

The Liver Disease Fellowship at Mount Sinai is the largest program of its kind in the United States.

## DIVISION OF LIVER DISEASES

DR. SCOTT FRIEDMAN serves on the governing board of the American Association for the study of Liver Diseases (AASLD) and will become its President in 2009.

**The Division of Liver Diseases Faculty Practice Associates reported receipts of nearly \$1 million in 2006, up from only \$134,000 in 2003. During the same period, research support from the NIH to the Division increased by 24 percent. This tremendous growth within just three years resulted from recruitment of outstanding junior and senior faculty who are building upon Mount Sinai's historic accomplishments in the field.**

Of this growth, and of planned future expansion, Division Chief, Scott Friedman, MD, Irene and Dr. Arthur M. Fishberg Professor of Medicine (Liver Diseases), emphasizes that the Division's goal is to become the premier division of liver diseases in the United States within five years. "Our success will be defined by excellence in both clinical and translational research," he says.

### **Building upon Greatness**

The Division of Liver Diseases is distinguished by its leadership in hepatic fibrosis, hepatocellular carcinoma, hepatitis C virus infection, primary biliary cirrhosis, and liver immunology.

Over the past decade, there has been an upswing in chronic liver disease, a growing incidence of liver cancer, and an ever-increasing shortage of organs available for liver transplantation. Basic, translational, and clinical research projects, as well as patient care initiatives within the Division, are geared toward finding solutions for each of these concerns.

### **Chronic Liver Disease**

A distinct target of Division research is the hepatitis C virus (HCV), a leading cause of liver disease. Research by Andrea Branch, PhD, Associate Professor of Medicine, and her associates within the Division's Hepatitis C Program, has brought increased NIH funding to investigate the pathogenesis, as well as novel modes of diagnosis, of HCV infection.

By uncovering the pathways through which liver cells process the hepatitis C virus, Dr. Branch's work is expected to help assess how seriously a patient's liver will be affected by disease progress, and to adjust treatment accordingly.

Of the nearly one million people in the US estimated to have human immunodeficiency virus (HIV), approximately 300,000 of them are believed to be co-infected with hepatitis C. The investigational work on co-infection by Douglas Dieterich, MD, Professor of Medicine, who joined the Division in 2003, has positioned Mount Sinai as an international leader in research and clinical care related to co-infection with HCV and HIV.

Dr. Dieterich has led numerous clinical trials at Mount Sinai, including a landmark study published in the *New England Journal of Medicine* in 2004<sup>1</sup>, which found the highest response rate ever achieved for a treatment designed for patients co-infected with hepatitis C and HIV.

Paul Martin, MD, Professor of Medicine, joined the Division in 2004 as Associate Chief. Dr. Martin is an international expert on the interactions between HCV and kidney disease, as well as on management of end stage liver disease.

Dr. Friedman's own investigations into liver fibrosis have significantly contributed to the recognition of the importance of the assessment of liver scarring (fibrosis) in the treatment of patients infected with HCV. Ongoing basic research on fibrosis spearheaded by Dr. Friedman and others in the Division is leading the way to discovery of highly effective medications that can slow—or even reverse—liver fibrosis. A search for a noninvasive test for liver fibrosis is another valuable and potentially lifesaving area of inquiry that is being pursued.

Research in fibrosis took an exciting and unexpected turn when Dr. Friedman, John Martignetti, MD, Associate Professor of Human Genetics, and

<sup>1</sup>N Engl J Med. 2004 Jul 29;351(5):438-50.

then-graduate student Goutham Narla identified a tumor suppressor gene that is missing or mutated in many forms of cancer.

The original research, demonstrating the role of the gene *KLF6* as a tumor suppressor, was published in *Science* in 2001<sup>2</sup>. In 2005 the team again published results from their investigations, this time in *Cancer Research*. Their work demonstrated how a single variant of *KLF6* may increase a man's risk of prostate cancer by 50 percent.

Kirsten Sadler-Edepli, PhD, Assistant Professor of Medicine, joined the Division in 2005 and established the first zebra fish facility at the Mount Sinai School of Medicine to explore novel models of acute and chronic liver diseases. This unique model organism allows rapid and direct evaluation of genetic defects and molecular mechanisms of disease. Dr. Sadler-Edepli works closely with several other Mount Sinai investigators who are using this unique model to study key biologic pathways in the liver and other organs.

Mount Sinai has had a major and productive interest in primary biliary cirrhosis (PBC) for nearly 50 years, harking back to landmark studies conducted by Drs. Hans Popper and Fenton Schaffner, who became the first Chief of Liver Diseases at Mount Sinai.

The work of Drs. Popper and Schaffner illuminated the clinical spectrum, natural history, and histopathologic evolution of PBC. It also uncovered the nature and significance of cholestasis. This tradition of groundbreaking PBC research continues in the Primary Biliary Cirrhosis Center, led by Joseph Odin, MD, Assistant Professor.

