



# Outlook

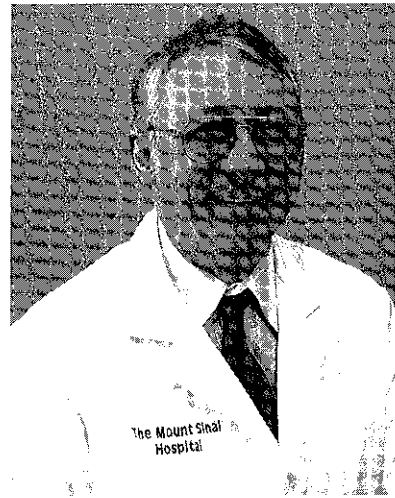
WINTER 2003

## Dr. William C. Koller to Direct Movement Disorders Program

*"We want to set  
up a full-service  
model that's highly  
patient-friendly."*

Bill Koller's big picture vision looks to the day when the Movement Disorders Program at Mount Sinai Medical Center will be unparalleled. A day, he believes, that is on the near horizon.

The newly-appointed director of the Movement Disorders Program at Mount Sinai's Department of Neurology came to New York in October 2002 with a clear agenda. "Our number one goal is to provide the best clinical care for patients with movement disorders, and that includes the best physicians, nurses, social workers, and rehabilitation."



*William C. Koller, MD, PhD*

He speaks quickly as he outlines the synergy and the components of this new patient-focused model. "It's a common complaint that doctors don't return phone calls. We want to help people with their questions and set up a full-service model that's highly patient-friendly. Our strength will be to offer the gamut – clinical care, genetic testing, new drug trials, an active surgical program ... all the elements to make it successful."

Dr. Koller believes that the time is ideal for the program's expansion. "There have been major advances in the field of movement disorders in the last five years and there's so much on the horizon ... new approaches, new treatments, new drugs," he says. "We understand what happens in the brain more and, when there's more understanding of the basic mechanics of the disease, there's more room for intervention."

While the roots of the program go back to the '70s, his aim is to guide it into a new era. The movement disorders program at Mount Sinai Medical Center first came into its own under Melvin Yahr, MD, the renowned Parkinson's disease specialist, whose groundbreaking research and clinical trials put the program on the map.

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## Many Thanks...

Generous supporters of two events this past fall will enable us to fund vital research and patient services

• Sold Out! That was the terrific response to our Parkinson's theater benefit of the Broadway play, *Man of La Mancha*. 140 people joined us for the event, which raised \$100,000.



The well-known New York City Zabriskie Gallery held an exhibition and silent auction of more than 60 works of art in December. The event, which was followed by a gala cocktail party, raised more than \$50,000 to benefit dystonia research and education. Gallery owner Virginia Zabriskie has three forms of dystonia that creates spasms of the muscles around her eyes, in her hands and her vocal chords.

## DON'T MISS OUT ...

Mark your calendar now  
**Young Professionals**

Have the best time and help fight dystonia and Parkinson's disease. Cocktail Reception Wednesday, February 26, 2003, 7-10 p.m. at Suite 16, 127 Eighth Avenue at 116th Street, New York City.

## Golfers

Get in the swing and sign up now for the 11th Annual Dystonia Invitational – Monday, June 16, 2003 at the Century Country Club in Purchase, NY.

To register call 212.241.5614 or email [Bachmann.Strauss@mssm.edu](mailto:Bachmann.Strauss@mssm.edu)

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## Dr. William C. Koller to Direct Movement Disorders Program

Dr. Koller is well-equipped to meet the road ahead. Prior to moving to New York, he was Professor, Department of Neurology and Department of Neurosurgery at the University of Miami, FL and, previously, Professor and Chairman, Department of Neurology at the University of Kansas Medical Center in Kansas City, KS. Schooled in Milwaukee and in Chicago, he holds an MS and PhD in Pharmacology and an MD from Northwestern University. He did his internship in internal medicine and his residency in neurology at Rush-Presbyterian St. Luke's Medical Center in Chicago. His focus has been on movement disorders ever since.

The author of more than 500 articles and numerous books, Dr. Koller's work is considered a definitive source in the field of neurology. His background includes 76 visiting professorships in this country and abroad. Among his awards are an NIH Predoctoral Fellowship, 1968-1974 and a Pillsbury Fellow, 1979-1980.

Building on past strengths, Dr. Koller's expansion plans include hiring expert nurses and more physicians with movement disorder experience. Collaboration and full service, he believes, are the keys to building a premier program.

