ACCELERATING THE CURE

The newsletter for friends and supporters of
The Michael J. Fox Foundation for Parkinson's Research

WINTER/SPRING 2008

$4.4 Million LEAPS Award Targets Glutamate System for New Class of Parkinson's Therapy

In December The Michael J. Fox Foundation awarded a $4.4-million *LEAPS* (*Linked Efforts to Accelerate Parkinson's Solutions*) grant to a multidisciplinary team of researchers led by Jeffrey Conn, PhD, of Vanderbilt University to jump-start the development of a new class of symptomatic Parkinson's disease drugs targeting the glutamate system and in particular a glutamate receptor called mGluR4.

Because the death of dopamine neurons is a hallmark of PD pathology, Parkinson's scientists traditionally have focused their efforts on modulating aspects of the dopamine system. But recent insights into the physiology of the basal ganglia (a brain region affected in Parkinson's disease) have shed light on the potential for treatments that could alleviate PD symptoms by "resetting" brain circuits. The glutamate system in particular has shown promise as a target for such treatments.

"Dopamine replacement therapies have long been considered the 'gold standard' of Parkinson's treatment. But they lose efficacy over time, alleviate only some of PD's symptoms, and cause side effects that can be as debilitating as the disease itself," said Katie Hood, CEO of MJFF. "Patients don't think this status quo is good enough, and neither does our Foundation. Dr. Conn and colleagues are aiming to bring about a 180-degree turn in PD treatment by developing an entirely new class of drugs that would bypass the dopamine system altogether."

In addition to Dr. Conn, the multidiscliplinary team of principal investigators comprises C. David Weaver, PhD; Colleen Niswender, PhD; Carrie K. Jones, PhD; Yoland Smith, PhD; and Craig W. Lindsley, PhD. All sit on the faculty of the Vanderbilt Program in Drug Discovery, with the exception of Dr. Smith, of the Yerkes National Primate Research Center.

What Is mGluR4?

Glutamate, like dopamine, is a neurotransmitter — a signaling molecule that plays a role in transporting brain messages and controlling body functions. Dr. Conn has shown in an animal model that increasing activity of a specific glutamate receptor, mGluR4, may alleviate symptoms of Parkinson's. In further work supported by MJFF's *Target Validation* initiative, his team identified molecules that increase mGluR4 activity. The researchers will now use a combination of medicinal chemistry, molecular biology, and animal studies to engineer these molecules into a compound that can be clinically tested for use as a drug that could provide sustained symptomatic relief.

Scientists do not yet fully understand how mGluR4 may work to alleviate Parkinson's symptoms. Research to date has indicated that mGluR4 activators may work by triggering a compensatory mechanism or process that allows the brain to send messages without the use of the dopamine receptors that die in Parkinson's disease.

The Business of Glutamate

Also in December, news media reported that two pharmaceutical companies, Addex Pharmaceuticals and Merck & Co., Inc. (through its affiliate Merck Sharp & Dohme Research Ltd.) had entered a collaboration and licensing agreement to develop a drug targeting mGluR4.

"The news of the Merck-Addex collaboration is very positive for us and our mGluR4 project," said Dr. Conn. "It will help stimulate activity in the area and could potentially drive interest from other drug companies in developing the compounds that will come out of our program. Pharma tends to follow its competition, so seeing Merck get into this area will make others want to do the same."

About *LEAPS*

LEAPS are multi-year, multi-million, multi-disciplinary projects that bring together "all-star" teams of researchers to address questions with significant practical impact on the treatment of Parkinson's disease. Continued funding is dependent on completion of predetermined milestones at specific stages.

More information on this and other *LEAPS* awards, including grant abstracts and researcher bios, is available at www.michaeljfox.org.

NEWS FROM THE CEO

In 2007 The Michael J. Fox Foundation funded about $25 million in Parkinson's research, bringing us over the $100-million mark in total research funded. While we're proud of the momentum and targeted activity that figure represents, the metric we find most meaningful is the same one you probably do: practical advances toward life-transforming treatments for Parkinson's disease.

With a new year under way, we are more committed than ever to doing whatever it takes to make those advances a reality.

We've recently announced over $8 million in funding for two *LEAPS* projects aiming to establish entirely new classes of PD therapies. You can read more about one of them at left. See pages 2 and 3 for information on our $2-million partnership with Merck Serono (EMD Serono in North America) to forge new treatments for those afflicted by PD-related cognitive and mood disorders, and to read a Q&A with an expert on the surprisingly common (and potentially debilitating) cognitive effects of Parkinson's disease. And see pages 6 and 7 for Foundation news and stories of Team Fox members and other friends who continue to apply limitless ingenuity and generosity to the fight for a cure.

