medical School:** Stritch School of Medicine of Loyola of Chicago

**Residency:** Cincinnati General Hospital and Boston City Hospital

**Fellowship/Post-residency:** Fellowship in Endocrinology at Georgetown University Hospital

**Areas of Interest:** thyroid disease, osteoporosis and Paget's disease

**Accomplishments:**

- Stanley Robbins Award for Excellence in Teaching (2002)
- One of the founding fathers of the National Organization, Clerkship Directors in Internal Medicine (CDIM)



MARIE MCDONNELL, M.D.

**Instructor of Medicine at Boston University School of Medicine;  
Director of Inpatient Diabetes Program**

**Medical School:** Boston University School of Medicine

**Residency:** New York Presbyterian Hospital, Columbia Campus

**Fellowship/Post Residency:** Fellowship in Endocrinology at Boston Medical Center

**Areas of Interest:** Diabetes and nutrition



THOMAS MOORE, MD

**Professor of Medicine at Boston University School of Medicine**

**Medical School:** University of Cincinnati College of Medicine

**Residency:** University of Cincinnati Medical Center

**Fellowship/Post Residency:** Research fellowship at Peter Bent Brigham Hospital and Harvard medical school

**Areas of Interest:** Nutritional aspects of hypertension

**Accomplishments:**

- Chairman of the DASH, multicenter, NIH-sponsored study showing that a diet rich in fruits, vegetables and low-fat dairy food can lower blood pressure
- Clinical Investigator Award for the National Institutes of Health
- Established Investigator Award from the American Heart Association
- Published the *Dash Diet for Hypertension: Lower Your Blood Pressure in 14 Days – Without Drugs*



ELIZABETH N. PEARCE, M.D., M.Sc.

**ASSISTANT PROFESSOR OF MEDICINE AT BOSTON UNIVERSITY SCHOOL OF MEDICINE**

**Medical School:** Harvard Medical School, Boston University School of Public Health

**Residency:** Beth Israel Deaconess Medical Center

**Fellowship/Post Residency:** Fellowship in Endocrinology at Boston Medical Center

**Areas of Interest:** Sufficiency of dietary iodine in the U.S., thyroid function in pregnancy, thyroid effects of environmental perchlorate exposure, the cardiovascular effects of subclinical thyroid dysfunction and thyroid disease

**Accomplishments:**

- Pfizer Scholar in Endocrinology
- Elected to Delta Omega, the public health honor society



**SARA PIETRAS, M.D.**

**INSTRUCTOR OF MEDICINE AT BOSTON UNIVERSITY SCHOOL OF MEDICINE**

**Medical School:** Dartmouth Medical School

**Residency:** Mount Auburn Hospital in Cambridge, Massachusetts

**Fellowship/Post Residency:** Fellowship in Endocrinology at Boston Medical Center

**Areas of Interest:** Diabetes, bone disease and thyroid dysfunction



**James L. Rosenzweig, MD**

**Associate Professor of Medicine at Boston University School of Medicine, Director of Diabetes Services at Boston Medical Center**

**Medical School:** Yale School of Medicine

**Residency:** Barnes-Jewish Hospital, Washington University School of Medicine, St. Louis, Missouri

**Fellowship/Post Residency:** Diabetes Branch, National Institute of Diabetes, Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland. Clinical Associate, U. S. Public Health Service. Lita Annenberg Hazen Fellowship in Clinical Research in Diabetes, Endocrinology, and Metabolism.

**Areas of Interest:** Diabetes disease management, prevention of diabetes and cardiovascular Disease, clinical quality improvement, physician

performance measurement, clinical guidelines and pathways, patient risk stratification.

**Accomplishments:**

- Dr Rosenzweig led a workgroup that developed nationally-recognized guidelines for the prevention of diabetes and cardiovascular disease in patients at risk.
- Dr. Rosenzweig is Chairman of the Performance Measures Committee and a member of the Clinical Affairs Committee of the Endocrine Society
- He was Chairman of the National Diabetes Quality Improvement Alliance



Neil Ruderman, M.D., D.Phil.

**Professor of Medicine, Physiology and Biophysics at Boston University School of Medicine;**

**Director of the Diabetes Research Unit at Boston Medical Center**

**Medical School:** University of Pittsburgh School of Medicine

**Residency:** Presbyterian Hospital, Pittsburgh, PA; Metropolitan Hospital, NY

**Fellowship/Post Residency:** Joslin Diabetes Research Laboratory, Harvard Medical School

**Areas of Interest:** Diabetes and Metabolic Disorders

**Accomplishments:**

- Internationally known for research in areas such as diabetes and exercise, vascular complications of diabetes and the metabolic syndrome, a disorder that predisposes people both to type 2 diabetes and coronary heart disease.
- Recipient of many honors, most recently the Albert Renold Award of the American Diabetes Association



ASISH SAHA, PHD

**Associate Professor of Medicine; Co-Director, Biochemistry and Molecular Biology Core**

**Graduate School:** University of Calcutta, India

Ph.D. in Biochemistry, University of Calcutta, India

**Post-doctoral:** University of Pittsburgh, Dept. of Biochemistry & Molecular Biology, School of Medicine

**Areas of interest:** Fuel Sensing and Insulin Resistance; AMPK/malonyl CoA mechanism in mammalian tissues and the role of its dysregulation in the pathogenesis of the metabolic syndrome

**Accomplishments:**

- Recipient of WHO Fellowship
- Established investigator of Boston area Diabetes Endocrinology Research Center



JOSHUA D. SAFER, M.D., FACP

**Associate Professor of Medicine and Molecular Medicine at Boston University School of Medicine; Director, Endocrinology Fellowship Training Program**

**Medical School:** University of Wisconsin School of Medicine, Madison

**Residency:** Beth Israel Medical Center, New York City

**Fellowship/Post Residency:** Fellowship in Endocrinology at Beth Israel Deaconess Medical Center - Harvard Medical School, Boston

**Areas of Interest:**

**Clinical** - treatment of thyroid disease, use of sex hormone therapies.

**Research** - use of thyroid hormone to treat skin disease and improve wound healing.

**Accomplishments:**

- Editorial Board member for Endocrine Practice, the journal of the American Association of Clinical Endocrinologists
- Fellow of the American College of Physicians



***Elliot Sternthal, M.D.***

*Assistant Professor of Medicine at Boston University School of Medicine*

**Medical School:** McGill University Faculty of Medicine, Montreal, Canada

**Residency:** Jewish General Hospital, Montreal, University of Massachusetts Medical Center,

**Fellowship in Endocrinology at University of Massachusetts Medical Center**

**Areas of interest:** diabetes

**Accomplishments:**

- Fellow of the American College of Physicians and the American College of Endocrinology
- Associate Editor of Endocrine Practice



***Lisa Usdan, M.D.***

**Instructor of Medicine at Boston University School of Medicine**

**Medical School:** University of Tennessee, College of Medicine

**Residency:** Residency in Internal Medicine, Thomas Jefferson University Hospital

**Fellowship:** Fellowship in Endocrinology, Boston Medical Center

**Areas of Interest:** Diabetes, Obesity, Thyroid and Pituitary Diseases



LYNN WHITE, RN-C, FNP-BC, CDE, BC-ADM

**Nurse Practitioner**

**Graduate School:** Master of Science from Boston College

**Areas of Interest:** Working with diabetes patients to manage their disease. Improving medication therapy while developing life skills to make medications work in the best way for each patient. Firm belief in working with the patient to find and reach their goals for health maintenance and diabetes control.

**Accomplishments:**

- Certified NCBDE, AANC in Family Nurse Practice, Advanced Diabetes Management, Diabetes Education
- Insulin Pump trainer Medtronic, Omnipod, Deltec Cozmo

BOSTON UNIVERSITY MEDICAL CENTER  
**DEPARTMENT OF MEDICINE**  
**ANNUAL REPORT**  
SECTION OF **Nephrology**  
**JULY 1, 2007 - JUNE 30, 2008**  
**FISCAL YEAR 2008**

**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 \$1.5 million in 2007-2008 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 Amgen Research 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 dialysis and to define the effects of homocysteinemia in patients with kidney failure.

**CLINICAL ACTIVITIES**

**DIALYSIS CARE**

Our outpatient dialysis unit is operated in conjunction with DaVita Healthcare, a recognized leader in dialysis services, under the direction of Dr. Laura Dember. DaVita Healthcare offers state-of-the-art dialysis care with a national reputation for establishing benchmark dialysis units in academic medical centers.

The DaVita Boston unit, the largest dialysis facility in Boston, is located immediately adjacent to Boston Medical Center. Our highly skilled physician, nursing and technical staff provide high-quality hemodialysis care.

The peritoneal dialysis program at the DaVita Boston facility is a regional leader in the provision of peritoneal dialysis therapy and is directed by Dr. V. Elizabeth Abernethy. Peritoneal dialysis is performed by patients at home under the supervision of the Peritoneal Dialysis Program team, enabling patients to remain independent and continue working. Thirty-five percent of the dialysis population served through the Boston DaVita facility uses peritoneal dialysis.

Providers in the outpatient dialysis unit are dedicated to caring for the many medical and social needs of the end-stage renal disease patient. The multidisciplinary care team consisting of physicians, nurses, social workers, dietitians and patient care technicians collaborate closely with the primary care physician to meet each patient's unique needs.

## TRANSPLANT CARE

Over the past decade, more than 400 cadaver and living-related-donor kidney transplants have been performed under the auspices of the Boston Medical Center Kidney Transplant Program. Our physicians provide medical support from the initial evaluation, through peri- and post-operative management and long-term transplant follow-up under the supervision of Drs. Jean Francis and Dr. V. Elizabeth Abernethy.

## INPATIENT CARE

Our inpatient service cares for patients with renal problems such as acid-base and electrolyte abnormalities, stone and hypertensive disorders, acute glomerulonephritis and vasculitis, post-operative and other forms of acute renal failure, chronic renal insufficiency and ESRD. All dialysis modalities, including continuous therapies (CVVHD), intermittent hemodialysis and peritoneal dialysis are available at Boston Medical Center.

## OUTPATIENT CARE

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. Annual visits increased by 15% over the past year

## VA BOSTON HEALTHCARE SYSTEM (VABHS)

VABHS-based Renal physicians provide consultative inpatient services at the West Roxbury VA, oversee the inpatient and outpatient dialysis unit, and conduct outpatient clinics at the Jamaica Plain VA in collaboration with nephrologists from Harvard programs.

## EDUCATION

Clinical faculty members deliver 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., Associate Professor of Medicine, serves as director of the GPMM.

Several Nephrology faculty at BUMC also serve as ward attending in the Department of Medicine as well as 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 also attend 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, now in its 35<sup>th</sup> year, supports the research training program and has been renewed through 2010. All positions were continuously filled through 2008, and 50% of program graduates have academic appointments. Postdoctoral fellows have also 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

- Six recent trainees have had first-author papers in Nature Cell Biol, JBC, J Exp Med, J Immunol and Kidney Int, two have received K awards, others have received career development awards from AHA, Amgen Research Foundation and private foundations.
  - Dr. Vipul Chitalia's Nature Cell Biol paper in 2008 with Dr. Herb Cohen on Jade inhibition of Wnt signaling was the subject of a *News and Views* review in the same journal and a three-page overview in Trends in Biochemical Sciences (TiBS) by Randall Moon, a Hughes Investigator and world leader in the Wnt field.
  - A paper by Drs. Rebecca Foy, Maria Panchenko and Cohen on the role of Jade-1 in the histone acetyltransferase HBO1 complex in J Biol Chem was cited as the *Paper of the Week*.
  - Drs. Tamar Aprahamian's January 2009 paper on PPAR agonists in murine lupus with Dr. Rifkin was selected for "*In this issue*", a forum that highlights the top 10% of papers published in J Immunol.
  - Dr. Larry Beck's discovery of the membranous nephropathy antigen together with Dr. Salant was presented at the annual meeting of the American Society of Nephrology to wide acclaim.
  - Dr. Chitalia has been awarded a K08 grant from NIDDK and a Young Investigator Grant from the National Kidney Foundation to study the role of Wnt signaling in uremic vascular disease.
  - Dr. Aprahamian has been awarded a K01 grant from NIAMS to study the mechanisms of accelerated atherosclerosis in lupus.
  - Dr. Beck received a Junior Faculty Development Award from Amgen Research Foundation for his research to define the molecular basis of human membranous nephropathy.
  - Tal Kopel, Research Fellow, received a fellowship grant from the National Kidney Foundation.
  - Katarina Illanes, Research Fellow, received a fellowship grant from the Amgen Research Foundation.
- Weining Lu, M.D., M.Sc., Assistant Professor of Medicine, received a new R01 grant from NIDDK and a March of Dimes grant to study genetic defects in kidney and urinary tract development.
- 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 has been awarded a new grant from NIDDK to continue her studies on vascular access patency, and she also serves as chair of the NIDDK Fistula Study Protocol and Quality Control Committees of the Dialysis Access Consortium. She was re-appointed as Co-Editor of the American Journal of Kidney Diseases.
- Dr. Salant delivered the William B. Waters lecture to the Georgia Kidney Foundation and the Abraham Rapoport lecture at the University of Toronto, and was visiting professor at Duke, UAB, Emory, University of Michigan and University of Toronto. He also serves the Education Committee of the American Society of Nephrology and chairs a test writing committee for the ABIM.
- 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

**Elizabeth Abernethy, M.D.** is an Assistant Professor of Medicine at Boston University. She completed her residency at the Cleveland Clinic and Nephrology training at Boston University Medical Center. She joined the Renal Section in 1999. Her research training was in macrophage and mouse proximal tubular epithelium signaling under Dr. Jerrold Levine. She oversees the home peritoneal dialysis training program and is the medical director of the renal transplant program at Boston Medical Center and the BMC UNOS representative.

**Edward A. Alexander, M.D.** is a Professor of Medicine and Physiology at Boston University and was Chief of Nephrology at Boston City Hospital for 25 years. He trained with Dr. Norman Levinsky and then with Dr. Joseph Hoffman in the Department of Physiology at Yale Medical School. He returned to Boston University - Boston City Hospital to become a member of the Renal Section in 1969. Dr. Alexander has published extensively in several areas of research. These include renal acidification mechanisms; electrolyte excretion; the relation of the adrenal and the kidney to hypertension; the effects of aging and of pregnancy on renal function. In addition he has authored several book chapters in clinical nephrology. Dr. Alexander's research is supported by a grant from the National Institutes of Health. He plays a major role in house-staff and fellow education and is the recipient of a Department of Medicine Teaching Award.

Dr. Alexander's Research Activities:

- [Control Mechanisms of Acid Secretion](#)

**Jasvinder Bhatia, M.D.** is an Assistant Professor of Medicine at Boston University. He completed his Internal Medicine residency and Nephrology fellowship at Boston Medical Center. His research training was with Dr. Laura Dember, examining thyroid function in patients with renal amyloidosis. He joined the Renal staff in 2003 and currently serves as the section's Clinical Director. He attends on the consult services, the dialysis and transplant service, and inpatient Medicine service. He also conducts a weekly clinic at the East Boston Neighborhood Health Center.

**Laurence H. Beck, Jr., M.D., Ph.D.** is an Assistant Professor of Medicine at Boston University. He completed his Internal Medicine residency and Nephrology fellowship at Boston Medical Center. He joined the Renal Section in 2006, and continues to conduct basic science research on the pathogenesis of membranous nephropathy. His clinical roles include a weekly clinic and attending time on the consult and dialysis/transplant services.

