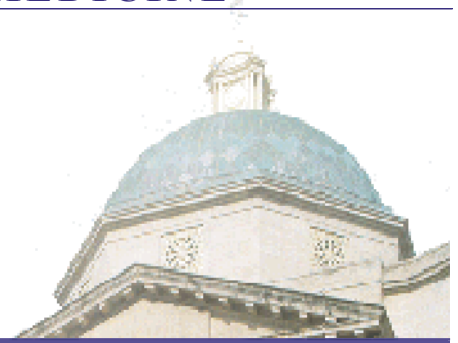


THE DEPARTMENT OF
**INTERNAL
MEDICINE**



Newsletter of the Department of Internal Medicine

Volume 2 • Number 1

Yale's Department of Medicine has a long history of distinguished clinicians and academic leaders among its faculty. These individuals have had an enduring effect on the values and character of the Department. We celebrate their legacy in this new section of the newsletter. Our intent is to honor their many gifts to the Department and to inform new members of the Department about these individuals.

David L. Coleman, M.D.
Interim Chairman

Profile: Robert M. Donaldson, Jr., M.D.

Since one of our teaching firms is named after Dr. Robert M. Donaldson, Jr., it might be of interest to those new to Yale to know something about this individual who was such a strong and important leader in our department from 1973 until his death in 2003. Bob grew up in Wellesley, Massachusetts, where he was a natural, gifted baseball pitcher, good enough to be invited to try out with the Boston Red Sox. But fortunately for us, his baseball career ended abruptly when he fractured his humerus throwing one of his wicked round-house curve balls and he decided to study medicine instead. He went on to graduate from Yale College in 1949 and received an M.D. degree from Boston University School of Medicine in 1952. Following residency at Boston University, he completed a fellowship in gastroenterology at the Peter Bent Brigham Hospital, later developing a distinguished early career as head of the gastroenterology section at Boston University Medical Center.

In 1973, Bob Donaldson came to Yale as Vice-Chairman of the Department of Internal Medicine. Appointed Chief of the medical service at the West Haven Veteran's Administration Hospital, he and Dr. Sam Thier set about to rejuvenate the training program of the Department of Medicine. Clinical excellence was their mantra and within a very short period of time, their enthusiasm for teaching, their personal support of housestaff and students, reawakened a latent energy in the entire department such that internal medicine at Yale became one of the most desirable training programs in the nation. Outstanding

young chief residents were recruited, many of them have stayed on as leaders in our present department. Individuals such as Vinnie Quagliarello, Dave Coleman, Cyrus Kapadia, Frank Bia, and Lynn Tanoue found an important mentor in Bob Donaldson during their days at the VA. He and I always worked well together and I shall never forget the happiness of our early days together at the VA where I first became aware of his intellectual and educational talents. In many ways, he was like a surrogate older brother to me. Throughout my days at Yale, he was always kind, supportive, and helpful, but at the same time, firm in his demand for excellence. Bob set high standards and generated a new vitality and excitement for learning that was contagious. As a true triple-threat, he also found time to run an active laboratory at the VA where he continued research on the role of certain bacteria in malabsorption, and on basic mechanisms in the absorption of vitamin B12 and the secretion of gastric intrinsic factor. His research is detailed in more than 100 publications. He was very active in the American Gastroenterological Association (AGA)



and in 1979, was elected president of that society and was later honored by the AGA with the prestigious Friedenwald Medal, their highest award. For seven years, he served as editor of *Gastroenterology*, and was on the editorial boards of several other prominent journals including the *New England Journal of Medicine*.

One of the highlights of his life was his marriage to Dr. Phyllis Bodell, a superb young physician-scientist who was one of the earliest and forceful advocates to improve the status of women in medicine at Yale. Bob shared her goal and worked tirelessly on behalf of women's issues throughout his professional career. He and Phyllis were very happy together, but sadly, within a few years, Phyllis developed acute leukemia and died long before her time. But just as things seemed to be at rock bottom, he found Ellen, who became his wife and brightened Bob's life once again and filled his days with love and support.

