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DIVISION OF NEPHROLOGY



DR. BARBARA MURPHY was voted President-Elect of the American Society of Transplantation in 2007.

Five years ago, Paul Klotman, MD, stepped down as Chief of the Division of Nephrology to become Chairman of the Department of Medicine. After a national search, Barbara Murphy, MD, Irene and Dr. Arthur M. Fishberg Professor of Medicine, was selected as the new Chief of Nephrology. Her research on transplant immunology has added another dimension to Mount Sinai's renowned transplant programs.

In 2007 Dr. Murphy was voted President-Elect of the American Society of Transplantation. Her term as President will begin in May of 2008.

Teaming Up for Clinical Excellence

Even before Mount Sinai was the first in New York to open a dialysis facility in 1957, the Hospital was already a major center for the care of kidney disease. Today, as a regional referral center, the Division provides consultation and comprehensive evaluation and treatment programs that include one of the largest peritoneal dialysis programs in the country.

Between 2001 and 2006, the number of inpatients cared for by nephrologists at The Mount Sinai Hospital increased by 51 percent. Over this same period, the severity of illness in kidney patients also increased as demonstrated by a significant increase in the case mix index, a measure of case complexity, between 2002 and 2006.

Strong in its own right, the care the Division provides patients is further enhanced through partnerships with other groups within Mount Sinai, particularly the Recanati/Miller Transplantation Institute, the Brookdale Department of Geriatrics, and the Division of Infectious Diseases.

Mount Sinai was one of the first in the region to perform kidney transplants. In 2006 Mount Sinai's outcomes for one-year and three-year survival rates for kidney transplantation were the best in the region despite the fact that many Mount Sinai patients have significant co-morbidities.

The coordination of care between nephrologists and transplant surgeons before and after surgery is a major factor in how well patients recover. Led by Dr. Murphy, Transplant Nephrology at Mount

Sinai has developed many of the cutting edge protocols for patients including ones for desensitizing recipients with high immunological risk factors, transplants for HIV positive patients, and immune monitoring as a means of risk stratification of transplant recipients.

The field of geriatrics was created at Mount Sinai and the Medical Center is consistently ranked in the top five in the nation in this discipline. Housed within the Brookdale Department of Geriatrics is one of the most renowned palliative care programs, the Herzberg Palliative Care Institute. So, it is only natural that Mount Sinai would be the first in the country to create a Geriatric Nephrology and Renal Palliative Care Program, which is directed by Mark Swidler, MD, Assistant Professor of Medicine, a nephrologist who is board-certified in both renal medicine and geriatrics and has palliative medicine certification thru the American Board of Hospice and Palliative Medicine.

Mount Sinai is one of only two New York State Department-of-Health-designated AIDS Centers. The work of nephrologists on HIV associated nephropathy (HIVAN) was highlighted in *New York* magazine's 2006 *Best Hospitals* issue.

HIVAN is now the third leading cause of renal failure in African Americans, the most common cause of chronic renal failure in HIV-1 infected individuals. Dr. Klotman is principal investigator on a program project grant from the National Institute of Diabetes and Digestive and Kidney Diseases to study the pathogenesis of HIVAN. Together with colleagues in the Divisions of

Nephrology and Infectious Diseases, he is testing the hypothesis that HIVAN is a disease in which HIV-1 infection of the renal epithelium is required but not sufficient to induce the disease. Genetic factors are believed to be responsible for susceptibility and progression.

Research and Discovery

Mount Sinai's clinical strengths in nephrology are largely an outgrowth of the active research programs in the field. The Division's funding from the NIH has increased from \$3.7 million in 2001 to over \$11 million in 2006.

Several researchers in the Division are studying the molecular genetics, cell biology, and pathophysiology of autosomal dominant polycystic kidney disease (ADPKD), the most common genetic disease in humans—affecting six million people worldwide.

Patricia Wilson, MD, Professor of Medicine, was recently awarded a US Patent for a method to assay the effects of potential drug therapies for ADPKD.

Peter Mundel, MD, Professor of Medicine, is investigating the cell biology and pathology of podocytes, highly differentiated cells, which play a crucial role in the physiology and pathology of the kidney glomerulus. In a 2006 paper in *Nature Cell Biology*, he and his colleagues identified a protein that is essential for the integrity of the podocyte cytoskeleton and for regulation of podocyte cell migration.¹

Transplantation

Building on Mount Sinai's leadership in transplantation, nephrologists are working to improve outcomes and increase the availability of donor organs. Dr. Murphy is the primary investigator on a program project grant awarded as part of the Genomics Consortium from the National Institute of Allergy and Infectious Diseases in 2006 to study the genomics of chronic allograft rejection, which remains the most common cause of graft loss.