### **Liver Cancer**

Hepatocellular carcinoma (HCC) is a major global health problem. It is now the third leading cause of cancer-related death worldwide.

Josep Llovet, MD, Visiting Associate Professor of Medicine, joined the faculty in 2005 as Director of HCC Research of the Mount Sinai Liver Cancer Program. The HCC research program is a new initiative undertaken in partnership with the Recanati/

Miller Transplantation Institute and the Division of Hematology and Medical Oncology to identify new molecular pathways of hepatocellular carcinoma as well as novel treatments for the disease.

An international randomized clinical trial recently led by Dr. Llovet places the Division in the forefront of clinical research in HCC. The trial, which compared the multikinase inhibitor sorafenib to a placebo, was terminated prematurely due to overwhelmingly positive survival results favoring treatment. According to Dr. Llovet, "Mount Sinai was the leading patient recruitment center in the United States. I am pleased to note that it is the first time in which the scientific community has had a positive trial in treating advanced HCC. It is also the first time that a molecularly targeted therapy has been tested in HCC during a phase III trial."

### **Transplantation**

In 1988 Mount Sinai surgeons performed the first liver transplant in New York State history. Since then, the Recanati/Miller Transplantation Institute at Mount Sinai has become one of the world's leading transplant centers. Medical specialists in the Division of Liver Diseases work closely with transplant surgeons to care for patients both before and after transplantation.

Thomas Schiano, MD, Associate Professor of Medicine, holds primary responsibility for the medical aspects of postoperative care for transplant patients and for identifying specific medical complications that may arise in the posttransplant setting.

Ever mindful of the communities served by Mount Sinai the Division and the Recanati/Miller Transplantation Institute began the Community Transplant Outreach Program, in 2004 led by Nancy Bach, MD, Assistant Professor. The program is designed to extend Mount Sinai's expertise to affiliate hospitals.

### **Training Initiatives in Hepatology**


The Division conducts nationally recognized training programs in liver disease for its medical house staff and fellows.

<sup>2</sup>*Science*. 2001; 294:2563-65.



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**DR. KIRSTEN SADLER-EDEPLI**  
is studying zebra fish models of  
liver disease in her laboratory at  
Mount Sinai.



DR. HANS POPPER

### **“A GIANT WALKED AMONG US”**

In the year 1957, the recruitment of Hans Popper, MD, to the Division of Pathology would greatly advance the study of liver diseases at Mount Sinai and help propel the Medical Center to international prominence.

The driving force behind creation of the Mount Sinai School of Medicine, Dr. Popper was Chief of Pathology at Mount Sinai and the first Dean of the Medical School. He wrote over 800 clinical articles and 28 books on liver disease.

Universally regarded as “The Father of Modern Hepatology” for his tireless research into liver function and pathology, Dr. Popper’s leadership of the Department of Pathology, and his work in helping create the Mount Sinai School of Medicine, would transform Mount Sinai into “the” place for the study and treatment of liver disease.

The Division’s commitment to training was recently highlighted by the awards of three AASLD/Schering Advanced Hepatology Fellowships to Divisional trainees, more than any institution in the country. In addition, Efsevia Albanis, MD, Assistant Professor of Medicine, an MSSM graduate, won the highly prestigious AASLD/AMGEN Physician Development Award in 2006.

The Division has recently created additional advanced training opportunities to prepare national and international leaders in the treatment of liver disease.

The Advanced Clinical Hepatology Fellowship Program is considered a national model for specialized training and advanced certification in the specialty. Directed by Meena Bansal, MD, Assistant Professor of Medicine, the Liver Disease Fellowship at Mount Sinai is the largest program of its kind in the United States. It provides fellows with an intensive year of advanced clinical training to prepare them as future teachers and researchers in hepatology. Trainees are eligible for a Certificate of Added Qualification, a category of expertise newly created by the American Association for the Study of Liver Diseases.

Mount Sinai is the only School of Medicine in the New York metropolitan area to receive a multi-year NIH Training Grant in Liver Diseases and Gastroenterology. This NIH grant funds an interdisciplinary program that prepares independent researchers in basic and clinical research, including cancer biology, immunology, liver injury, fibrosis, molecular basis of transport and gene therapy, and clinical research.

Together with unrestricted industry-sponsored support, the NIH training grant also funds a unique Visiting Professor Program led by Dr. Albanis. The program permits national and international leaders in hepatology to spend two days each visiting and exchanging ideas with Mount Sinai faculty, fellows, and staff.

In 2006 the Division inaugurated a postgraduate course, the First Annual Mount Sinai Hepatology Update, directed by Drs. Dieterich and Martin, which features presentations from internationally known liver disease experts.

**DR. DOUGLAS DIETERICH**

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