**Ramon Bonegio, M.D.** is an Assistant Professor of Medicine at Boston University. He graduated from the University of the Witwatersrand Medical School in South Africa and then trained in clinical nephrology in the renal section at the Johannesburg Hospital. After completing a clinical nephrology fellowship at Boston Medical Center, he undertook research training in the laboratory of Dr Wilfred Lieberthal where he examined the pathogenesis of proteinuria-associated tubulointerstitial fibrosis. He now works with Dr. David Salant and is completing a Ph.D. thesis on the role of notch signaling in renal development and the glomerular injury response. In addition to his research interests, Dr Bonegio was the recipient of the "Excellence in Teaching Award". He is an attending physician on the consult and dialysis/transplant services.

**Steven C. Borkan, M.D.** is an Associate Professor of Medicine at Boston University. He worked in the Renal Function Laboratory with Dr. Jordan Cohen and subsequently received training in clinical Nephrology at the University of Chicago with Dr. Fredric Coe. Dr. Borkan completed a three-year research fellowship in Nephrology at Boston Medical Center with Drs. John Schwartz (Renal Section) and Peter Brecher (Biochemistry) and then joined the Renal Section Faculty in 1989. His interests include education of nephrology fellows, medical students and house staff, basic research on the cellular mechanisms of ischemic acute renal failure and the care of patients with both general medical and renal diseases. Dr. Borkan is the senior author of numerous publications in the area of the cellular stress response to acute ischemia and has

been a Principal Investigator for the NIH for nearly 15 years. Dr. Borkan has also received several awards for excellence in teaching from medical students, house staff and colleagues at Boston Medical Center. Most recently he received the 2007 Grant V. Rodkey award from the Massachusetts Medical Society for significant contributions to medical student education and mentoring.

Dr. Borkan's Research Activities:

- [Gene expression associated with acute renal injury](#)
- [Cellular Mechanisms of Injury in Acute Renal Failure](#)

**Joline Chen, M.D.** is an Assistant Professor of Medicine at Boston University. She completed her Nephrology fellowship at Tufts-New England Medical Center and a Masters of Science in Clinical Research from Tufts University in 2006. Her research training was with Drs. Carmen Castaneda Sceppa and Andrew S. Levey, examining the effect of exercise in patients with chronic kidney disease. She was also an investigator in clinical trials that examined the effect of resistance exercise in patients with kidney failure treated with hemodialysis. She joined the Renal Section in 2006 and currently attends on consult and the dialysis and transplant services.

**Herbert T. Cohen, M.D.** is an Associate Professor of Medicine and Pathology and serves as Director of the Graduate Program in Molecular Medicine. He received advanced training in molecular biology and protein chemistry at Beth Israel Deaconess Medical Center and Harvard Medical School in the laboratory of Dr. Vikas P. Sukhatme. Earlier, he studied renal physiology and biochemistry with Dr. Adrian I. Katz and was a clinical fellow at the University of Chicago. His interests are in the molecular bases of renal cancer, renal cystic disease and renal development. From study of the von Hippel-Lindau (VHL) tumor suppressor, Dr. Cohen's laboratory has identified a new family of transcription factor and ubiquitin ligase proteins, the Jade family of proteins. His NIH-funded research projects are titled, "VHL, Jade-1 and protein stability in renal cancer" and "Jade-1 in cystic renal disease." Dr. Cohen is presently director of the Graduate Program in Molecular Medicine.

Dr. Cohen's Research Activities:

- [Molecular Biology of Renal Cancer, Polycystic Kidney Disease, and Renal Development](#)

**Laura Dember, M.D.** is an Associate Professor of Medicine at Boston University and Medical Director of the DaVita-Boston Dialysis Center. Dr. Dember received her nephrology training at the Hospital of the University of Pennsylvania and at Brigham and Women's Hospital where she was a Howard Hughes Medical Institute postdoctoral fellow in the laboratory of Dr. Paul Anderson. Dr. Dember's research focus is on intervention studies in end-stage renal disease with particular interests in hemodialysis, vascular access. She is a principal investigator for the NIH Dialysis Access Consortium established to design and conduct multi-center clinical trials evaluating pharmacologic approaches to improving hemodialysis vascular access outcomes, as well as an NIH-funded multicenter observational study investigating mechanisms underlying hemodialysis fistula maturation. As a member of the Boston University Amyloid Treatment and Research Program, Dr. Dember is conducting studies evaluating renal outcomes with new treatments for the systemic amyloidoses. Dr. Dember lectures at national nephrology courses, serves on committees and advisory groups of the American Society of Nephrology, and is a Co-Editor of the American Journal of Kidney Diseases.

Dr. Dember's Research Activities:

- [Clinical Investigation](#)

**Jean M. Francis MD** is an Assistant Professor of Medicine at Boston University. He completed his Internal Medicine residency and Nephrology fellowship at Hospital of Saint Raphael and Yale University. He subsequently did Kidney and Pancreas transplant fellowship at Beth Israel Deaconess Medical Center and Harvard Medical School. He is UNOS certified transplant nephrologist with primary focus on pancreas transplantation. His research interest is Bone Mineral Disorders in CKD, ESRD and transplant patients. He

joined the Renal Section in 2008 and currently attends on both consult services, the dialysis and transplant service, and inpatient Medicine service. He also conducts weekly transplant and general Nephrology clinics.

**Craig E. Gordon, M.D.** is an Assistant Professor of Medicine at Boston University. He completed Internal Medicine training at Beth Israel Deaconess Medical Center and served as an academic Hospitalist and Core Faculty member at BIDMC following residency. He completed Nephrology fellowship at Tufts Medical Center. His research training was with Drs. John Wong and Andrew S. Levey, investigating the treatment of hepatitis C virus in hemodialysis patients. He joined the Renal Section in 2008 and currently attends on the consult service, dialysis and transplant service and weekly continuity clinic. He serves as a Robert Dawson Evans Educator for the Department of Medicine and is actively investigating hepatitis C virus in chronic kidney disease.

**Andrea Havasi, M.D.** is an Instructor in Medicine at Boston University. She graduated from the Semmelweis University School of Medicine in Budapest, Hungary, and completed nephrology training at Boston Medical Center. At BMC, she undertook research training in the laboratory of Dr. Steven Borkan as a National Kidney Foundation Research Fellow Award recipient, investigating the cytoprotective mechanisms of Hsp27 in ischemic renal cell injury and apoptosis. She joined the Renal Section Faculty in 2008, and continues to conduct basic research in the area of renal cell injury using cell culture and animal models. Her clinical roles include a weekly clinic and attending time on the consult and dialysis/transplant services.

**Robert J. Hamburger, M.D.** is a Professor of Medicine at Boston University School of Medicine and is Chief of the Renal Section at the VA Boston Health Services. Dr. Hamburger received his nephrology training at the University of Pennsylvania. His interests are hypertension, electrolyte disorders and he is involved in the Veterans Affairs cooperative study program.

**James S. Kaufman, M.D.** is Professor of Medicine at Boston University School of Medicine. Dr. Kaufman completed a three year research fellowship at the Walter Reed Army Institute of Research and has been a member of the Renal Section at Boston University based at the Boston VA Medical Center since 1977. He is currently actively involved in clinical research with several projects involving hypertension and dialysis patients and is the chairman of two VA multi-center cooperative studies on the use of erythropoietin in hemodialysis patients and the other on the use of anti-platelet agents in the prevention of hemodialysis access thrombosis.

Dr. Kaufman's Research Activities:

- [Clinical Investigation](#)

**Weining Lu, M.D.** is an Assistant Professor of Medicine at Boston University. He graduated from Zhejiang University College of Medicine, China in 1989 and received a M.Sc. in Biomedical Sciences from Northeastern University in 1996. He completed postdoctoral research training in molecular biology with Dr. Jing Zhou and in developmental biology with Dr. Richard Maas at the Brigham and Women's Hospital. After serving as an Instructor in Medicine at Harvard Medical School, he joined the Renal Section at Boston University in 2004 to study the molecular basis of kidney development and congenital anomalies of the kidney and urinary tract. His research program is supported by grants from the NIH, March of Dimes and National Kidney Foundation.

Dr. Lu's Research Activities:

- [Molecular Genetics of Kidney Development and Congenital Anomalies](#)

**Ian R. Rifkin M.D., Ph.D.** is an Associate Professor of Medicine at Boston University. He graduated from medical school in South Africa and completed his Ph.D. at the University of Cambridge in England in the laboratory of Dr. Martin Lockwood where he studied T cell regulation and neutrophil activation in systemic vasculitis. Subsequently, he trained as a clinical fellow in this Renal Section and then worked as a research

fellow in immunology with Dr. Ann Marshak-Rothstein in the Department of Microbiology at Boston University. His research on the role of Toll-like receptor in autoimmunity, and SLE in particular, has received widespread international recognition. His research is funded by grants from the NIH, Lupus Research Institute and National Kidney Foundation.

Dr. Rifkin's Research Activities:

- [Autoimmunity](#)

**David J. Salant, M.D.** is Chief of the Renal Section and Professor of Medicine at Boston University. He obtained his medical degree from the University of the Witwatersrand in Johannesburg, South Africa and joined the full-time faculty at Boston University after completing research training with Dr. William G. Couser. Prior to that he was a member of the Renal Section at the Johannesburg General Hospital in South Africa where he gained extensive experience in renal transplantation, dialysis and other aspects of clinical nephrology.

Dr. Salant is a senior investigator whose research is supported by grants from the National Institutes of Health. His research into the mechanisms of glomerular injury is of considerable topical interest and has received national and international recognition. His work has been regularly presented at scientific sessions of the American Society of Nephrology and other scientific meetings. He has further contributed to the proceedings of these organizations by reviewing abstracts, chairing scientific sessions and symposia, and delivering invited lectures. He has also served for several years as a member of a NIH study sections and special emphasis panels.

In addition to more than 130 contributions to the scientific literature, Dr. Salant has written several clinical papers on diverse nephrological subjects and book chapters on glomerular diseases and vasculitis of the kidney. He was an author of MKSAP and chairman of the ABIM Subspecialty Board of Examiners in Nephrology. He also serves as chair of the Department of Medicine Appointment and Promotions Committee.

Dr. Salant's Research Activities:

- [Renal Immunopathology](#)

- [Antibody-mediated podocyte injury](#)

- [Mechanisms of post-inflammatory renal fibrogenesis](#)

**John H. Schwartz, M.D.** is a Professor of Medicine and has been a member of the Renal Section since 1977. He trained in the laboratory of Dr. Philip Steinmetz at Harvard Medical School. In 1971 he became a staff member of the renal unit at the Walter Reed Army Institute of Research and from 1973 to 1977 was chief of that unit. Dr. Schwartz has made research contributions in a number of areas including the cellular regulation of H<sup>+</sup> transport in renal epithelia, coupling in excitable cells and pathogenesis of acute renal failure. His research is supported by grants from NIH. He also plays a major role as mentor and research supervisor of pre- and post-doctoral students/fellows in the GPMM and Renal research training program.

Dr. Schwartz's Research Activities:

- [Control Mechanisms of Acid Secretion](#)

- [Gene expression associated with acute renal injury](#)

- [Cellular Mechanisms of Injury in Acute Renal Failure](#)

**Aylit Schultz, M.D.** is an Instructor in Medicine at Boston University. She received her medical training at Albert Einstein College of Medicine and then Columbia Presbyterian Hospital in New York. She joined the Renal Section in 2007 after completing her Nephrology fellowship at Beth Israel Deaconess Medical Center. Her clinical roles include a weekly clinic, attending on the consult and dialysis and transplant services, and

growing our new Short Daily Home Hemodialysis program. She also serves on the Department of Medicine Quality Council, and is involved in other Quality of Care related projects.

**Adam M. Segal, M.D.** is an Assistant Professor of Medicine at Boston University. He received his medical training in South Africa at the University of the Witwatersrand and later trained in the United Kingdom. He joined the Renal section in 2006 after completing his Nephrology fellowship at Beth Israel Deaconess Medical Center where he spent time in the laboratory of Dr. Stewart Lecker examining the molecular mechanisms behind the muscle wasting that occurs in uremia and other chronic illnesses. He currently conducts clinic at East Boston Neighborhood Health Center, Boston Medical Center and in the Amyloid center and attends on the consult and dialysis and transplant service. His interests include kidney stone disease, amyloidosis associated renal disease, geriatric nephrology and HIV associated renal disease.

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SECTION OF GERIATRICS  
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A) Education Activities

Medical Students. All medical students participate in the geriatrics curriculum that is part of the required third year Family Medicine Clerkship. Emphasis is placed on Geriatric Assessment skills development. During their required four-week fourth year Geriatrics and Home Medical Care Clerkship, 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 on-line directed learning exercises. Students may also elect to spend four weeks of their third year internal medicine inpatient clerkship and/or their Medicine subinternship on the Geriatrics Inpatient Service. The Section also provides faculty and staff support for the BUSM Student Chapter of the American Geriatrics Society.

Four clinical geriatrics experiences are included in our internal medicine residency program: 1) all Primary Care interns participate in a two-week block experience designed to introduce them to community-based services and our interdisciplinary primary care team model of geriatric care; 2) 26 residents per year complete a four-week outpatient rotation in geriatrics, whose sites include homes, nursing homes, and a Program of All-Inclusive Care of the Elderly (PACE) site; 3) an additional two to five residents in the Primary Care Training Program elect to follow home care or nursing home patients a "second clinic" over one to two years; and 4) 26 interns and 13 residents per year form the housestaff team for the Geriatrics Inpatient Service.

Since its inception in 1988, the Geriatric Medicine Fellowship (Sharon Levine, MD, Program Director) has trained academic geriatricians, the majority of whom are practicing in underserved areas. There are both one-year and two- to three-year training options. In 1991, with the support of a Bureau of Health Professions (BHP) Faculty Training Grant in Geriatric Medicine and Dentistry, the fellowship expanded to include dental fellows, and in 2000 further expanded to include psychiatry fellows. The fellowship includes a strong mentored research component, with all two-year fellows completing a research project that fulfills the thesis requirements for an MSc in epidemiology or health services through the BU School of Public Health. The Section also co-sponsors nationally recognized Geriatric Oncology Fellowship in collaboration with the Section of Hematology/Oncology. Two of our three 2008 fellowship graduates will join our faculty in July 2008: Drs. Ilona Kopits and Won Lee.

Our John A. Hartford Foundation Center of Excellence in Geriatrics faculty development program continues to train non-geriatrician faculty scholars (54 faculty members have been trained since 1998). The program is designed to equip clinician educator faculty members to become excellent teachers of geriatrics principles. Six faculty scholars have been accepted for the coming academic year, representing general internal medicine (including hospital medicine), ophthalmology, urology, and anesthesiology.

B) Research Activities

Dr. Rebecca Silliman leads a research group that conducts research on breast cancer etiology, disparities in breast cancer therapy, and the consequences of those disparities. Current grant funding includes two R01s and a K05 (all funded by the National Cancer Institute) that support mentoring and research collaborations both at BU and across the nation. Research findings published during this academic year highlight the untoward consequences of under treatment of breast cancer in older women. Dr. Silliman is also principal investigator of a National Institute on Aging (NIA) R01, in collaboration with Dr. Michael Paasche-Orlow from the Section of General Internal Medicine. It is testing the efficacy of a computer-based agent to increase the amount of walking done by older adults. Dr. Silliman serves as Vice-chair of the Research Committee of the American Geriatrics Society and is Chair of the Abstract Selection Committee for the annual national meeting. She also is an associate editor of the *Journal of Gerontology: Medical Sciences*.