No matter what we take on, we focus on one key question: How will this impact the lives of people with PD? Your friendship makes that focus possible. Together, I know, we're creating a future where Parkinson's disease is only a memory.

Katie Hood
Chief Executive Officer

IN THIS ISSUE

MJFF Partners with Merck Serono to "Invigorate Research and Therapeutic Development" for PD-related Cognitive Disorders

In December the Foundation committed up to $2 million for research toward therapies to alleviate Parkinson's-related cognitive dysfunction and mood disorders. Funding for the *Cognitive Deficits and Mood Disorders in Parkinson's Disease* initiative was made possible by generous leadership funding from Merck Serono (EMD Serono in North America), affiliates of Merck KGaA, Darmstadt, Germany.

"Most people think of Parkinson's disease as a motor disorder, but time and again, patients tell us that the cognitive and mood-related symptoms of PD — including depression, anxiety and executive dysfunction — are some of the most disabling aspects of the disease," said Katie Hood, the Foundation's CEO. "These symptoms frequently affect patients early in their disease and don't respond to dopamine replacement therapy. With the *Cognitive Deficits and Mood Disorders in Parkinson's Disease* initiative, we hope to invigorate research and therapeutic development in this very important area."

Cognitive dysfunction, which includes difficulty in planning, sequencing, initiating and sustaining behavior toward a given goal, and incorporating feedback to make adjustments along the way, is estimated to occur in up to 80 percent of people with PD. Depression is thought to affect up to 50 percent of Parkinson's patients. Anxiety and apathy also are often associated with PD.

"While treatments for classic forms of depression or anxiety have been developed, little evidence exists that they are optimal when used in Parkinson's patients," said Todd Sherer, PhD, the Foundation's vice president, research programs. "Additionally, while information from other fields must be leveraged in pursuing treatments for PD's cognitive and psychiatric symptoms, simple extrapolation of this knowledge to Parkinson's is not possible — perhaps due to the pathology of PD and its treatments."

Dr. Sherer noted that MJFF and Merck Serono hope, through their innovative partnership, to encourage Parkinson's scientists to collaborate with researchers from other areas, including psychiatry, in order to capitalize on work already done and to obtain different perspectives on cognitive and psychiatric disorders in Parkinson's disease.

While MJFF has funded research focused on cognitive dysfunction before, this initiative is the Foundation's first exclusively dedicated to this research area. Previous grants have examined aspects of cognitive dysfunction including acetylcholine deficiency, which has been linked to cognitive problems like concentration and executive functions, and approaches designed to test whether behavioral interventions can target the everyday action impairment that characterizes PD-related dementia. Other awarded grants have sought to test cognitive dysfunction as a risk marker or potential biomarker of Parkinson's disease.

In selecting research projects for *Cognitive Deficits and Mood Disorders in Parkinson's Disease*, MJFF hopes to address several cognitive issues, which include better understanding the pathophysiology of cognitive disorders, validating tools to predict or assess early development of cognitive dysfunction and evaluating the impact of existing PD treatments for these symptoms.

Elmar Schnee, president of Merck Serono, commented: "Merck Serono recognizes the urgent need for new therapies to alleviate PD-related mood disorders and cognitive dysfunction, and we look forward to supporting The Michael J. Fox Foundation in pursuit of effective treatments for these under-addressed aspects of Parkinson's disease. Our support of the Foundation is just one example of our commitment to driving the innovative science that will allow every individual to live a fuller and more satisfying life."

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>
> — Katie Hood

Quick Facts on PD-related Cognitive Dysfunction

- **Historically, the cognitive aspects of Parkinson's disease and its impact on patients' functioning and well-being have been under-recognized and overshadowed by the motor features of the disease.**
- **Using sensitive neuropsychological tests, cognitive dysfunction has been discovered to be common and present early in the course of Parkinson's disease.**
- **The cognitive dysfunction associated with Parkinson's disease differs significantly from Alzheimer's disease, tending to impact abstract reasoning, planning, visuospatial function, and verbal fluency more than memory.**
- **Clinical tools used to diagnose cognitive impairment are not currently as refined as those used to diagnose Alzheimer's disease and other dementias.**
- **Factors that may predispose Parkinson patients to develop cognitive impairment include older age, longer disease duration, male gender, lower education, and greater motor dysfunction.**
- **Patients with the following symptoms are more likely to develop cognitive complaints: poor balance, depression, delusions, and hallucinations.**
- **Cognitive dysfunction can worsen over time and progress to dementia.**
- **While there is one FDA-approved medication to treat dementia associated with Parkinson's disease, rivastigmine, no treatments currently exist for the less severe cognitive dysfunction that precedes progression to dementia.**