"There's so much potential," he says, looking out his window to the East River. "We have great laboratory science that can be translated to clinical care. By collaborating with other programs in genetic studies, we can more quickly make therapeutic advances. The opportunity is tremendous."

*The Movement Disorders Program can be reached at 212.241.5607. The Bachmann-Strauss Dystonia & Parkinson Foundation has provided funding for the Movement Disorders Program at Mount Sinai Medical Center since 1995 to support basic research and better treatment and patient care.*

## The Key to Inquiry and Understanding



BONNIE STRAUSS  
FOUNDER AND PRESIDENT



MARGIE J. WALDEN  
EXECUTIVE DIRECTOR

*If there is one word that defines the work of our organization, it is collaboration. The collective, cooperative efforts of our volunteers this past fall resulted in tremendous financial support for movement disorders research through our special events. That joint effort was key to our annual symposia on dystonia and Parkinson's disease,*

*which enables patients, families and caregivers to share questions and concerns and engage in a dialogue with clinicians and research scientists.*

*It was the launch of our dystonia research think tank that really underscored the critical role that collaborative effort plays in inquiry and understanding. This scientific meeting brought together top scientists working to uncover the causes of dystonia. By doing so – by providing a forum for discussing the most current knowledge, questions and results – we are moving one step closer to the day when we can find cures.*

*The greatest commendation of all came from the scientists at the meeting who expressed hope that this would be the first of an annual series focused specifically on dystonia and research into its causes and potential treatments and cures. In this year, we will do everything possible to make that a reality.*

## First Dystonia Research Think Tank Held

Noted specialists share theory and latest data

In the first initiative of its kind, The Bachmann-Strauss Dystonia & Parkinson Foundation brought together a world-class gathering of scientists involved in the basic research that might ultimately lead to a cure for dystonia. The group included noted specialists in dystonia, as well as neurobiologists, cell protein experts, molecular biologists, pathologists and physiologists. The seminar, held in October, provided scientists an opportunity to raise important questions, resolve problems and obtain the feedback they need to help move their research efforts forward.

There were three parts to the day's proceedings: In the first, scientists described the symptoms and classifications of dystonia, together with an overview of its neurophysiology and what is known of its molecular mechanisms. In the second part, they reported on the latest relevant findings, with special emphasis on the exciting work going on with the protein torsinA. The seminar concluded with a round table discussion focusing on the future directions of dystonia research. Several research priorities to maintain and accelerate progress were cited, including:

- The continued development of more and better animal models, such as bacteria, worms, flies and primates, for the study of abnormal proteins and genes.
- Ongoing basic research into the structure and function of torsin proteins. Understanding the role of normal torsin is vital to discovering how the mutant protein causes dystonia.
- The development of a system of brain banking that would provide brain tissue from donors whose medical history is well documented. Ideally, donors should include not only individuals who had dystonia in life, but also gene carriers who have escaped dystonia symptoms.
- Further opportunities and encouragement for scientists from a variety of disciplines to collaborate and exchange insights and findings, raise questions and solve problems so that research into a cure for dystonia can progress as quickly as possible.

The program made clear to all that some of the most vital and basic questions surrounding this debilitating condition have yet to be answered. In the last few years, remarkable progress has occurred in the study of dystonia, with new discoveries making breakthroughs in this disease seem tantalizingly imminent.

*This first dystonia research think tank was sponsored by the National Institute of Neurological Disorders & Stroke (NINDS), Allergan, and GlaxoSmithKline.*



Seminar co-chairs Susan Bressman, MD, of Beth Israel Hospital, and C. Warren Olanow, MD, FRCPC, of the Mount Sinai Medical Center in New York City.



Members of our Scientific Advisory Board enjoying the welcome dinner the evening before the seminar began. From left, José Obeso, MD, University of Navarra Medical School, Spain, Joseph Jankovic, MD, Baylor College of Medicine, C. Warren Olanow, MD, FRCPC, Mount Sinai Medical Center, and Robert Burke, MD, Columbia University.