Dr. Thomas Perls is Director of the New England Centenarian Study. 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 NIA is supporting the “Long Life Family Study”, a collaboration of Boston University, Columbia University, University of Pittsburgh, and 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, and to characterize the phenotypes associated with exceptional survival for eventual genetic linkage analysis.

Dr. Erica Bernstein is focusing her investigative work on the intersection of aging, oxidative stress, and diastolic dysfunction. She is a BIRCWH (Building Interdisciplinary Research Careers in Women’s Health) Scholar and will also be receiving funding from the Pepper Center (see below). Dr. Silliman is co-principal investigator (Karen Freund, MD, Director of the Center of Excellence in Women’s Health is principal investigator) of the BIRCWH (K12) program.

The Summer Institute in Geriatric Medicine, funded by the NIA and designed to provide a week-long intensive research experience, drew a class of 15 medical students from across the United States to the Boston University Medical Center campus in June. A competitive renewal application was funded for five years as of May 1, 2006 (Rebecca A. Silliman, MD, PhD, principal investigator). In addition, the Section supported three medical students who successfully competed for summer research funding through the Medical Student Training in Aging Research (MSTAR). All three (Emily Adams, Matthew Watto, and James Yeh) presented their research at the 2008 Annual Meeting of the American Geriatrics Society. Mr. Yeh won the prize for the best poster in the Biology of Aging category.

### C) Clinical Activities

Boston University (BU) Geriatric Services at Boston Medical Center, the clinical program of the Section of Geriatrics, has as its primary goal to provide ongoing primary care and case management to older Boston residents. Other goals include the provision of geriatric consultative services to BMC primary care physicians and specialists, and to promote geriatric education through the comprehensive training programs described below. A collaborative practice model is used, with care 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. Dr. Lisa Caruso is overall Clinical Director for BU Geriatric Services and Clare Wohlgenuth is our Director of Nursing. Each component of the practice also has a physician and nurse leader.

The Geriatric Ambulatory Practice (GAP) cares for older adults who are able to use available transportation. Approximately 1,000 patients are cared for during 10 geriatrician sessions/week, 2 Geriatric Medicine fellow

session/week, and 1 registered nurse session/week. Additionally, the GAP holds 2-3 Geriatric Assessment sessions per month. Dr. Heidi Auerbach is the physician leader and Ann McDonough is the nurse leader.

The Home Care Program cares for approximately 570 homebound frail elders living within the City of Boston. Many are eligible for nursing home placement, but are able to remain at home through an extensive network of formal and informal nursing and personal care services. Dr. Eric Hardt is the physician leader and Cathy Fabrizi is the nurse leader. BU Geriatric Services clinicians (physicians, nurse practitioners, and nurse case managers) work in close collaboration with patients' other caregivers, including the certified home health agency, community agencies, and family and friends. We have gained considerable experience with a special capitated program for patients with both Medicaid and Medicare and have expanded the use of Logician via wireless access to patients' homes.

The Nursing Home Program cares for approximately 450 patients in 10 Boston nursing homes, also using a nurse practitioner-physician collaborative model. Patients enrolled in the program typically require long-term care, and many are patients who were initially cared for in the Geriatric Ambulatory Practice or in the Home Care Program. The program also cares for short stay patients with skilled nursing or rehabilitation needs. Logician is also used in the Nursing Home Program. Use of Logician helps to smooth clinical transitions and minimizes duplicate laboratory and radiology testing. It also reduces the chances of lack of follow-up of hospital-initiated tests. Dr. Gary Brandeis is the physician leader of the Nursing Home Program and Monica Hogan serves as the nurse leader.

BU Geriatric Services is also responsible for the Geriatric Inpatient Service and most section physicians annually undertake two two-week rotations as the attending physician on the Firm. The service admits 24/7; the housestaff team of a resident and two interns is complemented by a nurse practitioner from the section who also serves as the service nurse leader (Julie Wentworth). Dr. Lisa Caruso is the physician leader. Whenever possible, patients within any of the section's programs who require inpatient care are admitted to the inpatient service.

We continue to use a range of strategies this year to improve clinical operations. Dr. Lisa Caruso and Ms. Clare Wohlgemuth are Co-leaders of our Performance Improvement Task Force. Current projects include falls risk identification/prevention; emergency room utilization reduction; improving medication prescribing; and improving advance directives documentation.

#### Major Accomplishments:

- During calendar year 2007, the section published 27 articles in peer-reviewed journals.
- Dr. Silliman was the Dr. John Meyers Visiting Professor in Geriatric Medicine at the University of Massachusetts Medical School in May 2008.
- Under Dr. Shalender Bhasin's leadership, we, along with investigators from Tufts University and the Joslin Clinic, submitted a successful Claude D. Pepper Older American Independence Center grant application to the NIA that will be funded this fall. Only one of 11 funded nationally, the Center will train early career investigators and support pilot and development projects focused on developing new strategies for enhancing the functional status of older adults. Dr. Silliman is a Co-Director of the Center and directs the Research Career Development Core (RCDC). The RCDC will support the research of four early career investigators.

- In follow-up of the section's biannual retreat, we developed a new initiative in interdisciplinary aging scholarship. Under the leadership of Dr. Victoria Parker, a faculty member in the Department of Health Policy and Management in the School of Public Health, this initiative will be fostering collaborative scholarship within the section, as well as with investigators in community-based organizations, such as the Visiting Nurse Association of Boston. A section-sponsored pilot project program is also under development.

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**SECTION OF CARDIOLOGY**  
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**FISCAL YEAR 2008**

SECTION CHIEF NAME: Wilson S. Colucci, M.D.

SECTION SUMMARY REPORT

**A. Clinical Activities**

In fiscal year 2007-2008, overall clinical activity decreased by approximately 5%, as reflected by a decrease in total work RVU's from 103,593 to 97,921. Ambulatory clinic volume increased to 15,127 clinic visits (37 % increase from 2007), whereas there were small decreases in consultations to 1,728 (3% decrease from 2007), and days of medical care to 6,567 (10% decrease from 2007). There were increases in non-invasive procedures, with 12,547 echocardiograms (13% increase from fiscal 2007), 4,356 exercise tests (6% increase from 2007) and 73,177 electrocardiograms (15% increase from 2007). We performed 1,555 catheterizations and interventional procedures, representing an 8% decrease from 2007. The Electrophysiology Program volume continued to increase with 1,155 procedures (a 22% increase from 2007), as did the Peripheral Vascular Interventional Program, which performed 392 procedures in 2007 (81% increase from 2007). The newly established Advanced Cardiac Imaging Program performed 41 cardiac MRI and 60 CT angiographic studies. Taken together, these trends in clinical activity volumes reflect our increased emphasis on ambulatory and diagnostic services, and the development of new programs in Vascular Medicine and Advanced Cardiac Imaging. Several new faculty were appointed as Assistant Professors of Medicine including Drs. John G. Carr, Naomi M. Hamburg, Andrew O. Maree, and Alisa B. Rosen.

**B. Research Activities**

The Section has been highly productive in its research activities. There were 5 new research grants, for a total of 36 on-going research grants in the Cardiovascular Section. The net annual direct research support to Section investigators in 2007 was \$9,701,282 with indirect support of \$4,179,505. The major source of funding was the NIH (\$8,633,635) with \$1,067,647 from other sources. Of the net direct funds, \$7,090,868 was attributable to physicians with a clinical appointment in the section, and \$2,144,713 was attributable to non-physician scientists. Section members published 94 journal articles, book chapters and review articles.

**C. Educational Activities**

The Cardiovascular Medicine Section is involved in extensive educational activities at all training levels involving medical students, residents, clinical fellows and post-doctoral research fellows. Medical student teaching includes direction of the Cardiovascular block of the Biology of Disease course and clinical electives in clinical cardiology for third and fourth year students. Medical residents rotate through the cardiology inpatient services and the consult service. In 2007-8 we trained 18 general cardiology fellows, 2 interventional fellows, one electrophysiology fellow and one cardiomyopathy fellow. Pre-doctoral Ph.D. and

post-doctoral MD's and PhD's are trained in numerous laboratory and clinical research settings throughout the Cardiovascular Medicine Section.

#### **D. Major Awards**

Drs. Gary J. Balady, Ravin Davidoff and Wilson S. Colucci were listed as Best Doctors in America – 2008 on the Castle Connelly List. Ravin Davidoff was also listed in Consumer A's Guidebook to Best Doctors in America (2008). Sheilah Bernard was listed as a Top Doctor by Boston Magazine (2008). Emelia Benjamin was elected to membership in the Association of University Cardiologists (2008). Joseph A. Vita received the Robert Dawson Evans Research Mentoring Award from the Department of Medicine at Boston Medical Center (2007). Sheila Bernard received the Robert Dawson Evans Clinician Award (Clinician-Teacher) from the Department of Medicine at Boston University School of Medicine (2007). Paul A. LeLorier received an Excellence in Clinical Teaching Award by the Section of Cardiology (2008). Subrata Chakrabarti received a Pilot Project Grant from the Department of Medicine at Boston University School of Medicine (2008)

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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 >100 faculty members, the Section continues to be highly productive in clinical, educational, and research realms.

Over the past year, GIM's research activities have grown. Direct research support to GIM faculty in 2008 increased by 3% and exceeded \$11 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 \$48.9 million. GIM faculty coauthored 72 medical articles in peer-reviewed journals in 2007, an increase from 58 and 46 in 2006 and 2005, respectively.

The **Women's Health Unit (WHU)** is under the direction of Karen Freund, M.D., M.P.H., Professor of Medicine and Epidemiology, and Associate Director of Boston University School of Medicine's (BUSM) Women's Health Interdisciplinary Research Center. The WHU's research activities continue to provide new insight through interventions to address health outcome 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. This work has now expanded to include navigation for cancer screening and chronic diseases, and within outpatient psychiatry to support coordination with primary care. Dr. Elizabeth Dupuis, Clinical Director of the Women's Health Group practice within the WHU, has demonstrated the benefit of tracking systems in follow-up after abnormal cervical cancer screening.

The WHU continues to receive funding for the Women's Health Fellowship, through its collaboration with the Boston Veterans Administration Health Care System. 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 junior faculty members yearly in a mentored career development program. The Unit is currently funding junior faculty in the Sections of General Internal Medicine, Geriatrics, Endocrinology, Pediatrics and Obstetric and Gynecology, on topics including the acceptance of the HPV vaccine in minority adolescents, longevity and end of life care issues for women, and both social and endocrinologic determinants associated with metabolic syndrome.

The WHU has increased its role in influencing health policy as it affects women's health and health disparities. Michele David, M.D., M.P.H., M.B.A., Associate Professor of Medicine, serves as Co- Chair of the Diversity Action Network, in collaboration with Massachusetts Health Care for All, developing policy initiatives focusing on the health of minority women. She was selected by Governor Deval Patrick to serve on the Massachusetts Department of Public Health's Public Health Council and by Elaine Ullian, CEO of Boston Medical Center to serve on the Commonwealth of Massachusetts Health Disparities Council.

The Women's Health Unit plays an active role in patient outreach and policy advocacy in addressing health disparities for minority women within the Women's Health Group practice as well as the other GIM practices. 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 and patient navigation services. Through funding from the Avon Foundation, the Unit provides patient navigation, tracking systems through the electronic medical record, and case coordination from screening mammography through diagnostic resolution for women with abnormal test results.

Dr. Teresa Cheng, WHG Fellow, in collaboration with the Department of Obstetrics and Gynecology, developed the new training module for first year medical students on the clinical breast examination. The module includes an interactive web based session, and video to illustrate proper technique. This innovation to the student curriculum includes the new clinical assessment module in the Clinical Skills and Simulation Center, where students are trained under supervision with genital teaching associates.

Dr. Michele David has received funding through the Soros Foundation to develop a new curriculum elective on advocacy for physicians. This training program will also be offered to all primary care internal medicine residents. During the elective, trainees will develop an advocacy position, and learn the role health care providers can play in advocating for the needs of our patients.

The Women's Health Unit, is also serving as a site for the new 4<sup>th</sup> year medical student ambulatory selective, under the leadership of Renee McKinney, Medical Education Director for the Unit.

The **Health/care Disparities Research Unit** was established in February 2008 under the leadership of Nancy Kressin, Ph.D., Associate Professor, with the mission of conducting high quality research to understand and alleviate inequities in health care, and to ensure the provision of exceptional health care without exception. The goal of the program is to facilitate the training of a new generation of healthcare equity researchers. Program faculty are to be intellectual advocates for and leaders of health equity research both locally, within this institution and city and nationally. Dr. Kressin is working to recruit the Unit's first faculty member. She is pursuing an internal marketing campaign to describe the program, develop or enhance relationships with faculty, to begin to foster and build new collaborations. Dr. Kressin is developing opportunities for collaboration in both research and training.

The **Clinical Addiction Research and Education (CARE) Unit**, an academic unit addressing the clinical, educational, and research aspects of alcohol and other drug use. The CARE Unit 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 Biostatistics at the Boston University School of Public Health; Theresa Kim, M.D., 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; Christopher Shanahan, M.D., M.P.H., Director of the Community Medicine Unit at Boston Medical Center (BMC), and Assistant Professor of Medicine; and Alexander Walley, M.D., MSc, Assistant Professor of Medicine and Program Director for the Facilitated Access to Substance abuse Treatment with Prevention and Treatment of HIV (FAST PATH) program, Medical Director of the BPHC Methadone Maintenance Treatment Program, and Medical Director of the Transitional Opioid Treatment (TOP) Program. CARE Unit projects directly employ approximately thirty staff members as well as several college and medical students, and they provide research

experiences for medical students, residents, and fellows. Drs. Alok Kapoor, Nancy Kressin, Amy Rubin, Sandra Gordon, and Robert Friedman, also in general internal medicine, have collaborated closely with CARE Unit faculty.

The CARE Unit collaborates with a number of other Boston University departments, other universities, and outside agencies. Dr. Saitz is Associate Director and Scientific 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, Brown University, the Boston and Bedford Veterans Affairs Medical Centers, the Massachusetts Department of Public Health, and the Boston Public Health Commission.

In 2007-2008, the NIH and the Robert Wood Johnson Foundation provided support for 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 primary care settings; a study of the interaction between PTSD and substance use in people with chronic pain; prescription drug abuse; pharmacological treatment for depression for patients beginning buprenorphine treatment of opioid dependence; drinking and health across the lifespan (in collaboration with the Framingham Heart Study); a study of an HIV prevention intervention in Russians with HIV who drink alcohol, a study of an HIV prevention intervention among uninfected Russian 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. Two large NIH grants support a randomized trial testing a health services delivery intervention---chronic care/disease management for alcohol and drug dependence. This study is currently responsible for the second greatest GCRC utilization of any study at BUMC. A large (approximately \$6 million) R-01 was awarded at the end of June 2008 to support a clinical trial to test drug screening and brief intervention in primary care settings.

Mentoring is a large commitment for CARE Unit faculty. Dr. Liebschutz is responsible for mentoring numerous residents and fellows in research. Drs. Saitz and Samet mentor research fellows, Dr. Saitz in his investigator role as well as in his role in the K30 Clinical Research Training Program, and Dr. Samet with his K24 from National Institute on Alcohol abuse and Alcoholism (NIAAA) for doing so. Dr. Samet also supports research training with a R25 award from the National Institute on Drug Abuse (NIDA) in its 7<sup>th</sup> year of funding. As a co-investigator on this award Dr. Walley mentors summer medical student research projects.