David Weiner, MD, talks to MJFF about PD-related Cognitive Dysfunction

This month The Michael J. Fox Foundation is reviewing grant proposals under its *Cognitive Dysfunction and Mood Disorders in Parkinson's Disease* program. This new initiative, launched in December, was made possible by generous leadership funding from Merck Serono (EMD Serono in North America), affiliates of Merck KGaA, Darmstadt, Germany. For practical answers to questions about the diagnosis, progression and treatment of cognitive dysfunction in Parkinson's disease, the Foundation spoke to David Weiner, MD. Dr. Weiner is an expert in drug discovery and development for human neuropsychiatric disease and a member of the MJFF Scientific Advisory Board.

Does cognitive dysfunction in Parkinson's disease differ from normal aging-related cognitive decline?

This is a very important point. It's true that a certain degree of impairment is associated with normal aging. In general, when we talk about cognition and the higher mental functions that are unique to humans, we do not categorize impairment or classify it as cognitive dysfunction or dementia until patients reach a level or scope of impairment that goes beyond what's seen in healthy aging.

How can a patient know what goes beyond normal? When is it appropriate to talk to one's doctor?

This can be difficult. In the early stages of any disease involving cognitive dysfunction or dementia — including PD and Alzheimer's disease — there is often a period of uncertainty. If there is a bigger problem, it tends to become clear over time.

Parkinson's-related cognition problems, unlike those seen in Alzheimer's, do not typically affect memory. Rather, in PD we talk about issues with what's called "executive function." Practically speaking, what you are looking for is difficulty with everyday activities that rely on mental functioning, such as balancing a checkbook or being able to concentrate on something even in the presence of distractions — think of focusing on a conversation at a crowded dinner table where people are talking across each other. Driving can also become extremely problematic because of PD-related problems with visuospatial functioning (the ability to process information about where objects are in space, how they fit together and where they are in relation to your body). This is entirely separate from tremor or other motor aspects of the disease.

In determining when it may be appropriate to present the problem to your doctor — you want to be on the lookout for problems like these that are frequently present, worsen over time and eventually make it difficult or impossible to just get through the basic activities of the day without undue hardship.

I'd also like to emphasize how important it is to see a neurologist or movement disorder specialist. Research into the cognitive and mood aspects of PD is very new. In fact, this avenue of research has opened up only in the past 20 years or so, with a major proportion of the work happening in the last five to seven years. What this means in practical terms is that a primary care physician or general practitioner is far less likely than a neurologist or movement disorders specialist to be up to date on the most recent developments and potential interventions that can impact treatment regimens.

You mentioned dementia. Is that different from cognitive dysfunction?

Clinically, we use the term "dementia" to indicate that cognitive dysfunction has reached a certain specific degree of severity. This is true both in Parkinson's-related and other forms of dementia. There are specific, structured clinical criteria that must be present to support a diagnosis of dementia. A neurologist can use neurobehavioral tests to determine whether or not these criteria are present.

In Parkinson's, we know that cognitive dysfunction can be present from the very earliest stages of the disease — for some patients, maybe even before a diagnosis of PD. If cognitive dysfunction is diagnosed, clinically we would expect it to worsen as the disease progresses and eventually lead to a diagnosis of Parkinson's-related dementia. The timeline for this varies across individual patients.

Is any particular type of PD patient at statistically greater risk of developing cognition problems?

Yes, there are a few known clinical risk factors. The first is age — the older you are, the more likely you are to have cognitive problems. The second is disease duration: the longer you have lived with the disease, the higher the likelihood. So, for example, if you surveyed 100 PD patients at random, those who had lived with the disease for one or two years would be statistically less likely to report cognitive issues than those who had been diagnosed 15 to 20 years before. People whose Parkinson's includes major problems with freezing, posture and gait also seem to be more likely to suffer from cognitive issues, although more research is required to understand why this is the case.

Finally, preliminary evidence suggests that a relatively higher level of education may protect against developing cognitive issues in PD. But this theory is not well established, and a great deal more research is needed to determine whether it is supported by a preponderance of scientific evidence.

Are patients with cognitive dysfunction more likely to experience PD-related mood disorders as well?

Yes. It seems that patients experiencing prominent problems with cognition are more likely also to be afflicted by hallucinations and mood disorders, such as depression or apathy. Cognitive problems are part of a neurobehavioral syndrome that occurs with some cases of PD.

These symptoms do not respond to dopamine replacement therapies, correct?