# Grant Awards

## New Grants Awarded to Advance Research and Knowledge

Based on recommendations by its Scientific Advisory Board, The Bachmann-Strauss Dystonia & Parkinson Foundation recently awarded grants of more than \$850,000 to further scientific inquiry in 2003. This includes funding for individual researchers at major institutions, as well as a grant to the Dystonia Medical Research Foundation. The following summarizes studies that will take place as a result of this key support:

### PARKINSON'S DISEASE

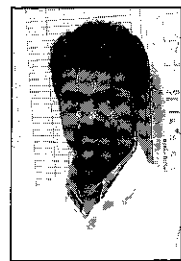


**Cause of Parkinson's Disease Probed-** The brains of people with Parkinson's disease show degenerated and dead neurons. These damaged neurons are associated with the accumulation of a long list of unwanted proteins, which then clump together to form the abnormal structures known as Lewy bodies, the hallmarks of Parkinson's disease. Dr. Kevin McNaught, of Mount Sinai Medical Center in New York City, suspects that a failure of the biochemical pathway responsible for cleaning out abnormal proteins – called the ubiquitin-proteasome system – may cause or contribute to sporadic cases of Parkinson's.

Dr. McNaught seeks to better understand what happens when molecules in the ubiquitin-proteasome system malfunction, and whether these malfunctions cause alterations in the normal expression of proteasomal components.

**Can Neurons Be Protected?-** Scientists know that the symptoms of Parkinson's disease are associated with the degeneration and death of dopamine-related neurons in the brain. If some way could be found to keep these neurons healthier longer, the course of the disease might be significantly improved.

Dr. Venugopalan Nair, of the Mount Sinai Medical Center, recently developed a laboratory model that mimics how the dopamine receptors of neurons respond in living brain tissue. This model will allow his research group to study whether certain dopamine-like compounds – called dopamine or D2 agonists, which have already been found to improve the symptoms of Parkinson's disease – might also keep neurons from degenerating or dying.



### DYSTONIA

**A Mouse Model of Dystonia-** Many breakthroughs in the understanding and treatment of human diseases would never have occurred without scientists developing an animal model of the disease. The first step toward real progress in studying many human diseases is finding a way to manipulate a strain of mice so that they will accurately manifest the human disease.

Recently, Dr. P. Shashidharan, of Mount Sinai Medical Center, announced that his group has generated what appears to be an accurate mouse model of childhood-onset dystonia. Like humans with dystonia, these transgenic mice carry a mutation in their DYT1 gene that causes them to express an abnormal form of the protein torsinA. These mice also exhibit symptoms of dystonia, and do so about as often as their human counterparts. Dr. Shashidharan is continuing to learn more about the effects the dystonia mutation has on motor function and physiology. In separate but closely related work, he is also investigating the cellular functions of torsinA.

**Normal and Mutant TorsinA: What Do They Do?-** Scientists know that childhood-onset dystonia is caused by a single mutation in a gene, called DYT1, which produces the protein torsinA. The role that normal torsinA performs in healthy people, and how abnormal (called mutant) torsinA causes the symptoms of dystonia, remain a mystery.

Dr. Xandra Breakefield, of Massachusetts General Hospital in Boston, is continuing experiments involving both the normal and mutant forms of torsinA. In her lab, both kinds of torsinA will be coaxed from cell cultures, and then the scientists will try to identify all the other genes that are affected by torsinA expression. They will seek to identify the proteins that interact with torsinA, or that participate in the same biochemical reactions as torsinA.

**Genes Involved in Adult-Onset Dystonia-** The most common form of dystonia is adult-onset, primary torsion dystonia (AOPTD). Scientists have long assumed that genetics must play a role in it, yet the vast majority of patients do not have any relatives with the same symptoms. For this reason, it's impractical to study dystonia using the standard methods employed in other inherited diseases – namely, to find all the people in a family with the same disease and then study what genes they have in common.

To overcome this, Dr. Laurie Ozelius, of Albert Einstein Medical Center, and Dr. Susan Bressman, of Beth Israel Medical Center in New York, are studying the genes of people with dystonia.

Recently, scientists discovered an association between a variation in the dopamine D5 receptor and patients with cervical dystonia or blepharospasm, the blinking form of the disease. This suggests that this gene, or perhaps a neighboring gene, could be involved. Drs. Ozelius and Bressman now plan to replicate this study, and then expand it to include other focal dystonias, such as writer's cramp and spasms of the vocal chord.

**Investigating the Role of TorsinA-** Scientists know that a mutation in the DYT1 gene, which codes for the protein torsinA, causes early-onset dystonia. But no one knows what normal torsinA does, or how abnormal (mutant) torsinA causes dystonia symptoms.