The CARE Unit has also been very successful at obtaining funds for clinical service delivery (along with research quality evaluations) from the federal Substance Abuse and Mental Health Services Administration (SAMHSA)(most notably the \$14 million MASBIRT project for screening and brief intervention (Alford PI), and the FAST-PATH project, to integrate substance abuse treatment into medical care for HIV-infected and high risk HIV-uninfected patients (Walley PD)).

To support its research dissemination and educational activities, the CARE Unit has two NIH R-25 grants, one completed this year from NIAAA and the aforementioned one from NIDA. They have supported drug abuse and alcoholism training for physicians, 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 improving addiction medicine clinical and teaching skills. These projects have

visible Web sites and produce a highly regarded electronic alcohol and health research summary newsletter. The current R-25 award supports an Addiction Medicine research track in the GIM fellowship program.

The Unit has not only been active with local and national education, and state programs, but also in the City of Boston, beyond the Boston Public Health Commission. After a fire during which two officers found to have been intoxicated, Dr. Chapman was appointed to an advisory panel by Boston's Mayor Thomas Menino to review the policies and procedures of the Boston Fire Department with specific attention to recommendations for mandatory random drug testing and wellness.

Drs. Alford and Saitz contribute to a national mentoring program for physicians prescribing buprenorphine for the American Society of Addiction Medicine(ASAM). Dr. Alford has led national efforts to train physicians in the use of buprenorphine in collaboration with ASAM. Dr. Samet serves as Program Chair for the annual national ASAM Medical-Scientific Conference. Dr. Saitz has served on a SAMHSA advisory committee addressing medical record confidentiality and serves on the Washington Circle to implement the report's recommendations.

Dr. Liebschutz, Associate Professor continued her work on an NIDA K23 career development award to study the intersection between drug abuse, PTSD, and primary care. She has begun, as part of that effort, a study of young adult victims of violence. 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.

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. Walley is Medical Director of the Methadone Clinic. Dr. Walley oversees the Transitional Opioid Program (TOP), which is an innovative 90-day treatment program that helps hospitalized, out-of-treatment opioid-dependent patients engage in substance abuse treatment. Dr. Sheila Chapman is the Medical Director of the pregnant women's program at the Methadone Clinic; Dr. Sandra Gordon also sees patients there..

CARE Unit faculty members also provide substance abuse treatment expertise to the Massachusetts Department of Public Health (DPH). Through the Office Based Opioid Treatment (OBOT) Program, Ms. LaBelle provides clinical leadership for its efforts in statewide training for the delivery of buprenorphine for opioid dependence in primary care settings. Dr. Walley is the Medical Director of DPH's Opioid Overdose Prevention Program Pilot, which trains potential overdose bystanders how to prevent, recognize, and respond to opioid overdoses.

In the past year, the CARE Unit published over 40 peer-reviewed articles and presented abstracts at numerous national and international scientific meetings of groups in general medicine, public health, and alcohol and drugs. CARE Unit faculty currently serve in leadership roles at the Society of General Internal Medicine, and the Association for Medical Education and Research in Substance Abuse.

Finally, it should be noted that CARE Unit faculty contribute substantial effort to institutional research, clinical and education infrastructure. Such efforts include, for example, but are not limited to, Dr. Saitz role in the Office of Clinical Research and in the newly-funded Clinical Translational Science (BRIDGE) Institute (including the K30, GCRC Advisory Committee and as Chair of the Division of Clinical Research Enhancements), general internal medicine fellowship leadership (Liebschutz), classroom teaching (Design and Conduct of Clinical Trials (SPH BS722), Cheng), and information technology (IT)/electronic medical record,

and community medicine leadership (Shanahan). Dr. Shanahan is Associate Medical Director for IT and has designed the IT infrastructure for MASBIRT project, which is gaining recognition as a model for sustainable implementations of large scale substance abuse screening programs. In the coming year we will add a new faculty clinician investigator, Dr. Judith Tsui, who has interests in HIV, HCV, pain and drug and alcohol abuse research.

### **Other Areas of Clinical Investigation**

Dr. Elaine Hylek, Associate Professor continued her work in the areas of prevention and treatment of arterial and venous thrombosis. Research has focused on risk factors for stroke and optimization of anticoagulant therapy. She participated in the consensus conference devoted to Antithrombotic and Thrombolytic Therapy: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines and several web-based programs sponsored by theheart.org and WebMD. Current research efforts include collaboration with investigators from Duke Cardiovascular Research Institute, University of Alabama, Veterans Affairs, and Geisinger Health System.

Dr. Michael Paasche-Orlow, Assistant Professor continued to develop his research in the role of health literacy in health outcomes. He was involved in a growing network of health literacy research projects. In addition to participating as a co-investigator in seven funded projects, he was the PI on an AHRQ funded ACTION network contract on the development of an Informed Consent and Authorization Toolkit for Minimal Risk Research. Michael was actively involved in mentoring fellows and junior faculty. In the past year, three of Michael's mentees obtained funding with his support.

The **Community Medicine Unit** (CMU) under the leadership of Dr. Christopher Shanahan, completed its sixth year since incorporation into the Section of General Internal Medicine (GIM) in 2002. The unit's mission remains directed towards support of development and management of community-focused clinical, educational, and research programs.

This past year the Joint Hire Program (JHP) provided continuing support for 14 physicians who together provided 28 weekly clinical sessions.

The CMU has worked actively with East Boston Neighborhood Health Center and South Boston Community Health Center to coordinate recruitment efforts and facilitate JHP arrangements for highly qualified community-based clinician educators including: Peter Smith, MD (Graduating GIM Fellow) - East Boston Neighborhood Health Center, Hernan Lopez-Morra, MD - East Boston Neighborhood Health Center and Lars Reinhold, MD - South Boston Community Health Center.

The CMU has continued to fund a Hospital-based Resident Education role for a Community-based Physician (Julie Crosson, MD). The position is dedicated to leading the Medical Interviewing Course for second and Third Year Internal Medicine House Officers during their Ambulatory Rotations.

CMU staff is refining the process for identifying community-based clinicians, communicating ongoing Clinical / professional evaluation standards, and compiling the results of these interrogatories. 102 BMC Medical re-credentialing applications and approximately 60 new applications for Medical Staff Appointments were handled in the last 12 months. Overall, the CMU maintains files for over 250 active BMC active staff.

The CMU director maintains an ongoing dialogue with Medical Directors, key staff physicians and other Providers and administrators at over 15 community-based sites. These relationships continue to provide a strong understanding of the current academic and practice environment across the Network regarding issues

affecting community medicine, the Metro-Boston Community Health Center Movement, and Primary Care Internal Medicine in these settings.

Dr. Peter Smith successfully completed a one year pilot of public PodCasting program featuring GIM Grand Rounds. The CMU provided funding for this project and will continue to support it. Twelve GIM grand rounds presentations were recorded and posted on the iTunes website <http://www.bmcrounds.com>.

**The Health Care Research Unit (HCRU)**, under the direction of Arlene Ash, Ph.D., Research Professor of Medicine 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 facilitating 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. These methods, developed by Dr. Ash and her colleagues, 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, 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 Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Program, and provides mentorship to departmental fellows and assistance to the Graduate Program in Molecular Medicine. Drs. Ash and Amresh Hanchate PhD, Research Associate, work with multiple BU Medical Center researchers on projects funded by the Centers for Disease Control and Prevention (CDC) ("Examining Quality of Epilepsy Care"); the Food and Drug Administration (glucose-monitoring study); the National Cancer Institute ("Impact of Breast Cancer on Older Survivors" and "Patient Navigation in the SafetyNet,"); and the National Institute on Aging ("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,," 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 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. Dr. Andrea Kronman, M.D., M.Sc., is a BIRCWH faculty scholar pursuing the following projects: "The Role of Primary Care at the End of Life" and "Improving Risk Adjustment Methods for Illness Burden."

The **Medical Information Systems Unit (MISU)** is lead by Robert Friedman, M.D., Professor of Medicine and Public Health. He directs 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 2007-2008, 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. 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.

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.

Mitchell Medow, M.D. has developed a focus in the areas of health outcomes, medical decision-making, and health informatics. Dr. Medow is pursuing research projects aimed at extending patient care outside of the clinic using telephony, with the addition of decision making tools for patients and health care providers.

## **CLINICAL ACTIVITIES**

Clinical activities within the Section of General Internal Medicine have been active. Guided by Peter Davidson, M.D., Associate Chief and Associate Professor of Medicine, ambulatory visits handled by GIM faculty exceeded 85,000 and GIM faculty were the attendings on 67% of all medicine inpatient blocks on non-

subspecialty services. Total outpatient visits have increased over the past year by 16% from 2007 in part due to the establishment of the Internal Medicine Pre-Operative Assessment Clinic, which is under the leadership of David Halle, M.D. A clinical incentive program has evolved in its fifth year of existence and measures work-RVUs (relative value units). Peggy Chou, M.D. was named Medical Director of Primary Care Services. She provides outpatient clinical leadership in all primary care practices in the Section of General Internal Medicine. In addition, she continues to provide clinical directorship in the DOB practice until a new director for that role is recruited. The YACC primary care practice is under the direction of Jason Worcester, M.D., Assistant Professor of Medicine. The Women's Health Group primary care practice is lead by 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 primary care 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 provides consultation to patients with breast problems or 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 Quincy Medical Center BU Medical Group primary care practice is now under the medical directorship of Nicolette Fontaine, M.D. The Medicine Consult Service at BMC, lead by David Halle, M.D., Assistant Professor of Medicine, has undergone extensive transformation and growth this past year with development of a newly constituted pre-operative evaluation center in collaboration with other hospital departments.

Elaine Hylek, M.D., M.PH., assumed the directorship of the Anti-coagulation clinic.

Raj Krishnamurthy, M.D., Associate Professor was recruited in a major leadership role as the Department of Medicine Outpatient Director.

The Section's **Hospital Medicine Unit (HMU)** has had a productive year. Under the direction of Jeff Greenwald, MD, Associate Professor of Medicine, the HMU grew in several areas. Nine faculty joined the Unit this year: Drs. Alok Kapoor, Charlene Weigel, Susan Kim, Robert Chehade, Karen Patterson, Versha Taparia, Sandhya Rao, Thomas Tadros and Henri Lee.

Clinically, in addition to staffing a 24/7 Hospitalist Service, co-directed by Andres Solorza, MD and Daniela Winston, MD, and PA service, the HMU staffed over a quarter of all the ward blocks and over a third of the Medical Consult Service blocks. Additionally, under the direction of Jennifer Hughes, MD, the Palliative Care Consult Service was designed and operationalized and now provides care campus wide to all services in the hospital.

HMU faculty ran an expert training session on transitions of care and quality improvement for Boston area hospitalists. Additionally, Subha Ramani, MD, MPH, MMEd coordinated the first BMC house officer OSCE, and helped organize the Departmental education retreat. Jeff Greenwald, MD is the Principal Investigator on an R13 conference grant from AHRQ. The HMU initiated a faculty teaching series and have a successful ongoing journal club.

At an organizational level, the HMU has also made significant strides. Charlene Weigel, MD, has been instrumental in working with Information Technology on the online clinical documentation project and with Quality Improvement, improving the systems for smoking cessation and pneumococcal and influenza vaccination. Nila Radhakrishnan, M.D., Assistant Professor, was appointed to a major leadership position as the first Inpatient Medical Director for the Department of Medicine.

GIM contributes to BMC Information Technology (IT) activities. Dr. Shanahan is the IT Medical Director. Two other general internists are supported by this hospital department 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 2007-2008. Craig Noronha, M.D., Assistant Professor and Victoria Hester, M.D. joined the YACC primary care practice. Daniel Chen, M.D., Assistant Professor and Mitchell Medow, M.D. joined the primary care practice in the DOB. GIM recruits Claudia Nader, M.D., Assistant Professor and Alexander Walley, M.D., Assistant Professor focus clinical contributions to both primary care and infectious diseases.

## EDUCATION

All program directors at BMC within the Department of Medicine continue to be GIM faculty. Angela Jackson, M.D., Associate Professor, continues in the role of Associate Program Director and Director of the Primary Care Training Program. David Halle, M.D. is an Associate Program Director. Beth Manning, M.D., Associate Professor is an Associate Program Director and Director of the Preliminary Program. Joel Caslowitz, M.D. is an Associate Program Director. Medical student education within the Department of Medicine is lead by Warren Hershman, M.D., M.P.H., Associate Professor of Medicine. Robert Dawson Evans Educators were appointed this year and GIM faculty, Drs. Peter Davidson and Elaine Hylek serve in these roles.

Medical students receive extensive clinical exposure in the primary care clinics, with GIM faculty providing one-on-one precepting in 502 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. Thirteen GIM faculty members attend at the Department's traditional resident morning report, and fourteen attend at the ambulatory morning report.

GIM faculty plays 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 continues 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 Frederick Brancati, M.D., M.H.C., Professor of Medicine and Epidemiology at Johns Hopkins School of Medicine and School of Public Health, who was the 2008 Mark Moskowitz Memorial 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. Associate 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. Eight fellows completed the program in 2008. 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 of General Internal Medicine, 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.

## **2007- 2008 Awards**

Daniel Alford, M.D., Associate Professor (MASBIRT) received recognition as one of BUSM's Top 15 grantees.

Sondra Crosby, M.D., Associate Professor received the Leonard Tow Humanism in Medicine Faculty Awards.

Theresa Kim, M.D., Assistant Professor received the Junior Investigator Travel Award, 2007 Addiction Health Services Research Conference, NIDA & NIAAA.

Subha Ramani, M.D., Associate Professor was awarded the Katherine Skinner Memorial Prize, BUSPH.

Eleven GIM primary care providers from BMC were recognized as Best Doctors in Best of Boston Magazine in 2008 more than any other single hospital in Boston.

BOSTON UNIVERSITY MEDICAL CENTER  
**DEPARTMENT OF MEDICINE**  
**ANNUAL REPORT**  
SECTION OF **Hematology-Oncology**  
**JULY 1, 2007 - JUNE 30, 2008**  
**FISCAL YEAR 2008**

## OVERVIEW

The Section of Hematology-Oncology continued to grow and flourish in 2008. David Seldin MDPHd was made permanent Section Chief, Gretchen Gignac MD became Firm Chief, and three new physician faculty members and two nurse practitioners were recruited. The Section now consists of 42 faculty, of which 37 are MDs and/or PhDs and 5 are NPs. Of the 37, 6 have their primary practice at the VAMC, where 4 additional Harvard faculty also practice in hematology and oncology. Of the 31 BUMC faculty, 24 have their primary appointments in Hematology-Oncology and 7 in the Cancer Center at BUSM. Of the 24 primary Heme-Onc faculty, 22 are full time. Ten are primarily clinical and clinical research faculty, 8 are primarily research faculty, and 6 are both attending physicians and laboratory PIs. Two Cancer Center faculty are also attending physicians at BMC. The affiliated Clinical Trials and Cancer Support Service Office is overseen by an MD and an RN/NP and has 11 additional full time staff. There are 13 clinical fellows in training and more than 16 postdocs, graduate students, and technicians carrying out research in the Heme-Onc labs, with additional personnel in the affiliated Cancer Center laboratories.

## CLINICAL

The Hematology-Oncology Section and affiliated programs in Surgery, OB/GYN, Dermatology, and other medical subspecialties provide the majority of the cancer care to the underserved, underinsured, and minority population of Boston and the surrounding area. The Section's clinical activity has grown steadily over the last several years. In 2008, there were approximately 24,000 outpatient visits to the hematology-oncology clinic in the Solomont Center for Cancer and Blood Diseases on Moakley 3; Ken Zaner MD serves as Clinic Director and Kathy Gere RN is the Nurse Manager. There were more than 800 hematology-oncology inpatient admissions and more than 500 consults seen. In response to the growth of the inpatient service, in 2008 the service was divided into a Hematologic Malignancies/Stem Cell Transplant Service (the Heme Team) and a solid tumor Oncology Service. Additional services include a combined Hematology and Oncology Consult Service and a Sickle Cell Inpatient Service.