In 1982, Bob moved across town to Yale where he continued to be a highly visible leader within the department, providing sage advice, direction, and support to hundreds of students, residents, fellows, and faculty. He was named the David Paige Smith Professor of Internal Medicine and coordinated all medical student educational activities within the department. When Dr. Thier left Yale in 1986, Dr. Donaldson served as acting chairman of the department, but within a year, was summoned by the Dean to become Deputy Dean of the School of Medicine. In 1991, the President of Yale appointed him Acting Dean of the School of Medicine where he was highly successful in maintaining the stability of the school and encouraging substantive change in the educational programs of students. His modesty and restraint as a leader and educator were widely admired. He had a vision about medical education that was innovative and refreshing. Although he was a laconic man of few words, those words were usually incisive and to the point. He was also a private person who shunned publicity and personal

recognition, and never sought the limelight although his many accomplishments deserved it. Characteristically, he was always willing to serve the university whenever and wherever needed, and he did so without fanfare or unreasonable demands. He was a behind-the-scenes man who made things work.

Prior to his retirement, he was appointed a VA Distinguished Physician by the United States Department of Veterans Affairs, and he returned to the VA as chief of general internal medicine. Not content to rest on these laurels, Bob then began an active practice in the AIDS clinic at Yale-New Haven Hospital, and became co-director of the professional responsibility course for first-year medical students, completely revamping the case-based seminars on medical ethics, health care policy, and legal medicine. He took enormous pleasure in being with students and showed them by example what a complete physician should be. He frequently taught in the doctor-patient-encounter course, meeting weekly with his students to teach them physical diagnosis. He was beloved by them. In fact, in the waning days of his time at Yale, medical students selected him as the most distinguished clinical teacher at the medical school, honoring him with the prestigious Bohmfalk prize. It is a measure of his character that he then proceeded to donate his \$5,000 teaching prize to a student-run community service program at the medical school. At that time, one of the students wrote, "It is hard to imagine a more outstanding doctor than Dr. Donaldson. He loves patients and they love him back. If I were one-tenth the doctor Dr. Donaldson is, I would be twice the doctor that I or any of my classmates are likely to become." Even while seriously ill with advanced pulmonary fibrosis, Bob continued to come to medical grand rounds, a passionate student of medicine to the very end.

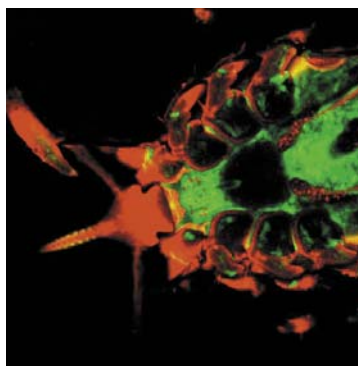
Robert H. Gifford, M.D.
Professor Emeritus

New Confocal Microscopy Facility in TAC

Dr. Ruth Montgomery announces "Good news for confocal microscopy at Yale!" We have just opened a new, shared facility for confocal microscopy in TAC. The principle of confocal microscopy is to collect fluorescent signals from only the plane of focus and eliminate any signal from above and below that plane.

We use laser optical sectioning to obtain sharp, detailed images with simple preparation of samples. Our new Zeiss instrument is similar to two in the Center for Cell Imaging in SHM, directed by Dr. Michael Nathanson. Confocal affords us tremendous power to quantify specific signals, determine co-localization of markers, and to do

3D reconstruction of cells. We have a META detector, which allows us to detect fluorescent dyes previously considered to be overlapping, like *gfp* and FITC, and we are also equipped with a Coherent 2-photon Chameleon laser. 2-photon microscopy allows penetration deep into living tissue with little damage to the surrounding area. This promises significant advances for intravital imaging studies. Interested users should contact the director, Dr. Ruth Montgomery (Ruth.Montgomery@yale.edu), for information and for training to use the instrument.