That's correct. More research is needed in this area, but dopaminergic drugs do not appear to significantly improve or worsen PD-related cognitive dysfunction.

What treatments are available?

Currently one drug, borrowed from Alzheimer's disease, has been approved to treat PD-related dementia. This drug, rivastigmine (sold under the brand name Exelon), is an acetylcholinesterase inhibitor. It causes nausea in some individuals, but it's generally well-tolerated. Its main limitation is that it's far from life-changing. And we are entirely without a drug that could treat early cognitive dysfunction — whether by alleviating symptoms or by slowing or stopping the underlying progression of the disease.

In addition to the lack of treatments, the field is hindered by a lack of certain very important clinical tools. For one thing, there is a critical need for a simple tool or test to measure cognitive function in the context Parkinson's disease over time. There is such a test for Alzheimer's, known as ADAS-Cog (Alzheimer's Disease Assessment Scale-cognitive subscale). We do not yet have a corollary for this in PD.

CONTINUED ON PAGE 8 >>

Note: The medical information contained in this article is for general information purposes only. The Michael J. Fox Foundation has a policy of refraining from advocating, endorsing or promoting any drug therapy, course of treatment, or specific company or institution. It is crucial that care and treatment decisions related to Parkinson's disease and any other medical condition be made in consultation with a physician or other qualified medical professional.

NEWSBRIEFS

THE MICHAEL J. FOX FOUNDATION ROUTINELY POSTS UPDATED INFORMATION ABOUT FUNDED PROJECTS ON ITS WEB SITE, **WWW.MICHAELJFOX.ORG**. FOR MORE INFORMATION ABOUT ANY OF THE PROJECTS LISTED BELOW — INCLUDING GRANT ABSTRACTS, RESEARCHER BIOS AND SUPPLEMENTAL GRANT INFORMATION (WHERE APPLICABLE) — PLEASE SEARCH OUR FUNDED GRANTS DATABASE LOCATED IN THE RESEARCH SECTION OF OUR WEB SITE AT WWW.MICHAELJFOX.ORG/RESEARCH.CFM.

RRIA Brings "Out of the Box" Ideas to Surface to Determine Scientific Potential

In December MJFF announced the launch of its $2-million *Rapid Response Innovation Awards (RRIA)* 2008 initiative. This program is designed to ensure that researchers have what they need to pursue good ideas without delay. *RRIA* accepts proposals on a rolling basis and speeds up to $75,000 to one-year 'high-risk, high-reward' basic, preclinical or clinical research projects in any Parkinson's-relevant arena. The program is intended to bring 'out of the box' ideas to the surface and quickly vet their therapeutic potential. The program targets projects that may have little to no preliminary data, but could significantly impact understanding or treatment of Parkinson's disease. The program has received a strong response from the scientific community, with 28 projects funded in 2007.

For more information, search the funded grants database at www.michaeljfox.org/research.cfm by program name Rapid Response Innovation Awards.

Biomarkers 2007 Awardees Announced

In December MJFF announced funding under the third round of its *Biomarkers* program, dedicated to developing objective biomarkers, or "biological fingerprints," of Parkinson's disease. In keeping with the Foundation's commitment to ensure that promising research moves forward as efficiently as possible, four of five projects under the 2007 initiative are extensions of work funded under earlier rounds of the *Biomarkers* program. The Michael J. Fox Foundation has been a field leader in spearheading the search for a PD biomarker, with approximately $8.5 million in biomarker research funded to date.

For more information on this project, search the funded grants database at www.michaeljfox.org/research.cfm by program name Biomarkers.

Clinical Research Projects Funded under Clinical Discovery Program 2007

Five clinical research studies were awarded funding under the Foundation's 2007 *Clinical Discovery Program*. This annual initiative funds clinical research projects with strong potential to yield new treatments for people living with PD. *The Clinical Discovery Program* is characteristic of the MJFF approach to translation: it vigorously aims to accelerate progress and directly benefit patients. The Foundation partners with teams that can execute clinical research critical to moving good ideas one step closer to people with Parkinson's disease. Each of the funded studies will focus specifically on improving patients' quality of life, addressing common and debilitating aspects of PD such as depression, dyskinesia (the uncontrollable movements that are a side effect of long-term levodopa treatment), sleep disorders and excessive salivation.

For more information on this project, search the funded grants database at www.michaeljfox.org/research.cfm by program name Clinical Discovery Awards.