To deliver state-of-the-art cancer care to the unique patient population at Boston Medical Center, many effective strategies are employed. Each patient receives individualized attention from an oncology nurse with tremendous support from social services for transportation and assistance with available services. In 2008, the Medical-Legal Partnership was extended to provide *pro bono* legal services to adults seen in the Solomont Center and in the other cancer programs at BMC. To provide state-of-the-art cancer care and capture as many patients as possible for clinical trials, the physicians in the Hematology-Oncology Section participate in a general multidisciplinary tumor board and in focused tumor boards dedicated to breast cancer, lung cancer, head and neck cancer, GYN oncology, hepatobiliary cancer, amyloidosis, and stem cell transplantation. Patients with any of these diseases are seen in the Multispecialty Center on Moakley 3 and cared for by physicians from Medical Oncology, Surgical Oncology, Radiation Oncology, Thoracic Oncology, Skin Oncology, GYN Oncology, and other departments as appropriate.

The Autologous Stem Cell Transplant Program at Boston Medical Center is internationally recognized as a leader in the treatment of AL amyloidosis. In collaboration with the Amyloid Treatment and Research Program 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, under the direction of Vaishali Sanchorawala, MD, maintains accreditation through the Foundation for the Accreditation of Cellular Therapy (FACT) and Massachusetts state licensure. The BMC Autologous Stem Cell Transplant Program has been an approved transplant facility through the Southwest Oncology Group since 1996. Patients with multiple myeloma, lymphoma, and leukemia also can be treated with high dose chemotherapy and autologous stem cell transplantation.

The Sickle Cell Center directed by Martin Steinberg MD oversees both the sickle cell research and clinical programs. The clinical services include an inpatient program, outpatient clinics, and a Sickle Cell “Day Hospital” unique in New England, which provides extended outpatient care to patients with sickle cell anemia and painful crises. Only about 10% of patients seen in the Day Hospital end up being admitted to the hospital. In 2008, the Sickle Cell Program began a Transition Clinic for adolescents, staffed by Lillian McMahon MD from adult hematology and Philippa Sprinz MD from pediatric hematology.

## RESEARCH

The Hematology-Oncology Section research programs include an extensive portfolio of clinical trials in all areas of hematology and oncology as well as diverse laboratory programs and unique centers of excellence. Extramural grant funding totaled approximately \$6,260,000 in 2008 for the Section with an additional \$2,225,000 of funding in hematology and oncology going to the Cancer Center. Major sources of funding include NIH, the American Cancer Society, the Leukemia and Lymphoma Society, the Department of Defense, the American Heart Association, and private foundations including Avon, Komen, and others.

The clinical research programs are overseen by the Clinical Trials Office, directed by Kathy Finn RN NP; in 2008 Timothy Cooley MD was recruited to Boston Medical Center to serve as Physician Director of the CTO. Also in 2008, Robert David was appointed Support Services Coordinator. The clinical trials program includes cooperative group trials through the Southwest Oncology Group (SWOG), the National Surgical Adjuvant Bowel and Breast Research Program (NSABP), the American College of Surgery Oncology Group (ACOSOG), and the Radiation Therapy Oncology Group (RTOG). Additional trials are investigator-initiated. There are also trials sponsored by pharmaceutical and biotechnology companies. The Clinical Trials Office also oversees the Cancer Support and Outreach Services. This program has been expanded tremendously in the last 5 years, such that the Office now conducts 9 regular patient support groups, two annual cancer screening days, a Survivor’s celebration, and mind-body activities ranging from yoga to prayer shawl knitting.

Particular programs of research excellence include the Sickle Cell Center, the Hemoglobin Reference Laboratory, and the Amyloidosis Treatment and Research Program. The Sickle Cell program directed by Dr. Steinberg has extensive laboratory and translational research programs in sickle cell genetics and pathophysiology of sickle cell disease, with extensive collaborations across the institution and city. The Hemoglobin Reference Laboratory, directed by David Chui MD is a national and international reference laboratory for the diagnosis of unusual hemoglobinopathies. The Amyloid Treatment and Research Program, directed by Dr. Seldin is an international referral center for the laboratory and clinical research and multidisciplinary care of patients with systemic amyloidoses. The Amyloid Program works closely with the Autologous Stem Cell Transplant Program, a FACT-approved program directed by Vaishali Sanchorawala MD on transplant and non-transplant trials for amyloidosis and related hematologic diseases.

## EDUCATION

The Hematology-Oncology Section provides teaching and training in all aspects of hematology and oncology, at all levels of pre- and post-graduate education. Kevan Hartshorn MD oversees an integrated fellowship training program operated in coordination with faculty at the Boston VAMC, as well as a unique fellowship pathway offering combined training in Geriatric Oncology in collaboration with the Geriatrics Section (Chief, Rebecca Silliman MDPhD). In addition, fellows have the opportunity to carry out laboratory research in Hematology under the aegis of a T32 grant for which Adam Lerner MD is the Principal Investigator; he successfully renewed the training grant in 2008. About four fellows each year enter these programs. Graduates of these programs have obtained excellent academic and private practice positions.

Residents as well as students are trained in the inpatient setting on the Hematology-Oncology inpatient service on 7E. Gretchen Gignac MD, appointed as the new Firm Chief in 2008, has revamped the teaching programs and the organization of the service, which now consistently receives excellent reviews for the teaching component, in spite of being a very demanding rotation. Residents can also do an outpatient elective, rotating through various subspecialty clinics, or on the consult service.

Medical students learn Hematology as part of the Diagnosis and Therapy longitudinal course in BUSMII. Nancy Andrea MD organizes an excellent lecture and laboratory experience for that course.

## MAJOR ACCOMPLISHMENTS IN 2008

### New Faculty

Timothy Cooley, MD, as Physician-Director of the Clinical Trials Office, with specialization in HIV malignancies and in lung and esophageal cancer

Mark Sloan, MD, specialization in benign and malignant hematology

Amy Fallon, MD, specialization in breast and gastrointestinal cancer

Dorothy Medeiros, NP, specialization in hematologic diseases

Lisa Yanarella, NP, specialization in stem cell transplantation

### New Grant Awards (N) and Renewals (R)

Isabel Dominguez, PhD: AHA Scientist Development Grant (R)

Adam Lerner, MD: Hematology T32 (R)

Carol Rosenberg, MD: Coulter Foundation Award (N), Mary Kay Ash Charitable Foundation (N), Avon Research Foundation Grant (N)

David Seldin, MD, PhD: Breast Cancer P01 (R, G. Sonenshein PI); Clinical and Translational Sciences Award (N, D. Center PI)

Martin Steinberg, MD: Comprehensive Sickle Cell Center Grant (R)

Xuemei Zhong, PhD: American Heart Association Health Sciences Student Research Project award (N)

### Affiliated Cancer Center Faculty

Douglas Faller, PhD, MD: DoD [N]; R01 [R]; Sackler Foundation Grant [N]

Gerald Denis, PhD: Leukemia & Lymphoma Society Translational Research Grant (N)

Yan Dai, PhD: NCI R21 [N] (fundable score)

Sheng Wang, PhD: Department of Defense [N]

### Promotions, Awards, and Other Significant Accomplishments

David C. Seldin, MDPH, appointed Section Chief

Gretchen Gignac, MD, appointed inpatient Firm Chief

Carol Rosenberg, MD, appointed to Komen Foundation Breast Cancer Research Award Scientific Review Panel, appointed Chair to Graduate Program in Molecular Medicine Admissions Committee and as Invited Faculty, Molecular and Translational Oncology Workshop

**BOSTON UNIVERSITY MEDICAL CENTER  
DEPARTMENT OF MEDICINE  
ANNUAL REPORT  
SECTION OF VA Boston Healthcare System  
JULY 1, 2007 - JUNE 30, 2008  
FISCAL YEAR 2008**

The VA Boston Healthcare System (VA Boston) is the primary tertiary care referral center for 5 New England states, as well as a large primary care system in eastern Massachusetts. VA Boston is comprised of three main Campuses, Jamaica Plain (JP), West Roxbury (WX), and Brockton plus 6 outpatient clinics in the greater Boston area. The WX Campus is the site for the acute inpatient Medical, Surgical, Neurological and Rehabilitation services. Acute Psychiatry, a Spinal Cord program, an inpatient hospice program, a transitional care unit, nursing home unit, and specialized substance abuse programs reside at the Brockton Campus. Together VA Boston has a total bed capacity of 647. The JP Campus is primarily an outpatient and research facility with and home to the majority of specialized clinical services and major research initiatives.

The Medical Service at VA Boston is closely affiliated with the Departments of Medicine at Boston University School of Medicine (BUSM) and at Brigham and Women's Hospital of Harvard Medical School (HMS). Many faculty members at both schools have full- or part-time appointments at VA Boston, where they work collaboratively in practice, teaching, and conduct some or all of their research. VA Boston 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.

Paul Conlin, MD, is the newly appointed Chief of the Medical Service. Jay D. Orlander MD, MPH serves as Associate Chief of Medicine and Vice Chair for Veterans Affairs in the BU Department of Medicine.

VA Boston is a thriving, clinical primary and tertiary care, educational and research center.

## **CLINICAL ACTIVITIES**

In the past fiscal year over 62,000 individual patients received care in our system making over 660,000 total visits to our primary and specialty clinics across all disciplines up over 6% from the preceding year. The inpatient service remains busy with more than 5700 admissions to medicine, but continues to evolve to meet the needs of our patients and trainees.

New initiatives on the clinical service are numerous and the theme of adding physician extenders has been evident in several areas. On the inpatient GIM service Anand Kartha MD, ScD, led a pilot project adding a Physician Assistant to two of the inpatient teams GIM medical team. These new staff rapidly developed a detailed knowledge of the VA systems of care and has been deemed by the housestaff and attending as facilitating and providing discharge planning, patient education and enhanced direct care. Formal evaluation of their impact on patient care efficiency, patient satisfaction and the housestaff educational experience was impressive. Recruitment of a full complement of physician extenders, one for each inpatient GIM team has been approved by the administration and recruitment is nearly complete.

Renal consultations continue to increase and addition of a fulltime PA to the ambulatory and chronic dialysis program has enhanced quality of care for patients and added capacity to the clinical service.

Pulmonary has just recruited a PA to help with its ambulatory program. In addition they have continued to expand the Sleep Medicine program under the leadership of Daniel Gottlieb MD. The Allergy and Immunology program at VA Boston now is part of the Pulmonary section and is expanding ambulatory clinics in this area. On the technology side, they have added bronchoscopic ultrasound technology to facilitate better detection and assessment of pulmonary malignancies.

Cardiology at VABHS provides tertiary care for VA facilities throughout New England. The division welcomed a new chief this year, Deepak Bhatt, MD. The program in vascular medicine started just last year has been enhanced by approval to begin cerebrovascular interventions. Funds have been approved to build a second cardiac catheterization/interventional lab to be shared with the growing electrophysiology program.

Cardiology and Pulmonary will be collaborating on a newly approved cardio-pulmonary rehabilitation program. Staff are currently being recruited for this new program.

## **RESEARCH ACTIVITIES**

VA Boston's research program continues to succeed even in this era of fiscally stringent research resources nationally.

With funding exceeding \$9 million this fiscal year, a total staff of nearly 100, and over 100 papers published or in press this past year, MAVERIC (Massachusetts Veterans Epidemiology Research and Information Center) continues to be the major center of research excellence at VA Boston and in Medicine in particular. MAVERIC is actually 3 major research related programs. It is one of only 3 Epidemiology Research Centers of Excellence in the VA nationally with special expertise in cardiovascular and pharmaco-epidemiology and a newly launched and funded genomics initiative with newly funded bio-informatics program that has been officially launched. MAVERIC is also one of 5 national Cooperative Studies Program Coordinating Centers (CSP CC) involved in planning and running a variety of clinical trials. While VA Boston is the youngest of the CSP centers joining the program in 2002, it has coordinated more than 22 large-scale trials and epidemiology studies in a wide range of chronic disease areas. Currently MAVERIC has collaborative projects with 29 other institutions including other VA's, the Department of Defense and other universities and academic institutions.

MAVERIC leadership is nearly synonymous with national VA research leadership in several key areas. Lou Fiore, MD, MPH, is Director of Informatics of Maveric and Chief of Informatics for the National VA Cooperative Studies Program Michael Gaziano MD, Directs the Epidemiologic activities of Maveric and for all of VA Cooperative Studies. Mary Brophy, MD, in the Section of Hematology oversees the 3<sup>rd</sup> component of MAVERIC, a national serum and tissue repository to support VA investigation across the country. At the behest of VA Research national office Mary and Maveric have been granted \$5 million dollars to further enhance the biorepository for high throughput processing. Half the funds will be used for a new building on the JP campus and half to equip the lab with robotic processing equipment for state of the art genomic research.

Major continuing programs include the VA Normative Aging Study. Pantel Vokonas, MD, Professor of Medicine and Public Health at BUSM, is the director, and David Sparrow ScD, (appointed in Pulmonary) is associate director. This prospective epidemiologic study recruited >2000 veterans in 1963 and continues today. This group collaborates with investigators across disciplines within VA and across several Boston area teaching hospitals. They have published over 400 manuscripts.

Clinical and laboratory science also are vibrant components to the Medical Services research portfolio across the multiple sections of the medical service. While not comprehensive the following is a list of highlights.

The GI section has a major research emphasis directed towards the development and clinical evaluation of novel imaging techniques. Satish Singh MD, a funded CIMIT investigator works in the area of Spectroscopic fiberoptic instruments and optical coherence tomography. These technologies are being evaluated for their ability to detect dysplastic, metaplastic and inflammatory abnormalities of gastrointestinal epithelia. Complementary imaging research in the section is done by Hiroshi Mashimo, MD who like his colleague Raj Goyal MD, investigates motility of the GI tract. Several clinical trials of Hepatitis C treatment are led by Marcos Pedrosa.

In GIM Antonio Lazzari, MD leads 3 current studies in the assessment, risks and treatment of osteoporosis in men. Anand Kartha, MD, ScD, is evaluating the impact of Hospitalists in the VA system nationally.

Deepak Bhatt Chief of Cardiology, has research interests which include the study of oral and intravenous antithrombotic medications, optimal management of patients with acute coronary syndromes, including myocardial infarction, and advanced techniques for cardiac, cerebral, and peripheral vascular intervention. Other research activities in the section include basic research into mechanisms of cardiac fibrosis and failure, and clinical trials on newer approaches to managing heart failure the latter under the guidance of Jacob Joseph, director of the Heart Failure program.

Kalpana Gupta, Chief of Infectious Disease, studies prevention of urinary tract infections in ambulatory woman and prevalence and molecular epidemiology of MRSA infections in the veteran population.

Daniel Jacobson, Chief of Oncology, studies genetic aspects of amyloidosis and the cell biology of lymphoma. Clinical trials in lung and colon cancer (Valia Boosalis MD) prostate cancer (Carlos Vera MD) and Multiple Myeloma (Nikil Munshi MD). Gary Gilbert MD investigates mechanisms through which blood coagulation proteins interact with membrane phospholipids.