Ixodes scapularis, the tick vector of Lyme disease. Ticks were microinjected with fluorescent dyes to label surface structures and midgut cells and imaged live 24 h later by laser scanning confocal fluorescent microscopy

New Grant Awards

Dr. Jonathan Bogan, Assistant Professor in the Section of Endocrinology, has received a three-year grant from the American Diabetes Association. The grant entitled “Regulation of Glucose Transporter Trafficking” continues Dr. Bogan’s work focusing on how insulin controls glucose uptake by muscle and fat. In these cell types, insulin redistributes glucose transporter proteins from an intracellular location to the cell surface. The increased number of glucose transporters at the cell surface enhances the rate of glucose uptake. Dr. Bogan’s group identified a protein that binds glucose transporters and retains them deep within cells, so that they are inactive, in the absence of insulin. Insulin disrupts this interaction, untethering the glucose transporters from their intracellular site of sequestration and targeting them to the cell surface, so that they can transport glucose into the cell. This research award will fund further investigations into this mechanism, and allow the group to study how this tethering protein traps glucose transporters in an intracellular, insulin responsive complex. These studies will set the stage for longer-term work to determine if alterations of these proteins may contribute to the development of insulin resistance and diabetes.



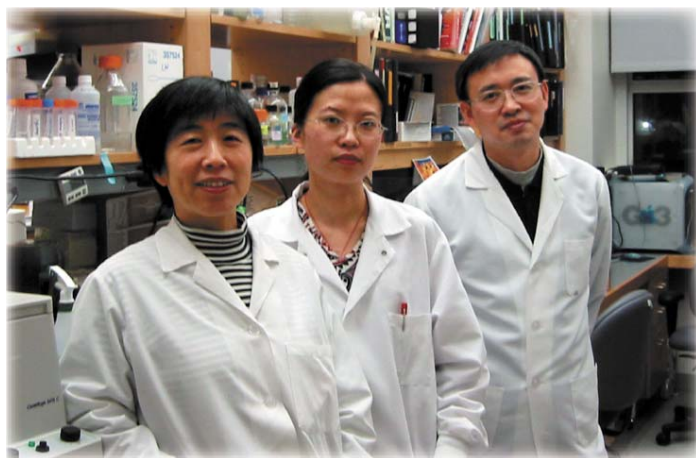
Dr. Bogan’s research group

Dr. Daniel Goldstein, Assistant Professor in the Section of Cardiovascular Medicine, was awarded a one-year grant from the Roche Organ Transplant Research Foundation for his project entitled “Role of Toll Like Receptor Signaling in Neonatal Transplant Tolerance.” This funding will enable Dr. Goldstein to obtain preliminary data to investigate whether the neonate has impaired innate Toll Like dependent signaling. Toll like receptors are critical innate immune receptors and it is not known whether reduced immune function in neonates is due to impaired Toll Like receptor function. Determining this will be the basis for further work to investigate the immune mechanisms of neonatal induced tolerance. Working with Dr. Goldstein on this project will be Wendy Walker, postdoctoral associate, and Bethany Tesar, research assistant.



Dr. Li Wen, Research Scientist in the Section of Endocrinology, has recently achieved a “hat trick” in securing three research grants. The first of these is an American Diabetes Association research grant to investigate the role of innate immunity on autoimmune diabetes development in two animal models, induced and spontaneous disease. This is a relatively new area of immunological study and could have potential impact beyond the pathogenesis of diabetes. The proposed studies could also have important implications for understanding innate immune responses in islet transplantation and in diabetes complications.

The second research grant award from the Juvenile Diabetes Research Foundation International focuses on a new T regulatory cell TCR transgenic mouse generated recently in Dr. Wen’s group. Cells from these mice protect from autoimmune diabetes in NOD mice. Her new JDRF research grant is to study the mechanism of this T