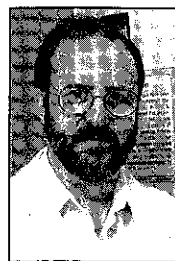
Dr. Kevin McNaught suspects that normal torsinA acts as a kind of molecular chaperone, enabling other biochemicals to degrade proteins that are no longer useful to the cell, but whose accumulation causes interference with normal nervous system functioning. To examine this, his laboratory will (1) determine whether mutations in torsinA interfere with the biochemicals that are responsible for proper protein housekeeping in cells; and (2) determine if excess proteins do indeed accumulate and aggregate in cultured cells that carry mutant torsinA, and in the brains of patients with dystonia. If his hypothesis proves accurate, scientists will know why torsinA is important to the nervous system, which could be the first step toward developing a treatment for dystonia.

**PET Brain Imaging in Dystonia-** Although the DYT1 mutation is a known cause of some forms of dystonia, only about 30% of people with the mutation actually exhibit noticeable symptoms. Dr. David Eidelberg, of North Shore University Hospital in Manhasset, N.Y., is using positron emission tomography (PET) to image living human brains to try to understand how those carriers of the mutation with the disease differ from those who have escaped it.

Dr. Eidelberg's group has obtained PET images of the brains of people who carry the DYT1 mutation, and found that despite the absence of symptoms, they show distinct abnormalities in brain organization under certain conditions. They have also found these brain abnormalities in carriers of non-DYT1 dystonias, but no one knows whether there are additional anatomical or functional changes in the brain that must occur prior to the onset of dystonia symptoms.

The group will continue to expand their studies to discover whether the alterations in brain function they have observed are linked to particular abnormal anatomical features, and whether they can be corrected by deep brain stimulation.

**Protein Under Study in Myoclonus Dystonia-** Scientists recently discovered that myoclonus dystonia, characterized by "lightening-like" muscle contractions, is caused by genetic mutations that disrupt the function of the protein epsilon-sarcoglycan. This protein is also involved in muscular dystrophy.



Using high-tech molecular techniques, Dr. Stuart Sealfon, of the Mount Sinai Medical Center, has begun studies of the function of epsilon-sarcoglycan. His research group aims to eliminate the protein from a neuronal cell line, and then study what effect this has on the cells' ability to survive, express genes, and communicate with each other. The scientists have also begun studying the mouse brain in hopes of discovering which neurons express the epsilon-sarcoglycan gene.

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*The Bachmann-Strauss Dystonia & Parkinson Foundation, Inc. was established in 1995 to find better treatment and cures for the movement disorders dystonia and Parkinson's disease, and to provide medical and patient information. An independent, nonprofit, 501(c)(3) organization, its funding is made possible through the generosity of individual and corporate contributors.*



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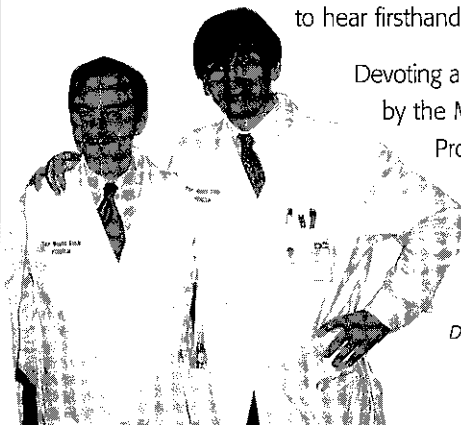
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## Hearing First-Hand about the Latest Advances

### Annual Dystonia & Parkinson's Symposia Shares Key Information

When Bonnie Strauss opened the annual Dystonia & Parkinson's Symposia this past fall, she addressed the broadest mix of patients, family members, researchers, medical students, laboratory technicians, doctors and other healthcare providers. Their common ground was to share information and to learn about the most up-to-date medical research, breakthroughs and insights, as well as current treatment and advances in drug therapies.

"Patients want to know where we are with treatment," said Margie Walden, The Bachmann-Strauss Dystonia & Parkinson Foundation Executive Director. "They're particularly interested in what's new on the horizon, especially any intervention that can slow the progression of their disease. This annual symposia enables everyone to hear firsthand about the latest developments and to ask questions."



Devoting a half day to each disease, the 2002 Dystonia & Parkinson's Symposia, presented by the Mount Sinai Medical Center, Department of Neurology, Movement Disorders Program and The Bachmann-Strauss Dystonia & Parkinson Foundation, Inc., was sponsored by Medtronic, Pharmacia, Boehringer Ingelheim, Allergan, and Teva NeuroScience. The next symposia are planned for fall 2003.

*At the Parkinson's symposium: From Mount Sinai Medical Center Department of Neurology, (L to R) Horacio Kaufmann, MD, Associate Professor of Neurology and Director of the Autonomic Disorders Research and Treatment Center, and Jean-Michel Gracies, MD, PhD, Assistant Professor.*