In a recent clinical trial, Elizabeth Ommen, MD, Instructor of Medicine, was able to increase by 73

percent the number of eligible kidney donors by using ambulatory blood pressure monitoring to differentiate between individuals with white coat hypertension and those with sustained hypertension. Her work examining cardiovascular risk in living kidney donors has recently been funded by the NIH.

Peter Heeger, MD, Professor of Medicine, was recruited from the Cleveland Clinic in 2006. He is building a comprehensive translational research program in transplant immunology as Director of the newly created Transplant Immunology Research Program. Dr. Heeger developed an assay that offers the potential to identify individual patients at risk of developing rejection, information that may be used to determine when the risks of immune complications warrant the side effects often seen with medication.

Islet cell transplantation is a focus of much research in the Division. Currently donations are often needed from multiple donors because the process of physically manipulating the cells can cause them to release substances that stimulate inflammation. In a paper published in the *Journal of the American Society of Nephrology* in 2005², Mount Sinai nephrologists reported on a technique that significantly increased islet cell function post-transplantation.

A Personalized Approach

Erwin Böttinger, MD, Vice Chair of Research for the Department of Medicine and a member of the Division of Nephrology, is heading up Mount Sinai's efforts in personalized medicine as Director of the newly established Charles Bronfman Institute for Personalized Medicine. He is currently focused on developing a biobank of over 100,000 DNA samples that will be linked to clinical information, allowing researchers to connect genotype and phenotype to begin to tailor treatments to specific needs.

Work in this area is already well advanced in the Division. Several years ago Michael Lipkowitz, MD,

¹Nat Cell Biol. 2006 May;8(5):485-91.

²J Am Soc Neph. 2005 Feb; 16(2):444-51.

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COMMUNITY ADVOCACY

Dr. Murphy and Jonathan Winston, MD, Associate Professor of Medicine, launched a campaign to identify individuals at risk for chronic kidney disease (CKD) early and to intervene to slow the progression of the disease. "African Americans and Hispanics, two groups that comprise the majority in our local community, are at increased risk of CKD," said Dr. Murphy. "Diabetes, hypertension and family history of kidney disease, all of which increase risk of CKD, are all very common in our community. Yet, few of our patients, or for that matter their physicians, were aware of their risk."

Initiatives to change this include community lectures, screenings at health fairs and other community events, presentations to caregivers, and a new process to report glomerular filtration rate on The Mount Sinai Hospital reporting system. Several research abstracts related to public awareness of CKD were presented by the Division at the 2006 National Kidney Foundation meeting. "We initiated this program to help our local community, but the problem of undiagnosed CKD is certainly not limited to East Harlem," said Dr. Murphy. "Through our research and recently through media coverage of our efforts, including the *Boston Globe* and WABC TV we are broadening our reach beyond our local community."

Associate Professor of Medicine, had the foresight to collect DNA samples from the African American Study of Kidney Disease and Hypertension trial, a large multi-center trial run by the NIH.

Now that the technology is available, he is using these samples to conduct genetic and pharmacogenomic studies to understand the genetic basis for susceptibility to hypertension, progressive renal failure, and their sequelae such as cardiac hypertrophy, coronary artery disease, and atherosclerosis, as well as effectiveness of drug therapy.

Fellow to Faculty

The stated goal of most fellowship programs is to train the future leaders in academic medicine. The question is: Are they succeeding?

OF THE 31 FELLOWS TO GRADUATE FROM THE NEPHROLOGY FELLOWSHIP PROGRAM AT MOUNT SINAI SINCE 1999, 23 HOLD FULL-TIME ACADEMIC POSITIONS AND COMBINED THEY HAVE WELL OVER 90 PUBLICATIONS INCLUDING SEVERAL IN THE *NEW ENGLAND JOURNAL OF MEDICINE & NATURE GENETICS*.

Over 240 applications are received for the five spots open in the program each year. The fellows entering in 2006 were graduates of Columbia University, Mount Sinai School of Medicine, University of Chicago, University of Texas, and University of Miami.

The strength of the Program led to receipt of a prestigious NIH Training Grant in Molecular Basis of Renal Disease. This grant helps support fellows conducting basic, clinical and translational research in a wide variety of areas including virology, immunology, transplantation, genetics, and developmental and stem cell biology. Working with faculty mentors, the fellows receive the support needed for a smooth transition from fellow to junior faculty member.

With graduates so well prepared for academic careers, the Division has not had to look far when seeking to recruit exceptional new faculty. Eight of the last ten faculty members to join the Division have come from its own Fellowship Program and many have already taken on leadership roles. These new recruits have also been tremendously successful in competing for research funding as evidenced by the receipt of eight prestigious career development awards from NIH.

DR. PETER HEEGER developed an assay that offers the potential to identify individual patients at risk of developing rejection, information that may be used to determine when the risks of immune complications warrant the side effects often seen with medication.



DR. ELIZABETH OMMER is educating the community about Chronic Kidney Disease