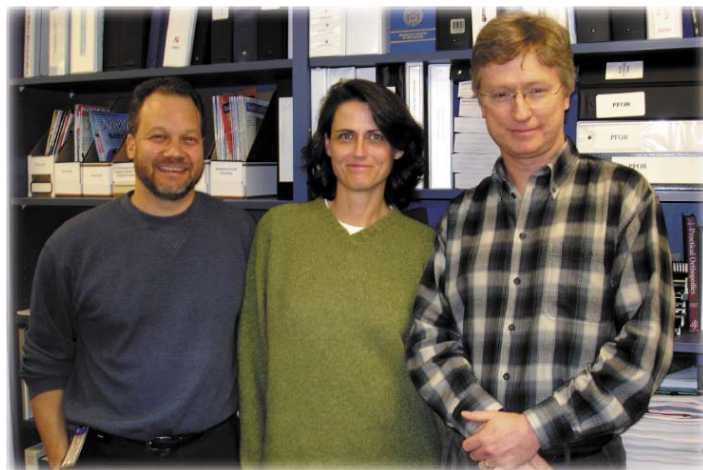


Dr. Li Wen and her research team

regulatory cell mediated autoimmune protection. These studies will also test the ability of these T regulatory cells to protect islet transplants. In addition, Dr. Wen has received a Seaver Institute award at the beginning of this year. This award will allow her to expand her interest in therapy for type 1 diabetes. She and her group will study dendritic cell-based therapies in autoimmune diseases, such as type 1 diabetes. They will test this therapy using their unique humanized mouse model. By doing these preliminary studies in an animal model, they hope to work out conditions that could then be applied to human dendritic cells to form the basis for future preventative therapy for autoimmune diseases.

David Fiellin, M.D., Lynn Sullivan, M.D. and Patrick O’Connor, M.D. from the Section of General Medicine, and Richard Schottenfeld from the Department of Psychiatry will form a clinical expert team that will provide support to a group of nation-wide HIV physicians treating opioid addiction in their patients. Dr. Fiellin is a co-investigator on a grant for the evaluation and support center for a federal project funded by the Health Resources Services Administration’s. The Yale team will work with the New York Academy of Medicine to assist in the implementation and evaluation of treatment with buprenorphine at 10 HIV primary care demonstration sites across the country. In addition, an award was made to Yale as one of the demonstration sites, with Rick Altice, M.D. as the principal investigator and Dr. Fiellin as co-principal investigator. The Yale demonstration site will involve Drs. Doug Bruce, Jerry Friedland, Patrick O’Connor, Lynn Sullivan, and Krystn Wagner in addition to clinicians at the Nathan Smith Clinic of Yale-New Haven Hospital.

Dr. Fiellin was also named Medical Director of the Physician Clinical Support System (PCSS) in a grant from the Substance Abuse Mental Health Services Administration to the American Society of Addiction Medicine. He will provide guidance on the implementation and evaluation of a nation-wide system of 60 researchers and clinical experts designed to expand access to treatment of opioid addiction with buprenorphine.



Drs. Fiellin, Sullivan and O’Connor

Medical Grand Rounds

- January 27, 2005 *“Understanding the Cholangiopathies: Bile Ductular Proliferation in Health and Disease”*
Jonathan Dranoff, M.D., Assistant Professor, Section of Digestive Diseases
- February 3, 2005 36th Annual Samuel D. Kushlan Lecture
“Clinical Implications of Host-Microbe Interactions in Inflammatory Bowel Diseases”
Fergus Shanahan, M.D., Professor and Chairman, Department of Medicine
National University of Ireland
- February 10, 2005 *“Art and Medicine”*
Barry Zaret, M.D., Robert W. Berliner Professor of Medicine
Section of Cardiovascular Medicine
- February 17, 2005 Samuel Their Lecture in Health Policy
“Professionalism and the Marketplace: Can They be Reconciled?”
Jerome Kassirer, M.D., Distinguished Professor of Medicine
Tufts University Medical School
Professor of Medicine, Adjunct, Yale University School of Medicine
- February 24, 2005 *“57 Year Old Man with Hypercalcemia, ARF and Metabolic Acidosis”*
Manoocher Soleimani, M.D., Professor and Chief, Section of Nephrology
University of Cincinnati Medical School

Grand Rounds begins at 8:30 a.m. in the Fitkin Amphitheatre.

Special Lectures

February 21, 2005

Seminar in Biomedical Research

TOPOISOMERASES, DNA DAMAGE, AND AGING IN THE IMMUNE SYSTEM

Albert Shaw, M.D., Ph.D., Assistant Professor, Section of Infectious Diseases

12:00 noon, Fitkin Amphitheater – lunch will be served

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Yale University School of Medicine

<http://info.med.yale.edu/intmed/newsletter/>

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