

DR. LLOYD MAYER'S research into gut immunology may help patients suffering from inflammatory bowel disease and related autoimmune disorders.

THE JEFFERY MODELL

DIVISION OF CLINICAL IMMUNOLOGY



The Division of Clinical Immunology is highly regarded for its superior leadership in immunobiological research and patient care. Patients travel from all over the United States—and around the world—seeking the expertise of Mount Sinai immunologists, fueling a 25 percent upsurge in faculty practice revenues over the past three years. In research support, funding from the National Institutes of Health to the Division more than doubled between 2002 and 2006.

In terms of education and training, Lloyd Mayer, MD, Dorothy and David Merksamer Professor of Medicine, Chief of the Divisions of Clinical Immunology and Gastroenterology, and Director of the Center for Immunobiology, notes that the Division's reputation consistently attracts exceptional candidates to compete for places in its fellowship program.

Leading the Way

Mount Sinai's involvement in the new science of immunology began in the 1920s. That's when Dr. Gregory Schwartzman, a Mount Sinai physician and researcher, first developed the concept of immune system hypersensitivity, a condition that later became known as the "Schwartzman Phenomenon."

In the years spanning from Dr. Schwartzman's work on hypersensitivity, to the Division's contemporary status as the leading center in the country for research into primary immune deficiency disorders, numerous other discoveries about immune-related disorders have been made by gifted and dedicated researchers and clinicians at Mount Sinai.

Primary Immune Deficiency Diseases

Much of the cutting-edge investigation into the more than 70 primary immune deficiency disorders has been spearheaded by Charlotte Cunningham-Rundles, MD, PhD, Professor of Medicine. Her pioneering scientific inquiries into this area have helped make Mount Sinai a major referral center for primary immune deficiency diseases, and continues to spark NIH support for this pivotal area of investigation.

In 2004 Dr. Cunningham-Rundles was awarded a program project grant from the NIH to develop unique models of primary immune deficiency diseases to study the distinct stages of B cell maturity and function.

"The program is visionary in scope. Such a global approach to a complex set of diseases is bound to yield immensely valuable information regarding both immunodeficiency and the normal regulation of immunity," remarked Dr. Mayer upon learning of the NIH award.

Dr. Cunningham-Rundles is also the principal investigator in another NIH-funded program project grant focused on the analysis of immunodeficiency patterns in racial and ethnic groups, employing sophisticated computer screening methods. She was recently elected President of the prestigious research consortium, the United States Immunodeficiency Network (USIDNET), which advances research into primary immune deficiency diseases and funds peer-reviewed research grants in this area.

Immune System Function

Dr. Mayer is also the recipient of a significant grant from the NIH that combines his tandem interests in immunology and gastroenterology to the study of innate and adaptive immune interactions in the human digestive system. Dr. Mayer and colleagues are investigating the diverse mechanisms involved in controlling the inflammatory process. These include immune and nonimmune factors that interact to suppress inflammation in the gut. It is expected that this research will have translational value for patients suffering from inflammatory bowel disease (IBD) and related disorders.



Recently, Drs. Mayer and Cunningham-Rundles were awarded the prestigious Jeffrey Modell Foundation Lifetime Achievement Award for their contributions to the field of Immunology.

Another important area of investigation within the Division is the role that T cells and related factors play in the earliest stages of immune responses to infection. Julie Magarian Blander, PhD, who joined the Division in 2006 as an Assistant Professor of Medicine, published a study in *Nature* in 2006 that provided insights into how structures known as toll-like receptors (TLRs) are activated to orchestrate the appropriate immune response¹. "With results from this research," says Dr. Blander, "it may be possible to identify 'breakpoints' during disease progression and work toward finding microcellular solutions to mend them."

Also recruited in 2006, Christopher Dascher, MD, Assistant Professor of Medicine, is investigating cell surface molecules known as CD1. In a 2005 paper published in the *Proceedings of the National Academy of Sciences*², he demonstrated that these molecules appear very early in the evolutionary history of terrestrial vertebrates and therefore clearly play a long standing regulatory role in immune response.

Asthma & Allergy Research and Treatment

There is a strong emphasis within the Division on the study of the underlying causes of asthma and allergies, and on the evaluation of new treatments for this disorder.

Beth E. Corn, MD, Assistant Professor of Medicine, has participated in numerous clinical trials of medications for the treatment of asthma and allergic rhinitis currently on the market. Dr. Corn, who is director of the Allergy/Asthma Clinic and a member of the Asthma Program, was elected as President of the New York Allergy and Asthma Society in 2006.