Supplemental Funding Awarded toward Better Treatments for Gastrointestinal Symptoms of PD

Gastrointestinal (GI) symptoms of Parkinson's such as nausea, bloating and constipation do not respond to dopamine replacement therapies. They detract from patients' quality of life and can affect other aspects of PD — for example, they can cause erratic absorption of oral medications, contributing to motor fluctuations and medication side-effects. The development of improved treatments for GI symptoms in PD is hindered by the lack of an animal model that mimics these symptoms. In 2006 Jim Greene, MD, PhD, of Emory University School of Medicine was awarded funding under MJFF's *Dopamine-non-responsive Symptoms of Parkinson's Disease* program to develop such a model. At the one-year assessment meeting in December, Dr. Greene reported that he had achieved project milestones and promising results to date. To keep this work moving forward, the Foundation quickly approved supplemental funding to allow Dr. Greene to fully characterize GI disorders in rodent models of PD. If successful, Dr. Greene's work could result in a critically needed research tool and spark new interest in this topic from the research community at large, accelerating progress toward new treatments.

For more information on this project, search the funded grants database at www.michaeljfox.org/research.cfm by researcher last name Greene.

Critical Challenges Awardees Work to Clarify Role of **LRRK2 and Alpha-Synuclein Genes** in Parkinson's Disease

In January, The Foundation announced approximately $2 million in total funding for seven research studies aiming to advance the ability of the Parkinson's research field, and drug makers, to therapeutically target two genes — LRRK2 and alpha-synuclein. The funding was awarded under MJFF's *Critical Challenges in Parkinson's Disease* program.

"*Critical Challenges* is uniquely designed to increase researcher focus on specific research challenges standing in the way of therapeutic progress," said Katie Hood, chief executive officer. "In this round, our research staff canvassed the world's leading PD experts to identify the precise issues holding up LRRK2 and alpha-synuclein drug development. We then structured our funding to incentivize scientists to look for the exact answers that will break down those roadblocks and allow work to move forward with greater impact. As in everything we do, our ultimate goal is to advance scientific solutions that can tangibly improve patients' quality of life."

Why LRRK2 and Alpha-Synuclein?

LRRK2 and alpha-synuclein were selected for study under the first funding round of MJFF's *Critical Challenges in PD* program following a survey of the field by the Foundation's research staff and advisors. Alpha-synuclein was the first gene associated with PD, and pathological clumping of the protein product of the alpha-synuclein gene within cells of the brain represents a nearly universal thread linking multiple forms of Parkinson's. The association of the LRRK2 gene to PD was discovered more recently but appears to contribute to a substantial number of Parkinson's cases — as high as 40 percent in some ethnic groups.

Alpha-Synuclein Challenge

Investigators funded under the alpha-synuclein challenge will look at various ways in which disease-related modifications of alpha-synuclein might lead to toxic effects. Hilal Lashuel, PhD, of Swiss Federal Institute of Technology Lausanne in Switzerland and Chris Rochet, PhD, of Purdue University will determine which modified forms of alpha-synuclein have the greatest effects on aggregation and toxicity to dopamine neurons. A third investigator, Deniz Kirik, MD, PhD, of Lund University in Sweden, will test the hypothesis that the toxicity of alpha-synuclein may be enhanced by interaction with dopamine itself, which might help further explain the selective vulnerability of these cells in PD.

LRRK2 Challenge

The four investigators funded under the LRRK2 challenge all seek to test whether an abnormal increase in LRRK2's enzymatic function triggers toxicity. Chenjian Li, PhD, of Weill Medical College of Cornell University and Zhenyu Yue, PhD, of Mount Sinai School of Medicine are each developing mice genetically engineered to express mutant forms of the LRRK2 gene, including a form that lacks enzymatic function, to directly test the hypothesis. Two other investigators, Romain Zufferey, MD, PhD, of Swiss Federal Institute of Technology and Andrew West, PhD, of the University of Alabama at Birmingham, will perform similar studies but will instead deliver the modified LRRK2 gene directly to brain cells using modified viruses, technology similar to that used in gene therapy.

Grant abstracts and researcher bios for all projects are available on the Foundation's Web site, www.michaeljfox.org.

Irene Hegeman Richard, MD, Appointed Senior Medical Advisor to MJFF

In November the Foundation announced the appointment of Irene Hegeman Richard, MD, associate professor of neurology and psychiatry at the University of Rochester School of Medicine and Dentistry, as Senior Medical Advisor — a newly created role that formalizes her participation in helping to inform and develop MJFF's clinical agenda.

"Irene's clinical research perspective complements the scientific expertise of Gene Johnson, PhD, MJFF's Chief Scientific Advisor, and her input will be a boon to our research staff and advisors in continually raising the bar on the patient-relevant outcomes we expect from every project we fund," said Katie Hood. "Additionally, as a clinician with an active neurology practice, Irene has a deep understanding of the challenges faced every day by people living with PD — something the Foundation values deeply, since patients are at the center of every activity we undertake."