In Pulmonary, Daniel Gottlieb, MD, MPH, Director of the Sleep Disorders Program studies effect of sleep disorders on cardiovascular disease. Eric Garshick, MD, studies the impact of spinal cord injury and environmental toxins on lung function. Marilyn Moy MD, is investigating the impact of exercise on COPD.

Rheumatology (Samar Gupta, MD) is involved in a multi site clinical trial of novel treatments of Rheumatoid Arthritis.

Endocrine research under Paul Conlin MD has 3 current clinical trials related to management of diabetes. One line of research is looking at cost effectiveness of web-based management protocols for patients with poorly controlled diabetes, another is investigating the impact of intensive diabetic management perioperatively in vascular surgery, and a third evaluates telemedicine roles in diabetic eye examinations.

The Renal Section has funded research projects from the VA, National Institute of Diabetes & Digestive & Kidney Diseases, and industry. Current studies include dialysis vascular access and a study of a new agent for the treatment of diabetic nephropathy. James Kaufman, MD is the principle investigator on a new Cooperative Studies Program (CSP) study on the effects of the addition of an ARB to an ACE-I in diabetic nephropathy. David Mount, MD, pursues basic of chloride transport, a mechanism that appears to be relevant in both kidney and brain tissue and studies uric acid transport characteristics.

## **EDUCATION**

Together, Boston Medical Center, Brigham and Women's Hospital, and Beth Israel Deaconess Medical Center rotate more than 200 interns and residents and 80 third year medical students through the VA Boston Medical Service each year. Clinical and research fellows in GIM and all medical subspecialties received training at VA Boston. BUSM trainees constitute greater than 50% of the trainees on the medical service. Under the direction of the BUSM and HMS resident and student program directors at the VA, these individuals work together to present a cohesive educational program and support to all trainees regardless of affiliation.

VA Boston is also a site for BUSM and HMS Second-year students, as well as a special MIT Biomedical engineering students to receive training in physical diagnosis at the VA.

The VA provides a couple of unique ambulatory training rotations including the Ambulatory Diagnostic Treatment Center (ADTC) and the Pulmonary Acute Care Clinic (PACC), which provide patients with active medical issues ease of access while providing trainees with a concentrated learning experience, placing them in intensive ambulatory treatment and teaching environments.

Our novel Patient Safety led by Dr. Anand Kartha (Hospitalist) along with David Thornton (Assistant Program Director), was introduced into the medicine residency program last year was expanded and cited as a best practice by several external review organizations including JACHO.

### **Major Accomplishments**

MAVERIC's \$5 million mandate to expand capacity for high throughput sample processing to support genomic research and funding of core bioinformatics staff.

VA joined CIMIT (Center for Integration of Medicine and Innovative Technology) a consortium of Boston area research institutions. Satish Singh, MD is a funded CIMIT investigator researching the development of a novel, optically-guided biopsy device for lower gastrointestinal endoscopy.

New position/recruit, Chief of Palliative Care, L. Michal Skarf, MD. Michal completed fellowship training in Palliative care in the Harvard Dana Farber program. Within 6 months of joining the staff, she obtained a 3 year, \$3 million grant from VA to expand palliative care services at VA Boston.

James Kaufman, MD in the Renal Section was appointed as Co-Editor of American Journal of Kidney Disease.

Michael Gaziano, MD, Director of MAVERIC, was appointed as an Associate Editor of JAMA.

Ambulatory and Patient Safety Rotation for BU Residents at the VA was expanded and won best practice commendations from several organizations.

New Chief of Medicine, Paul Conlin MD. Paul is the immediate past Chief of Endocrine here at VA Boston. He is an accomplished Health Services researcher with a focus on improving diabetes care.

New Section chief in Cardiology, Deepak Bhatt MD. Deepak was recruited from the Cleveland Clinic. He is an interventional cardiologist with added qualification in peripheral and cerebrovascular procedures. An accomplished researcher management of acute vascular thrombosis.

New Chief of Women's Health, Megan Gerber, MD, MPH. Megan was recruited from Harvard Vanguard Medical Associates and the Division of Ambulatory Care and Prevention. Megan's research interests are in the impact of domestic violence and intimate partner violence on women's health.

BOSTON UNIVERSITY MEDICAL CENTER  
**DEPARTMENT OF MEDICINE**  
**ANNUAL REPORT**  
SECTION OF **Vasculitis Center**  
**JULY 1, 2007 - JUNE 30, 2008**  
**FISCAL YEAR 2008**

## **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; Paul Monach, MD, PhD, 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, the Mayo Clinic Foundation, and the University of Toronto; these five centers are the leading vasculitis clinical research centers in North America. Several secondary centers in the United States, Canada, and Europe are also participating in VCRC activities. The VCRC has Longitudinal cohort studies enrolling in 6 type of vasculitis at the 5 Primary VCRC Centers. The VCRC is also conducting therapeutic clinical trials in Wegener's granulomatosis, giant cell arteritis, and Takayasu's arteritis; each of these trials is supported by additional NIH funding. 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 U01 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 grant. 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 trails are: The Wegener's Granulomatosis Etanercept Trial (WGET), the first randomized, double-blind, 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 papers

describing ancillary projects utilizing data and specimens from the WGET have been published, with several more in preparation; Vasculitis Center faculty and trainees have been the lead/senior authors 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 leading in the developmental of new clinical trials of novel therapeutics for Churg-Strauss Syndrome, several life-threatening ANCA-positive vasculitis, and Behçet's disease.

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, including directing the Vasculitis Working Group of the OMERACT program (Outcome Measures in Rheumatology Clinical Trials).

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, Nephrology, 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 the clinical volume, both established patient and new referrals, continues to grow at a steady pace. The Center receives national and international referrals. Several faculty members have clinics primarily dedicated to the evaluation and treatment of patients with vasculitis. Although based in the Section of Rheumatology, the Vasculitis

Center has a dedicated team of specialists within the Department of Medicine; 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.

## **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. Several Rheumatology fellows have chosen to conduct their mentored research projects with Vasculitis Center faculty and the faculty are active participants in the Rheumatology T32 training grant, the K30 program, and the BU Vascular Medicine training program.

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 were the lead group that organized and implemented a novel educational initiative: "Clinical Research for Rare Diseases". This one-day meeting held in Bethesda in September 2007 focused on research methodology in rare diseases. The hundreds of attendees ranged from trainees (fellows) and junior faculty to senior NIH scientists. Boston University received a grant from the NIH (NCRR) to support this program as well as funds from a variety of patient support groups. The conference was extremely successful and will, at the urging scheduled to be repeated in 2009.

## **FACULTY**

G. Alessandra Farina, MD, PhD	Visting Scholar
Eugene Y. Kissin, M.D.	Associate Professor
Michael LaValley, Ph.D.	Associate Professor
Alfred P. Mahr, MD, MPH	Research Associate
Peter A. Merkel, M.D., M.P.H.	Associate Professor
Paul A. Monach, MD, PhD.	Assistant Professor
Tuhina Neogi, M.D.	Assistant Professor
Robert W. Simms, M.D.	Professor

## **GRANTS**

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

Agency: NIH/NCRR 5 U54 RR19497

Project Title: Vasculitis Clinical Research Consortium (VCRC)

Total Direct Cost: \$4,704,256

Direct Cost Current Year: \$951,499

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

Agency: NIH NIAMS/ R01 AR051874

Project Title: Vasculitis Outcome Measures: Development and Validation

Total Direct Cost: \$99,579

Direct Cost Current Year: \$32,403

Agency: NIH NIAMS/ 2P60 2P60 AR047785

Project Title: The Interlay of Thrombosis and Vasculitis

Total Direct Costs: \$126,515

Direct Costs Current Year: \$621,527

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

Agency: NIH-NIAMS

Project Title: Concurrent Pilot Studies in Giant cell arteritis and Takayasu's Arteritis to Examine the Safety, Efficacy, and Immunologic Effects of Abatacept (CTLA4-Ig) in Large Vessel Vasculitis.

Total Direct Costs: \$3,800,000

### **Paul A. Monach, MD, PhD**

Agency: Arthritis Foundation

Project Title: Arthritis Investigator Award

Total Direct Costs: \$320,000

Direct Costs Current Year: \$70,000

BOSTON UNIVERSITY MEDICAL CENTER  
**DEPARTMENT OF MEDICINE**  
**ANNUAL REPORT**  
SECTION OF **Hypertension and Atherosclerosis**  
**JULY 1, 2007 - JUNE 30, 2008**  
**FISCAL YEAR 2008**

**1. A brief history**

The Section of Hypertension and Atherosclerosis at the Boston University School of Medicine has a long and distinguished history.

It all started in the late 1940's under the leadership of Dr. Robert Wilkins, then Chief of Medicine at the University Hospital, who had a particular interest in the field. After President Roosevelt died from malignant hypertension for lack of treatment to lower his blood pressure, there was a burst of interest in therapeutic approaches to control this condition. The proposed approaches ranged from injections of poisons and pyrogens that produced circulatory collapse, to sympathectomy by severance of sympathetic tracts—the Smithwick procedure introduced by the Boston University School of Medicine surgeon—which did save lives at the price of inducing debilitating orthostatic hypotension. Dr. Wilkins is credited with introducing the first orally effective antihypertensive agents: the rauwolfia derivatives (such as reserpine) and thiazide diuretics. His collaborators in these studies were Dr. Edward Freis who later gained recognition for his VA studies that first proved the long-term benefits of blood pressure control and who also introduced the concept of afterload reduction by sympathetic blockade for treatment of congestive heart failure, although this did not become accepted at the time; Dr. William Hollander, who subsequently became the first Chief of the newly established Section of Hypertension and Atherosclerosis, and who is recognized for his contributions to the role of lipids in atherosclerosis and cardiovascular disease; and Dr. Aram Chobanian, then a research fellow under Dr. Wilkins, who later succeeded Dr. Hollander as Chief of the section and served on NIH committees and Advisory Boards that produced the guidelines for treatment of hypertension and who later went on to a distinguished career as Dean of the BUSM and President of BU.

After the Boston City Hospital became solely affiliated with the BUSM, Dr. Chobanian decided to establish there a separate section for hypertension and atherosclerosis, and in 1975 he hired as its chief Dr. Haralambos Gavras, a young associate professor from Cornell University, who had made a name for himself with his experimental studies on the effects of inhibition of the renin-angiotensin system. In collaboration, they established one of the five newly NIH-funded national Specialized Centers of Research (SCOR's) in Hypertension, which actually remained the only one continuously funded for the next 30 years by successfully renewing its grants every five years, until the program was officially terminated by the NIH. In 1989 Dr. Chobanian became the Dean of the BUSM and Dr. Gavras succeeded him as Chief of Hypertension in both the University Hospital and the Boston City Hospital; and in 1996 the two hospitals merged to the current Boston Medical Center, and Dr. Gavras became the chief of the unified section.

**2. The Present**

The mission of the Section is to provide specialized patient care, to train young physicians and basic scientists, as well as conduct clinical and experimental studies and basic research in hypertension.

**Clinical Activities:** The Section conducts three outpatient clinic sessions per week. The majority of our patients are “tertiary referrals,” i.e., difficult diagnostic or treatment cases referred by other clinics or by

their primary care physicians. Once the patient's problems have been resolved, i.e., the causes of "resistant" hypertension have been clarified, whether due to underlying pathology causing secondary hypertension or due to suboptimal treatment (e.g., inadequate dosing, inappropriate drug combinations, conflicting therapies for multiple comorbidities, etc), and the blood pressure is under control, the patient may return to the care of the referring physician and/or be followed routinely at our clinic on a bi-annual basis for updates or adjustments. We also offer inpatient consultations for difficult cases at the admitting physicians' request. Patients referred only for ambulatory blood pressure monitoring (ABPM) are usually seen only twice in clinic, one day by the nurse who places the monitor and the next day by the physician who interviews the patient in order to provide interpretation of the ABPM tracing.

**Education:** Educational activities consist of monthly electives taken by 4<sup>th</sup> year medical students, bedside teaching of housestaff during inpatient consults, lectures ranging from informal group meetings as requested by departments or sections of the BMC or other hospitals to formal Grand Rounds given by the Section's senior faculty in hospitals around town and nationally, as well as lecture tours internationally. But the most intense and successful educational activity is the training of Research Fellows in clinical and experimental research activities. Most fellows are young physicians from the US or abroad, who have completed their residency and wish to pursue an academic career in cardiovascular research, whereas a few are PhD post-docs and, less frequently, graduate students pursuing their PhD.

Typically, they are assigned their own research project and work under the tutorship and supervision of an experienced faculty member. They are taught the application of a variety of procedures, including animal handling and surgery to produce specific experimental models in rats and mice (e.g., coronary artery ligation, renal artery clipping, subtotal nephrectomy, positioning of telemetry probes, osmotic minipumps, etc) hemodynamic measurements (e.g., indirect or direct BP recordings, echocardiography, metabolic studies, etc), as well as cellular and molecular biology techniques to investigate the properties (kinetics, signaling mechanisms, gene expression, etc) of cardiovascular factors. Many young physicians have subsequently used their assigned project as the basis of their PhD thesis and the first step for an academic career. Indeed, most of our past trainees have gone on to become leaders in the field, with distinguished academic careers.

**Research:** Hypertension research is the activity that has earned the Section and its leader, Dr. H. Gavras, national and international reputation. Earlier studies were mostly devoted to pathophysiologic studies in experimental animals and clinical inpatient or outpatient trials exploring various aspects of the inhibition of the renin-angiotensin system in hypertension and heart failure. Treatment of these conditions with the earliest experimental angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, when first introduced in the 1970's was regarded with skepticism, but by the 1980's became widely accepted and is now standard practice. Blockade of other vasopressor factors, such as components of the sympathetic nervous system and of vasopressin, are also approaches that have been explored successfully in experimental studies, even though they have not yet gained wide acceptance in daily practice. Nevertheless, an approach for the treatment of congestive heart failure that we championed in the 1980's but eventually abandoned for lack of support—namely, the use of vasopressin antagonists—has recently come around again after the development of a novel class of V<sub>2</sub> receptor antagonist, the "vaptans," by the pharmaceutical industry.

In 1995 our Section became one of the six NIH funded SCOR's in the Molecular Genetics of Hypertension and in collaboration with the Boston University School of Medicine Center of Human Genetics, the Department of Neurogenetics and the Framingham Heart Study, as well as the Jackson Laboratories in Bar Harbor, Maine, discovered a number of genetic variants associated with abnormal blood pressure regulation.

In recent years the Section's research has become more heavily oriented towards basic science, including gene expression studies in specific hypertensive disorders, as well as cellular and molecular research

of factors involved in cardiovascular complications. Ongoing projects include elucidation of the molecular mechanisms mediating a number of non-enzymatic activities of the angiotensin converting enzyme, such as its effects on gene expression of vasoactive factors, and investigation of the role of a novel gene discovered by us, the *Cmya 3* or myomaxin, induced by angiotensin II and involved in myocardial structure and function.

The Section's senior faculty is actively involved in national and international scientific societies and organizations: Dr. H. Gavras has served as Chairman of the Council of High Blood Pressure Research of the American Heart Association, President of the American Society of Hypertension and of the InterAmerican Society of Hypertension, regular or ad hoc member of NIH Study Sections and NIH Advisory Committees and is currently a member of the European Research Council. He has received numerous awards by these societies, as well as honorary doctorates by medical schools. Dr. Irene Gavras has also served on Executive Councils and various professional education and publication committees of these societies, as regular 4-year member and as ad hoc member of NIH Study Sections and is currently a member of the ASH Specialists Examination Committee. Both are on the editorial boards of most major journals in the field of hypertension.