¹Nature. 2006 Apr 6;440(7085):808-12.

²Proc Natl Acad Sci USA. 2005 Jun 14;102(24):8674-9.

DR. CHARLOTTE CUNNINGHAM-RUNDLES
is President of the prestigious research
consortium, The United States
Immunodeficiency Network (USIDNET).

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IMMUNOLOGY INSTITUTE

As the body's major defender, the immune system plays a role in almost every human disease.

Whether the response to infection or an autoimmune response caused by overreaction of the system, conditions from HIV to allergies, diabetes to cancer, and asthma to inflammatory bowel disease all have an immune component.

As medical science has increasingly recognized the involvement of the immune system in human disease, medications re-directing or modifying immunity have exploded. Unfortunately, many of these newer agents possess limited efficacy or produce unwanted side effects.

The Immunology Institute at Mount Sinai School of Medicine was established in 2007 to bring together a multidisciplinary team to define abnormal pathways in human disease and develop the next generation of immunotherapeutic agents.

Under the leadership of Co-Directors Dr. Mayer and Sergio Lira, MD, PhD, Professor of Immunobiology, this Institute is building on Mount Sinai's historic strengths in immunology research and diverse expertise in patient care to build new translational programs in inflammation and immunoregulation. Because of the particularly crucial role of immunomodulatory therapies in transplantation, the Immunology Institute also includes extensive transplantation research programs.

When it comes to asthma pathophysiology, researchers have come to understand that hypersecretion of mucus plays an important role in the pathogenesis and severity of the disease. However, the central question is, what causes this hypersecretion?

It had been known that a cytokine called tumor necrosis factor-alpha (TNF-alpha) increases airway mucus gene expression *in vitro*. However, in a 2005 paper published in the *Journal of Allergy and Clinical Immunology*³, Paula Busse, MD, Assistant Professor of Medicine, was the first to demonstrate that this also occurs *in vivo* in two mouse strains. Citing scientific precedent, Dr. Busse stated that blocking the effects of TNF-alpha may prove successful in asthma treatment, just as it has in a number of other chronic inflammatory diseases.

Mount Sinai's Jaffe Food Allergy Institute is one of the leading centers in the world for clinical care and research on food allergies. Currently, a multidisciplinary team has been assembled that includes renowned food allergy expert Hugh Sampson, MD, Professor of Pediatrics, and faculty from the Division of Clinical Immunology, the Department of Pediatrics, and the Jaffe Food Allergy Institute.

The team is leading a project to examine the basic immunologic mechanisms of food allergy in humans and animal models. The results are expected to produce insights into multiple allergic mechanisms in humans that, in turn, may lead to the development of new strategies to treat and prevent these disorders.

Training Physician-Scientists

Under a ten-year NIH training grant, the Division partners with allergists in the Department of Pediatrics to prepare highly-trained pre- and postdoctoral candidates to become outstanding academic scientists in the field of Immunobiology.


Through laboratory and didactic training, working in translational research programs relating to cytokine biology, HIV-related disorders, autoimmunity and primary immunodeficiency, these trainees acquire the intellectual and technical skills needed to advance the specialty at Mount Sinai and elsewhere.

The program is one of the most sought after by trainees graduating from prestigious institutions, says Dr. Mayer, because of the enormous growth that is occurring in the basic sciences at Mount Sinai; its overall excellence in research; diverse patient population; a protective and nurturing mentoring environment; and an unequivocal commitment to postdoctoral fellowship training.

³J Allergy Clin Immunol. 2005 Dec;116(6):1256-63.

A photograph of Dr. Julie Magarian Blander in a laboratory setting. She is wearing a white lab coat and is focused on her work at a biosafety cabinet. She is holding a pipette and appears to be transferring liquid into a small container. The background shows various lab equipment and a clean, professional environment.

DR. JULIE MAGARIAN BLANDER

A close-up photograph of Dr. Beth Corn. She has long dark hair and is looking slightly to the left of the camera with a thoughtful expression. She is wearing a dark turtleneck sweater under a white lab coat.

DR. JULIE MAGARIAN BLANDER,
PUBLISHED A STUDY IN *NATURE*
IN 2006 THAT PROVIDED INSIGHTS
INTO HOW STRUCTURES KNOWN
AS TOLL-LIKE RECEPTORS (TLRS)
ARE ACTIVATED TO ORCHESTRATE
THE APPROPRIATE IMMUNE
RESPONSE.

DR. BETH CORN
President of the New York
Allergy and Asthma Society