Dr. Richard runs a research program and clinical practice at the University of Rochester focusing on the psychiatric aspects of Parkinson's. She is currently leading SAD PD (Study of Anti-Depressants in Parkinson's Disease), a large-scale multi-center clinical trial evaluating the treatment of PD-related depression. Her efforts have brought new clinical and research attention to the previously overlooked area of mood disturbances in Parkinson's. Establishing her as Senior Medical Advisor will help ensure that MJFF's increasing involvement in clinical trials is as efficient and targeted as possible. She will also provide important feedback on pre-clinical experimental design, helping to ensure that all studies funded by MJFF — not only those requiring the active involvement of patients — are designed with potential clinical issues in mind.

Dr. Richard has served on the Foundation's SAB since 2006. She also has been a member of the review committee for the Foundation's annual *Clinical Discovery Program*, which funds high-impact clinical projects in PD, since the program was first launched in 2004, and has played a key role in continually refining its specific criteria for patient-relevant grant selection. Additionally, she has frequently spoken to MJFF friends and supporters at the Foundation's Research Roundtable events across the country.

"As a grant reviewer for the Foundation and a member of its Scientific Advisory Board, I've been impressed by The Michael J. Fox Foundation's extraordinary commitment to speeding scientific solutions to the clinic and patients — a commitment I share," said Dr. Richard. "The Foundation understands that it's never too early in the drug development process to think clinically, and I'm thrilled to take on formal responsibility for working with its staff and advisors to continually improve our ability to do this across the board."

Dr. Richard's biosketch, as well as a Q&A the Foundation conducted with her focusing on mood disorders in Parkinson's disease (originally published in the Summer 2007 edition of *Accelerating the Cure*), are available at www.michaeljfox.org.

Party for Parkinson's

Friends Brenda Mifsud and Diane at the event

When Kathy Zweifel of Seville, Ohio, was diagnosed with young-onset Parkinson's disease at age 35, she was in shock. At first, she tried to hide her disease from others. But after learning more about Michael J. Fox's story, the Foundation and Team Fox, Kathy made a decision: She wasn't "going to sit around and not do anything while Team Foxers were busy fighting for a cure."

In December, Kathy hosted her Second Annual Party for Parkinson's Fundraiser and Silent Auction. Over 200 items were donated to the auction, along with food and the actual event space. The event was for women only as a chance to get some early holiday shopping done and catch up with friends. Participants were encouraged to bring handmade items for the silent auction and the chance to win an LCD/HDTV. As part of the event, Kathy also had a jewelry sale of her handmade Parkinson's awareness bracelets.

Kathy credits Team Fox for "bringing the community together and really supporting the cause." The event raised over $5,000 for Parkinson's research.

Michael J. Fox and Stephen Colbert backstage at "A Funny (Groovy) Thing Happened on the Way to Cure Parkinson's," held Saturday, December 1, at the Sheraton New York. Mr. Colbert hosted the event, which raised $5.5 million for Parkinson's research. Lisette Ackerberg, Donna Karan, Jennifer and Marc Lipschultz, and Kim and Jim Pallotta co-chaired the Woodstock-themed event featuring musical performances by John Mayer, Joan Osborne, Levon Helm, Gavin DeGraw and house band The Soul Ramblers. Over 1,000 guests, including Julianne Moore, Lance Armstrong, Rachael Ray, Governor of New York Eliot Spitzer and Mayor of Newark Cory A. Booker joined Michael J. Fox and Tracy Pollan for the Foundation's 2007 gala.

Friends and Family Put the "Fun" in Fundraising

Even before Team Fox was officially launched in 2006, MJFF was deeply fortunate to benefit from the commitment of community fundraisers all over the country who put their time, energy and creative spirit into raising money for Parkinson's research. Gary Umetsu was one of those fundraisers who ultimately inspired the creation of Team Fox (of which he quickly became a charter member).

Seven years ago, when the mother of Gary's close friend was diagnosed with PD, Gary's motivation was sparked. He got to work planning his first golf tournament to raise money for MJFF as a way to give back. That first event began with 28 people and raised $5,000 — already an impressive total — but Gary had set his goals high and decided to work toward one day holding a full golf tournament.

In December 2007 Gary achieved his goal, attracting 144 guests, including the original 28 golfers from the very first tournament he had organized. To date, he has raised an amazing $30,000 for Team Fox. But this tireless fundraiser keeps his accomplishments in perspective. "It's a great feeling," Gary says, "to know that getting together with friends for a good day out is raising money that will benefit MJFF."