Over the years, several Research Associates from the section have won Young Investigator Awards for their presentations in scientific meetings of the AHA or the ASH.

### **Major Accomplishments**

The most widely recognized accomplishment of the Section's faculty is the research on the effects of the renin-angiotensin system and its inhibition. These original studies were first carried out in experimental animals and in small clinical studies and provided the "proof of concept," which led to the introduction of angiotensin converting-enzyme inhibitors and angiotensin-receptor blockers for the treatment of hypertension and congestive or chronic heart failure. These original studies were subsequently reproduced by other investigators in the field and their results were confirmed by numerous large clinical trials that have now established this approach as standard therapy for these cardiovascular conditions. In this respect, the Section's faculty has continued the tradition of its earlier leaders by being the first to introduce a novel approach to the treatment of hypertension and heart failure: with the introduction of rauwolfia derivatives and thiazides in the 1950s and the first inhibition of the renin-angiotensin system with angiotensin converting enzyme inhibitors and angiotensin II receptor blockers in the 1970s, this Section has pioneered four new classes of antihypertensive agents.

The other major accomplishment of our Section is the training and nurturing of young scientists, our past Research Fellows who became expert clinicians and renowned educators and research scientists in their own right. We are proud of the fact that many current leaders in the field of hypertension, nationally and internationally, are our alumni: Examples are Dr. Donald DiPette, President of the University of North Carolina, Dr. Artur Ribeiro, current President of the Brazilian Society of Hypertension, Dr. Michael Bursztyn, current President of the Israeli Society of Hypertension, Dr. Bernard Lammek, Dean of the Medical School of Gdansk (Poland), Dr. Athanasios Manolis, current President of the Greek Society of Cardiovascular Diseases and Secretary of the European Society of Hypertension.

Many others are currently on the faculty of medical schools in the US as well as in Europe and Latin America.



Chief of Section

### **Feature of Faculty**

Dr. Haralambos Gavras obtained his medical degree from Athens University School of Medicine in Athens, Greece, and his postgraduate training at the Hippocraton Hospital in Athens and the Western Infirmary, Glasgow, Scotland, UK, as a British Council Scholar. He has received numerous awards for his research in the renin-angiotensin system.

Dr. Irene Gavras received her medical degree from Athens University School of Medicine in Athens, Greece, and her postgraduate training at Hippocraton Hospital in Athens and the Royal Infirmary, Glasgow, Scotland.

Dr. Hector Lucero received his PhD degree in Biochemistry from the University of Buenos Aires, Argentina and his postgraduate training in the Section of Biochemistry, Molecular and Cell Biology at Cornell University, Ithaca, New York.

Dr. Ekaterina Kintsurashvili received her PhD degree from the Institute of Molecular Biology, Moscow, Russia and her postgraduate training at the University of Toronto, Toronto, Ontario, Canada and the Laval University Cancer Research Center in Quebec, Canada.

### **Selected recent Publications**

Kintsurashvili E, Shenouda S, Ona D, Ona L, Ahmad S, Ravid K, Gavras I, Gavras H: Hypertension in transgenic mice with brain-selective overexpression of the  $\alpha_{2B}$ -adrenoceptor. *Am J Hypertens* 22 : 41-45, 2009.

Duka A, Kintsurashvili E, Duka I, Ona D, Hopkins TA, Bader M, Gavras I, Gavras H: Angiotensin-converting enzyme inhibition after experimental myocardial infarct: role of the kinin B1 and B2 receptors. *Hypertension* 51:1352-1357, 2008.

Silva VS, Martin LC, Franco RJ, Carvalho FC, Bregagnol EA, Castro JH, Gavras I, Gavras H: Pleiotropic Effects of Statins May Improve Outcomes in Atherosclerotic Renovascular Disease. *Am J Hypertens* 21:1163-1168, 2008.

Sun B, Kintsurashvili E, Ona D, Ignjacev-Lazich I, Gavras I, Gavras H: Inhibition of the  $\alpha(1D)$ -adrenergic receptor gene by RNA interference (RNAi) in rat vascular smooth muscle cells and its effects on other adrenergic receptors. *Vascul Pharmacol* 46:367-372, 2007.

Duka A, Schwartz F, Duka I, Johns C, Melista E, Gavras I, Gavras H. A novel Gene (Cmya3) induced in the heart by angiotensin II dependent but not salt dependent hypertension in mice. *Am J Hypertens* 19: 275-281, 2006.

Shenouda SM, Johns C, Gavras I, Gavras H: Long-Term Inhibition of the Central alpha(2B)-Adrenergic Receptor Gene Via Recombinant AAV-Delivered Antisense in Hypertensive Rats. *Am J Hypertens* 19:1135-1143, 2006.

Cardoso de Carvalho F, Bregagnollo E, Santos Silva V, Brunie A, da Silva Franco RJ, Martin LC, Gavras I, Gavras H: Frequency of coronary artery disease in patients with renal artery stenosis without clinical manifestations of coronary insufficiency. *Am J Hypertens* 19:1125-1128, 2006.

BOSTON UNIVERSITY MEDICAL CENTER  
**DEPARTMENT OF MEDICINE**  
**ANNUAL REPORT**  
SECTION OF **INFECTIOUS DISEASE**  
**JULY 1, 2007 - JUNE 30, 2008**  
**FISCAL YEAR 2008**

SECTION CHIEF NAME: Paul R Skolnik, M.D.

**RESEARCH ACTIVITY**

Faculty in the Section of Infectious Diseases continued research programs to study bacteria, chlamydia, and viruses, focusing especially 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.

Studies of bacterial pathogenesis were carried out by Drs. Frank Gibson, Lee Wetzler, and Paola Massari through NIH-funded research projects. Drs. Gibson, in conjunction with others at Boston University, studies the mechanisms by which invasive bacteria accelerate atherosclerosis through innate immune recognition receptors (Toll-like receptors, TLRs). These studies utilize two principal model systems: the ApoE-knockout mouse model and primary cultures of human aortic endothelial cells (HAEC). Dr. Gibson, through independent NIH funding, has focused on understanding the immuno-stimulatory effects of *Porphyromonas gingivalis* capsular polysaccharide (CPS) using a murine macrophage-based system. Dr. Gibson published several articles describing his work this year.

Drs. Wetzler and Massari continue to work on the use of the Neisserial major outer membrane proteins, termed porins, as vaccine candidates and immune stimulants. The B subunit of cholera toxin is also being investigated as an immune adjuvant. Dr. Wetzler is principal investigator for a project to devise vaccines against tularemia. Dr. Guillermo Madico, in addition to work on Neisseria, continues to run a core for the *Francisella tularensis* program project, including work on a PCR method for detection and quantification of sub-species of *F. tularensis* and expression of pilin genes as candidate antigens for protective vaccines.

Dr. Madico and Dr. Robin Ingalls continued work on aspects of pathogenesis concerning *Neisseria meningitidis* and *N. gonorrhoeae*. Dr. Ingalls' research, in collaboration with other faculty from the Section of Infectious Diseases, the broader 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's work is supported by two NIH R01 grants.

Dr. Lisa Ganley-Leal has added a new dimension to the research efforts in the Section of Infectious Diseases. Her area of interest is parasitology, especially the study of *Shistosoma mansoni*. Her interests are synergistic with others in the section and elsewhere at Boston University—she pursues immunologic investigations of host-pathogen interactions concerning the function of B cells during parasitic infection, and during other chronic inflammatory diseases.

Dr. Klempner continued to direct the construction, and planned opening, of the National Emerging Infectious Diseases Laboratory (NEIDL), and is recruiting faculty and staff to work in the various core and operations facilities of the NEIDL.

Drs. Carol Sulis, Tamar Barlam, and Philip Carling pursue research related to infection control. Dr. Sulis studied mechanisms to reduce the incidence of errors in the use of antimicrobial prophylaxis as part of a national group. She is active in the Surveillance Task Force, a citywide consortium of hospital epidemiologists studying bioterrorism preparedness and the efficacy of syndromic surveillance. Dr. Carling uses a unique dye method, visible only by UV light, to detect areas that have been inadequately cleaned in a variety of medical and non-medical settings (e.g., cruise ships, patient care floors, and chemotherapy infusion facilities).

## CLINICAL ACTIVITY

The section provides substantial primary and consultative care in the outpatient and inpatient settings. The outpatient Center for Infectious Diseases (CID) continues to expand its services. The CID comprises the clinical activities of the Center for HIV/AIDS Care and Research (including the STD program), and the international health program which includes both refugee care and travel medicine. Dr. David Hamer continued to significantly expand the travel medicine program. 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, is supported by an organized, multidisciplinary approach, and one which also attends to the social needs of patients.

ID Section faculty provided inpatient care on the general medical service and infectious diseases consultation service at BMC and the VA Boston Health Service (VABHS). Faculty who provide these clinical services at BMC include Drs. Tamar Barlam, Anita Barry, Ioana Bica, Carling, Deborah Cotton, Hamer, Robert Horsburgh, Sulis, Margaret Sullivan, and Catherine Yu, as well as Drs. Ingalls, Klempner, Skolnik, Thomas Treadwell, and Wetzler. Drs. Kalpana Gupta, David Thornton, and Richard Serrao provide these services at the VABHS, and support the clinical infectious diseases program. Drs. Tandon and Yu provide infectious diseases consultative services at Radius Healthcare, and Dr. Skolnik provides HIV consultative services at Whittier Street Health Center.

Dr. Barlam provides antibiotic oversight at BMC. She chairs the Antibiotic Subcommittee of the Pharmacy and Therapeutics (P&T) Committee, sits on the P&T committees at BMC, runs an antibiotic stewardship program, and works with the Microbiology Laboratory to insure that diagnostic procedures support the appropriate use of antibiotics.

Dr. Sulis runs the infection control program for BMC, BMC affiliates, and Radius Healthcare. She also sits on many hospital and other agency committees representing the ID section and the hospital. This included participation on a Pandemic Influenza Task Force convened by Dr. Robert Brown to bolster programs throughout Boston University. Dr. Barlam has joined Dr. Sulis in the hospital infection control program.

Dr. Alan Sugar provides clinical care in the HIV/AIDS clinic at Cape Cod Hospital, and runs the Hepatitis C and Hepatitis B programs there, focusing on diagnosis and treatment.

## EDUCATION

The Section of Infectious Diseases provides education in multiple venues, and for many levels of students. Mentoring occurs in all components of the outpatient Center for Infectious Diseases, on the inpatient services, in the basic and clinical research venues, and during lectures, small classes and seminars for pre- and post-doctoral students, and medical and dental students. Teaching was provided on the inpatient services by Drs. Barlam, Barry, Bica, Carling, Cotton, Hamer, Horsburgh, Ingalls, Klempner, Skolnik, Sulis, Sullivan,

Treadwell, Wetzler, and Yu, and on the outpatient service by Drs. Bica, Hamer, Skolnik, Sullivan, and Yu. Our ongoing ID conference series provides educational opportunities for fellows, junior and senior faculty, and outside visitors at all levels of training. Dr. Barlam has created an interactive teaching series for the medical house staff that focuses on clinical pharmacologic issues. These teaching responsibilities, comprising over 1,000 contact hours of teaching for hundreds of students, are shared by all members of the section.

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

The section helped train pre-doctoral students. Drs. Wetzler taught courses in the microbiology department and the dental school. Teaching and mentoring were also provided by Drs. Gibson and Ingalls for Master degree candidates in the Graduate School of Medical Sciences and post-doctoral students.

The ID Section faculty at the VABHS are heavily involved in teaching. Dr. Kalpana Gupta mentored an infectious diseases fellow in a project to investigate the prevalence of methicillin-resistant *Staphylococcus aureus* using a PCR-based technology. Dr. David Thornton is Associate Program Director for the BU Internal Medicine Residency Program in charge of VA rotations. He also teaches and precepts BU medical students rotating through the VA for their third-year clerkships, and precepts BU ID fellows rotating through the VA on the ID 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 at the VABHS.

Dr. Sugar continues to precept medical students and 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 federal grant support during this time of limited funding. Dr. Ganley-Leal received a NIAID R21 award to study CD23+ B cells in schistosomiasis, a Broad Medical Foundation award to explore the role of B cells in chronic inflammatory diseases, a Becton-Dickinson award, and a Boston University Ignition Award to develop a non-invasive assay to predict inflammatory bowel disease severity.

Dr. Davidson Hamer continued his successful international work, serving on the Steering Committee for the Young Infants Clinical Signs Study (co-funded by the World Health Organization, Saving Newborn Lives, and the Applied Research on Child Health Project). Results of this study were used by the WHO to modify the Integrated Management of Childhood Illness algorithm. Dr. Hamer, with Dr. Elizabeth Barnett of the Department of Pediatrics, was awarded a CDC grant for the Boston Area Travel Medicine Network—this research project now has 6 active protocols and nearly 5,000 patients enrolled. Dr. Hamer was elected to Fellowship in the Infectious Diseases Society of America.

Dr. Philip Carling continued to investigate environmental hygiene and healthcare-associated infections using a fluorescent marker, visible only with UV light, to detect surfaces that are not adequately cleaned. This has generated national and international interest. Dr. Carling, collaborating with an epidemiologist at the University of Iowa, uses the procedure in 18 acute care hospitals in that state and will test the method in other settings.

Dr. Tamar Barlam expanded the clinical and research activities of the antimicrobial stewardship program. She developed, in collaboration with others, a database with unit-based information to better target interventions and teaching. She extended this program to offer fellow research opportunities and successfully mentored a fellow in this area.

Dr. Robin Ingalls presented data concerning site-specific innate immune responses to Chlamydia at international and national meetings. A post-doctoral fellow in her laboratory was awarded second place in the Evans Day basic research poster competition. Dr. Lee Wetzler revised a chapter on *Neisseria meningitides* in Harrison's Textbook of Medicine.

We welcomed Dr. Kalpana Gupta as the new Chief of Infectious Diseases at the Veterans Administration Boston Health Care System (VABHS). She added to the clinical care, education, and research endeavors at the VABHS. Dr. Richard Serrao was a visiting faculty member in Kampala, Uganda, for the Infectious Diseases Society of America/HIV Medical Association AIDS Treatment program.

The reconfiguration of the Infectious Diseases Fellowship Program, under the direction of Drs. Skolnik and Sullivan, has enhanced teaching within the Section and helped recruit strong ID fellows. The program hosted a site visit in June 2008 and received full accreditation with no citations from the Accreditation Council for Graduate Medical Education (ACGME). Many faculty and staff came together to make this effort successful.

The volume of patients seen in the CID continued to grow as new initiatives in travel medicine, administrative reorganization, and other improvements enhanced its reputation, quality, and breadth of services.

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

### RESEARCH ACTIVITY

Dr. Andrew Henderson continued his basic research on transcriptional regulation of HIV replication and implications for HIV latency. His research is supported by an NIH R01 award. Dr. Montano studies molecular and genetic aspects of HIV pathogenesis. He received an R01 award to study muscle stem cell biology. This work has implications for the lipodystrophy that complicates HIV infection in many patients. Dr. Montano also studies the differences between muscle changes in patients with HIV infection and those that occur during aging.

Dr. Skolnik and Dr. Marlynne Quigg-Nicol 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 HIV+ persons. The laboratory is also interested in changes in innate immunity (Toll-Like Receptors, TLRs) during HIV infection, and the effects of these changes on functional aspects of the immune response. Mathematical modeling of these networks, in conjunction with Dr. James Collins of the BU College of Engineering, is undertaken 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. These efforts were supported by an NIH R01 award.