(L-R:) Steve Cecil, Lisa Ezra, Charly Woods and Eric Tabak spend a day out on the course for a good cause

Ride for a Cure

When Jo Martinelli hosted her first Team Fox event in "Ride for a Cure" in Sunland, California, in November, she didn't start small. Jo and her team of helpers sent out newsletters, created posters and used word of mouth to let the community know about her event. Her successful outreach and publicity efforts attracted nearly 1,500 people, and this western-themed family event raised over $14,000 for Parkinson's research.

Horseback rider Jessica John gallops for a cure

The all-day benefit featured live music, great food, guest speakers and western specialties including barrel races and donkey rides.

When Jo first started planning, she "was really determined and just went for it." She thought the Ride would be a one-time thing. But the success and excitement have inspired her to make it an annual event. She and her guests are already looking forward to an even bigger and better rodeo-style event later this year.

Andrew S. Grove, Co-Founder of Intel, Dedicates Portion of Estate to MJFF

In January Andrew S. Grove, co-founder of technology giant Intel and senior advisor to The Michael J. Fox Foundation for Parkinson's Research, announced that he would bequeath a portion of his estate, up to $40 million, to the Foundation. Mr. Grove's gift will establish **The Grove Circle** (see sidebar, *right*), a society to honor those who provide for the Foundation through their wills or other planned gifts.

"Andy's gift is not only an incredible vote of confidence in MJFF, but will also have a dramatic impact on our ability to fund paradigm-shifting PD research," said Katie Hood, CEO of The Michael J. Fox Foundation. "Andy's generosity, and his leadership in establishing The Grove Circle for planned gifts, will further strengthen our longtime partnership in pursuing our common goal — to do whatever it takes, including driving change of a flawed system, to speed delivery of transformative treatments and a cure for Parkinson's disease."

A longstanding relationship

Mr. Grove has worked closely with MJFF's leadership since May 2001. He formalized his role, accepting the title of Senior Advisor to the Foundation, in January 2006.

"Despite decades of research, we have no known cure for any neurodegenerative disease today," said Mr. Grove. "Coming up with new treatments may require creative and even unorthodox approaches. Every interaction I've had with The Michael J. Fox Foundation over the years has demonstrated their willingness to go where others may hesitate. There is no one I trust more than the Foundation's leadership and staff to direct my contribution effectively."

Mr. Grove specifically pointed to the Foundation's progress in building an in-house scientific team that actively injects itself into the research process, drives collaboration between academic and industry researchers and, increasingly, targets funding to identify and advance the most promising therapeutic targets for PD.

A "cultural revolution" for biomedical research

Following his diagnoses of prostate cancer in 1995 and Parkinson's disease in 2000, Mr. Grove's has become a major voice calling for a "cultural revolution" in biomedical research to speed the delivery of cures.

In November 2007 he spoke at the annual meeting of the Society for Neuroscience, arguing that finding new treatments for disease requires different attitudes toward failed experiments and a major rebalancing of research spending.

Concluded Michael J. Fox: "Andy has been an incredible benefactor to our Foundation throughout our years of working together. Leave it to him to find one more way to maximize the impact of his generosity and foresight on behalf of PD patients everywhere."

The Grove Circle for Planned Giving

Mr. Grove's gift will provide a further boost to MJFF's momentum by establishing The Grove Circle, a new planned giving society honoring the Foundation's many friends who plan their estates to support The Michael J. Fox Foundation after their families' needs have been met.

Deborah W. Brooks, co-founder of MJFF, commented, "The Michael J. Fox Foundation's mission has always been to put itself out of business by curing PD. Needless to say, this key Foundation value is not changing with the establishment of a planned giving effort. Rather, the planned giving established by The Grove Circle's members will provide a major, long-term funding source around which we can plan and which we can leverage immediately to accelerate groundbreaking research."

Members of The Grove Circle will be listed in the Foundation's annual report and will receive regular updates from MJFF on the PD therapeutics development efforts made possible by their support.

For details on becoming a Charter Member of The Grove Circle — in strict confidence and with no obligation — please contact Karen Leies, MJFF's vice president for Development, at kleies@michaeljfox.org or (800) 708-7644.

Katie Hood Appointed CEO of The Michael J. Fox Foundation

On December 14, the Foundation announced the appointment of Katie Hood as chief executive officer. Ms. Hood had served as interim CEO since October.

"I'm proud and passionate to lead an organization that puts patients' interests squarely at the center of every one of its activities," said Ms. Hood. "Over the past seven years this Foundation has built a unique expertise about Parkinson's research that we will continue to leverage in our mission to aggressively translate research into transformative therapeutic results."