Clinical research activities are supported by federal, state, and industry funding, and include epidemiologic, prevention, and experimental therapeutic trials. Funding from the NIH, CDC, HRSA, SAMHSA, and the Massachusetts Department of Public Health (MDPH) supports investigations into linkage to care, retention in

care, and health disparities, as well as service-related activities such as counseling and testing, enhanced medical management, prevention and education, and home health care.

Dr. Horsburgh increased his efforts in helping to develop and evaluate new treatments for tuberculosis as part of the TB Treatment Consortium. He is co-investigator on an NIH-funded study of HIV and HCV coinfection, for which Dr. Deborah Cotton is now principal investigator. This study follows a cohort of subjects initially enrolled nine years ago. Conducted in collaboration with Drs. Bica, Skolnik, and others in the Department of Medicine and the BU School of Public Health (BUSPH), this study yielded important insights into predictors of liver pathology, and differences between those infected with HCV alone and those with HIV/HCV coinfection.

Dr. Hamer and Dr. Donald Thea at the BUSPH, 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, along with Dr. H el ene Hardy who directs the HIV Pharmacotherapy program in the CHACR, collaborated on an NIH grant using cell phone technology to improve adherence to therapy during HIV disease. Drs. Anela Stanic, Hardy, and Skolnik are collaborating with Dr. Allen Gifford in the BUSPH on an NIH-funded R01 award to study interventions, using computerized, interactive technologies, to improve adherence to antiretroviral medications.

Dr. Skolnik is site leader, 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. Industry-sponsored trials of novel therapeutic agents provide cutting edge treatment opportunities for patients. This year, trials of integrase inhibitors and chemokine receptor antagonists were completed or continued, along with strategy studies of how to best employ these therapies for treatment-na ive and -experienced subjects. Dr. Skolnik continued as protocol immunologist for an ACTG trial of a chemokine receptor inhibitor (A5211).

## CLINICAL ACTIVITY

CHACR clinical care comprises the majority of clinical activity in the CID. The approach is multidisciplinary. Often, the needs of patients go beyond the medical, and include social and behavioral issues. Care is organized in teams. Each team includes a case manager, nurse, and physician. This team follows the patient from initial encounter, often after discovery of HIV infection during rapid HIV testing, 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.

Our pharmacy and clinical studies teams are an integral part of the overall care we provide for patients. We have specialty care available within the CID, including pulmonology, hepatology, and psychiatry. Dr. Kanno provides STD services within the CHACR. Physicians involved in outpatient efforts include Drs. Jon Fuller, Hamer, and Beth Zeeman, and Drs. Bica, Skolnik, Sullivan, and Yu. Drs. Sondra Crosby, Julita Mir, and Jon Pincus from General Internal Medicine, Dr. Harrison Farber and Dr. Michael Jeong from the Pulmonary Section, and Dr. David Nunes from the GI Section also provide care within the CHACR.

The HIV pharmacotherapy team, led by Dr. H el ene Hardy, contributes to the overall care of patients by enhancing adherence, which is central to 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 interactions with other drugs.

Dr. Sullivan leads a multidisciplinary team, in conjunction with the Departments of Pediatrics and Obstetrics/Gynecology, in the care of HIV+ pregnant women. She spearheaded the initiation of studies and services regarding human papillomavirus infection in HIV+ men and women in the CID. Dr. Sullivan also leads a study to provide reproductive health care to HIV sero-discordant couples, in collaboration with Dr. Deborah Anderson of the Department of Obstetrics and Gynecology, which utilizes “sperm washing” and intrauterine insemination to help HIV+ couples conceive safely. Dr. Sullivan continues to lead the Northeast mother-to-child-transmission provider group, which she founded as a forum to bring together clinicians from multiple institutions for educational and research opportunities.

The refugee health program, led by Dr. Elizabeth Barnett of Pediatrics, refers HIV+ patients directly into care in the CHACR. This provides consistency of care that is especially important to patients with multiple health and social challenges. Dr. Crosby, along with a case manager who focuses on refugee care, are central to our efforts to care for refugees, asylees, 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 many levels of their careers. Drs. Skolnik, Henderson, and Montano mentor undergraduate, pre-doctoral, postdoctoral, and junior faculty in HIV-related research. Some of these trainees are supported through NIH K series or T32 awards. The CHACR basic research laboratories are sought-after venues for students in this program to complete their required theses.

Formal lectures for medical and dental students concerning HIV/AIDS are given by Drs. Bica, Skolnik, and Yu in the medical microbiology and pharmacology courses at the BU School of Medicine, and in graduate and post-graduate courses at the BU Goldman School of Dental Medicine.

Third-year medical students rotate through the CHACR/CID, as part of their medicine clerkship, to learn principles of outpatient care, and HIV care in particular. Dr. Yu serves as mentor for this activity. Because of the size and reputation of our program, and its location in an urban medical center, medical students and residents from BUSM and BMC, and other medical schools and hospitals, look to the CHACR as a prime HIV training site. Dr. Fuller coordinates these outpatient educational activities.

Dr. Hardy, in conjunction with the Massachusetts College of Pharmacy and Health Sciences, leads an accredited residency program for PharmD students who desire specialized training in HIV pharmacotherapy.

Training in clinical HIV research is supported by an NIH T32 training award, the BU-CHART, for which Dr. Cotton was principal investigator (she has transferred this responsibility to Dr. Skolnik). This is done in conjunction with the K30 curriculum award to Dr. David Felson of the Clinical Epidemiology Research and Training Unit, and now as part of the recently awarded NIH Clinical and Translational Science Award (CTSA), for which Dr. David Center is principal investigator. Trainees can receive the MSc or ScD from the BUSPH at the end of this training. In this program, each trainee has an ethics co-mentor, drawn from the world-renowned medical ethics department in the BU School of Public Health, and can focus on epidemiologic, interventional, substance use, or health policy areas of clinical research. Dr. Hamer serves as mentor for BU-CHART fellows who are interested in international HIV research.

Our status as a regional center to teach STD prevention and care also continues to be an important part of the overall mission of the CHACR. The large volume of clinical material available within the STD program in the CID provides ample opportunity for learning experiences, and the STD nurses provide much of the hands-on teaching to trainees who come from all over New England to partake of this educational opportunity.

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

## MAJOR ACCOMPLISHMENTS

Dr. Andrew Henderson continued his cross-cutting research and infused new educational opportunities into the CHACR. A Proceedings of the National Academy of Sciences paper received a great deal of attention in the popular press and was selected by Nature Publishing Group as one of four papers to be presented for the Boston Science Café in June 2008. Dr. Monty Montano's R01 award to study the molecular genetics of muscle remodeling received a first percentile score. He was also elected as Director of the Exploratory Sciences Core for the Pepper Center.

Dr. Richa Tandon successfully finished the first two parts of a research study on anal PAP smears in HIV-infected women. Findings from this study were presented at the IDSA meetings. Dr. Marlynne Quigg-Nicol obtained a Department of Medicine pilot grant to study Toll-Like Receptors in the lungs of HIV+ persons, published a major article in the Journal of Virology in collaboration with Dr. Skolnik, was accepted for membership in the American Association of Immunologists, and was appointed Instructor of Medicine.

Dr. Deborah Cotton served as Chief Medical Officer, and Director of the Center for Strategic HIV Operations Research, for the Clinton Foundation HIV/AIDS Initiative (CHAI). Dr. Cotton was also appointed Chair of the National and Global Public Health Committee for the Infectious Diseases Society of America (IDSA). Dr. Jon Fuller continues to expand his educational activities. He published a "Clinical Crossroads" in JAMA concerning HIV-associated lipodystrophy, and continued to provide technical assistance for HIV projects to numerous Catholic Development Agencies.

Dr. Paul Skolnik continued his leadership of the Section and the CHACR. The interdisciplinary clinical care programs leverage both public and private funding as a national model for outpatient HIV care. Dr. Skolnik is protocol immunologist for a ACTG trial of a CCR5 inhibitor—this exemplifies the "bench-to-bedside" translational research that epitomizes the CHACR basic research effort. Dr. Skolnik also joined the NIH AIDS Immunology and Pathogenesis Study Section as a member this year.

Funding to the CHACR from the Massachusetts Department of Public Health HIV/AIDS Bureau was maintained despite national and state economic adversity, which is a testament to the central role that CHACR plays in providing HIV care to those most in need in Massachusetts, and in studying the most effective ways to provide this care.

Dr. Mettasebia Kanno joined the STD program within the CHACR, and will serve as medical director of the CID; her special expertise in STDs should bring new opportunities to the CHACR. The CHACR counseling and testing programs identify, and link to care, more newly diagnosed HIV+ patients than any other program in the Commonwealth.

The HIV pharmacotherapy residency program achieved full re-accreditation as one of only two such accredited programs in the country. 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.

**BOSTON UNIVERSITY MEDICAL CENTER  
DEPARTMENT OF MEDICINE  
ANNUAL REPORT  
SECTION OF THE VASCULAR BIOLOGY UNIT  
FISCAL YEAR 2008**

SECTION CHIEF NAME: Richard A. Cohen, MD

**SECTION SUMMARY REPORT**

The Vascular Biology Unit led by Dr. Cohen was established in 1990 as an independent research Unit in the Department of Medicine. The mission of the Unit is to maintain a diverse research program in vascular biology with special emphasis on basic mechanisms of vascular dysfunction and disease. The Unit currently comprises six faculty members with expertise in various aspects of the role of oxidant stress in vascular diseases associated with atherosclerosis, diabetes mellitus, and aging. The staff of the Unit, including its faculty, fellows, students, and technicians, represents a talented group with varied backgrounds and experience that complements the work of the Unit. Dr. Cohen, the Jay and Louise Coffman Chair in Vascular Medicine, directs the Unit and many of its research programs. His current research work is focused towards understanding the effects of endogenous oxidant/antioxidant systems in diabetic, atherosclerotic and aging associated vascular disease including the involvement of hypercholesterolemia, angiotensin II, thromboxane A<sub>2</sub>, and NADPH oxidase. Research programs are directed at the regulation of oxidant regulated cardiovascular proteins, including SERCA, p21ras, and sirtuin-1. Dr. Cohen also is co-principal investigator of the BUMC NIH-funded Cardiovascular Proteomics Center that focuses on oxidant-induced post-translational protein modifications in cardiovascular disease. The research funding to the Unit is currently composed of 6 NIH project grants, including component projects on an NIH program project on endothelial oxidants led by Dr. Kenneth Walsh, and an NIH-funded program project in diabetic complications led by Dr. Neil Ruderman. Dr. Cohen is also PI of two R01 grants from the National Heart Lung and Blood and the Institute on Aging. Dr. Zang is PI of a new NIH R01 grant. In addition, grants from the American Heart Association and a Strategic Alliance with Institut de Recherche Servier provide funds for the Unit. Total annual funding to the Unit currently exceeds \$1.3M in direct costs.

Dr. Bingbing Jiang is an Assistant Professor of Medicine and an expert in inflammatory cytokine signaling via NF- $\kappa$ B. His independent research on smooth muscle cells has been funded by a Scientist Development Grant from the American Heart Association. His research 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. Reiko Matsui, an 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.

Dr. Mengwei Zang, an Assistant Professor of Medicine, focuses her research on the regulation of hepatic lipid metabolism in diabetes by AMP-dependent protein kinase. Last year, she demonstrated key roles for the histone deacetylase longevity factor, sirtuin-1, and the tumor suppressor, LKB1.

Dr. Markus Bachschmid, an Assistant Professor of Medicine, studies the role of oxidants in the vascular disease associated with aging. His research addresses the role of endogenous peroxynitrite in regulating platelet function via its effects on cyclooxygenase. He also studies oxidant-induced damage of mitochondrial DNA.

Dr. XiaoYong Tong, an Assistant Professor of Medicine, is experienced in transgenic mice and electrophysiology. She is studying the physiological dysfunction caused by oxidation of the calcium ATPase,

SERCA, in type 2 diabetes. She is currently studying the oxidation of SERCA in diabetic animal models and patients as it relates to excessive growth of atherosclerotic plaques and restenosis observed in diabetic patients.

#### MAJOR ACCOMPLISHMENTS:

The past year had several highlights. Dr. Cohen was named a Robert Dawson Evans Scholar, a 5-year appointment in the Department of Medicine to enable the initiation of new research programs. Dr. Zang was named a recipient of a Robert Dawson Evans Junior Faculty Merit Award, a 2-year Department of Medicine grant to encourage early faculty career development.

This year was also a very successful year in terms of both research funding and publications. Two new NIH R01 grants were funded in the Unit on oxidant regulation of sirtuin-1 and AMP kinase (PI: R. Cohen, Co-I's Bachschmid, Zang) and on regulation of lipid metabolism by sirtuin-1 and AMPK kinase (PI: Zang).

During the year, papers from the Unit have been published in the *Arteriosclerosis, Thrombosis and Vascular Biology*, *Journal of Biological Chemistry*, *Journal of Molecular and Cellular Cardiology*, and *Free Radical Biology and Medicine*. Research in the past year has highlighted the fact that vascular function in diabetes is modulated by oxidant modification of key vascular endothelial and smooth muscle cell proteins that participate in cell signaling. As an example, we made the novel observation that oxidation of SERCA in diabetic arteries is associated with a high degree of protein degradation. Dr. Tong showed that exposing smooth muscle cells to clinically relevant concentrations of high glucose was sufficient to oxidize a key cysteine residue in SERCA that normally regulates cellular responses to nitric oxide. As another example of the importance of oxidant-mediated changes in protein function, Dr. Bachschmid's research demonstrated that endogenous peroxynitrite formed from nitric oxide and superoxide anion in platelets regulates cyclooxygenase and thromboxane levels, thereby regulating platelet aggregation. Dr. Zang's research demonstrated the novel finding that polyphenols regulate hepatic lipid metabolism via sirtuin-1, LKB1, and AMP kinase. In addition, Dr. Bayat and Jiang showed how thromboxane enhances vascular inflammation via Jun kinase signaling.

#### SELECTED PUBLICATIONS FROM 2008:

- 1: Ying J, Sharov V, Xu S, Jiang B, Gerrity R, Schöneich C, Cohen RA. Cysteine-674 oxidation and degradation of sarcoplasmic reticulum Ca(2+) ATPase in diabetic pig aorta. *Free Radic Biol Med*. 2008 Sep 15;45(6):756-62.
- 2: Hou X, Xu S, Maitland-Toolan KA, Sato K, Jiang B, Ido Y, Lan F, Walsh K, Wierzbicki M, Verbeuren TJ, Cohen RA, Zang M. SIRT1 regulates hepatocyte lipid metabolism through activating AMP-activated protein kinase. *J Biol Chem*. 2008 Jul 18;283(29):20015-26.
- 3: Tong X, Ying J, Pimentel DR, Trucillo M, Adachi T, Cohen RA. High glucose oxidizes SERCA cysteine-674 and prevents inhibition by nitric oxide of smooth muscle cell migration. *J Mol Cell Cardiol*. 2008 Feb;44(2):361-9.
4. Schildknecht S, van der Loo B, Weber K, Tiefenthaler K, Daiber A, Bachschmid MM. Endogenous peroxynitrite modulates PGHS-1-dependent thromboxane A2 formation and aggregation in human platelets. *Free Radic Biol Med*. 2008 Aug 15;45(4):512-20.
5. Bayat H, Xu S, Pimentel D, Cohen RA, Jiang B. Activation of thromboxane receptor upregulates interleukin (IL)-1beta-induced VCAM-1 expression through JNK signaling. *Arterioscler Thromb Vasc Biol*. 2008 Jan;28(1):127-34.