As chief executive officer, Ms. Hood will build on the Foundation's strategy of inserting itself proactively into the research process to advance scientific breakthroughs. She will be active in the expansion of current MJFF initiatives which include validating promising drug targets, increasing investment in pre-clinical research, selectively supporting clinical projects with the potential to improve patients' lives in the near-term, and driving high-risk, high-reward attempts to uncover critically needed new research tools.

David Golub, chairman of the MJFF Board of Directors at the time Ms. Hood's appointment was announced, said: "We are committed to a strategy of working relentlessly to close critical gaps in the process of moving potential treatments from the laboratory to Parkinson's patients, and have worked with Katie and the entire executive team to develop a compelling vision of how that approach should be enhanced and extended for greater impact. The Board is confident that Katie is the right person to lead the MJFF forward and is sure that our efforts will result in scientific breakthroughs that ultimately translate into novel and effective therapies."

"MJFF gave me the opportunity to be part of creating something I feel incredibly strongly about"

More About Katie Hood

Katie Hood joined the staff of MJFF in September 2002 as research manager and was promoted to vice president, research programs, in January 2005. She was promoted again, to the position of deputy CEO, in June 2006. Her rise to the uppermost levels of Foundation leadership was directly proportional to her passion for the organization's mission to bring better treatments to those touched by Parkinson's disease: "I had been fortunate to hold interesting and challenging positions before joining the Foundation, but my role at MJFF gave me the opportunity to be part of building and creating something I feel incredibly strongly about — helping drive development of treatments that could defeat a devastating disease and transform millions of lives," Ms. Hood says.

Prior to joining the Foundation, Ms. Hood was employed as a consultant at Bain & Company in New York City, doing work in the consumer products, financial services, and nonprofit sectors; she also served as an analyst in the Credit Department of Goldman, Sachs & Co., and as a program coordinator with Duke University's Hart Leadership Program.

Ms. Hood graduated from Harvard Business School and holds a BA in Public Policy Studies from Duke University in Durham, North Carolina. She lives near New York City with her husband and two children.

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WINTER/SPRING 2008 NEWSLETTER

David Weiner, MD, talks to MJFF about PD-related Cognitive Dysfunction

(CONTINUED FROM PAGE 3)

You're describing a simple test that could be administered in a doctor's office to test cognitive function?

Correct. There's an obvious patient benefit to such a test being available when you see your doctor. But this is also a critical component of drug development for PD. Think of it this way: If we had a simple and reliable way to study cognitive function over time in people with Parkinson's, it's possible that cognition could be used as a clinical trial endpoint — a tool that would help us measure disease progression and tell us whether drugs in clinical trials are exerting a neuroprotective, not just symptomatic, effect.

This is where the research comes in. I'm so excited about the *Cognitive Dysfunction and Mood Disorders* program that MJFF is reviewing this month. It's going to encourage PD researchers, as well as experts in cognitive matters outside of the context of PD, to jump in and propose high-impact research to get us closer not only to new treatments but to new clinical tools that will help advance the entire field that much faster.

Why aren't we further along today in addressing the cognitive aspects of PD?

It's clear that the treatment landscape is less than optimal, and this is deeply frustrating for people living with Parkinson's. But you have to remember that we're overcoming nearly two centuries of Parkinson's being thought of as primarily a motor disease. When James Parkinson first described PD in 1817, he thought it was a movement disorder that left the "senses and intellect intact." We know so much more today than we did only 10 years ago, and programs like *Cognitive Dysfunction and Mood Disorders* will help to make strides in understanding and treating this part of the disease. I'm optimistic about the progress we've made in a relatively short time, and I'm confident that we're going to make inroads into this problem in the foreseeable future.

Dr. Weiner is senior medical director of the Neurology Global Development Unit at EMD Serono, Inc., Rockland, Massachusetts. His biosketch is available at www.michaeljfox.org.

ACCELERATING THE CURE is published three times a year by The Michael J. Fox Foundation. The spring and summer issues are mailed to donors of $25 or more within the past 12 months. The fall issue is mailed to all MJFF friends and supporters. All issues are available on our Web site, **www.michaeljfox.org**. To subscribe or unsubscribe, or with questions or feedback, please e-mail the editor at the address at right.

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THE MICHAEL J. FOX FOUNDATION IS DEDICATED TO FINDING A CURE FOR PARKINSON'S DISEASE WITHIN THE DECADE THROUGH AN AGGRESSIVELY FUNDED RESEARCH AGENDA AND TO ENSURING THE DEVELOPMENT OF IMPROVED THERAPIES FOR THOSE LIVING WITH PARKINSON'S TODAY.