THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

ACCELERATING THE CURE

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

SUMMER 2008

Michael J. Fox Foundation Awards **$5.6 Million** for Phase 2 Clinical Trial of **Inosine/Urate**

In April The Michael J. Fox Foundation announced that it would furnish $5.6 million, its single largest award to date, to drive a Phase 2 clinical trial investigating the potential of inosine — a naturally occurring chemical that gives rise to urate in the body — to slow or stop the progression of Parkinson's disease.

The work is being funded under the Foundation's *LEAPS (Linked Efforts to Accelerate Parkinson's Solutions)* 2007 initiative. *LEAPS* 2007 was funded with a lead gift from the Edmond J. Safra Foundation, one of the most steadfast supporters of The Michael J. Fox Foundation since its inception.

Urate is a natural metabolite and major antioxidant in humans. Past studies have found that healthy people with higher urate levels in the blood had a reduced risk of developing PD. More recent work, including a study published in the journal *Archives of Neurology* by two of the principal investigators on this *LEAPS* award, have linked higher urate levels to a possible slower progression of the disease.

"These findings, combined with prior knowledge of urate's protective properties in laboratory studies, raise the possibility that urate-elevating strategies could be used to slow the neurodegeneration of Parkinson's disease," said Michael Schwarzschild, MD, of the Massachusetts General Hospital Institute for Neurodegenerative Disorders and Harvard Medical School. Dr. Schwarzschild is lead author of the April *Archives of Neurology* paper and coordinating principal investigator of the *LEAPS* award.

MJFF moves quickly to amass data around preliminary findings from epidemiology

Studies linking urate and Parkinson's are based on interesting epidemiological observations that clearly warrant further research. But because inosine is a publicly available compound, no corporate entity has the financial incentive to fund costly clinical trials definitively assessing its potential to protect patients from the effects of PD.

"This *LEAPS* project is precisely the sort of work that The Michael J. Fox Foundation exists to identify and drive forward for patients' benefit," said Katie Hood, the Foundation's CEO. "We believe it is our obligation to the PD community to step in where other funders may be unwilling to go, and ensure that innovative approaches like this one do not stall for lack of resources."

The goals of the *LEAPS* award are to determine the safety of using inosine to raise urate levels, and to assess optimal dosage for therapeutic effect. Ninety people recently diagnosed with Parkinson's disease will be enrolled in a randomized, double-blind clinical trial to determine whether and at what dose inosine can safely elevate levels of urate in cerebrospinal fluid. Three months after enrollment, cerebrospinal fluid will be tested for urate levels. If a tolerable dose of inosine adequately increases urate in the cerebrospinal fluid, subjects will continue on treatment for up to two years to assess long-term safety.

A cautionary note for patients

Inosine is widely available to consumers in dietary supplement form. The researchers emphasize, however, that people with Parkinson's should not take inosine unless they are participating in a clinical trial.

"Potential benefits of urate have to be tempered against the known risks of elevated urate levels, which include gout and kidney stones," said Alberto Ascherio, MD, DrPH, of the Harvard School of Public Health and senior author of the *Archives of Neurology* paper, who joins Dr. Schwarzschild as a principal investigator on the *LEAPS* award. "From what we know now, urate elevation should be attempted only in the context of a closely monitored clinical trial, in which potential benefits and risks are carefully balanced."

Dr. Ascherio noted that the evidence to date surrounding inosine and PD does not prove a cause-effect relationship. Additionally, elevated urate levels are known to carry certain health

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NEWS FROM THE CEO

Another spring has passed, and with it, one of the busiest seasons in The Michael J. Fox Foundation's annual calendar. In spite of the feverish pace, I've been reflecting on a quote I read in a recent *Wall Street Journal* Op-Ed written by Jack Kemp, the former congressman and HUD secretary.

Mr. Kemp wrote: "All great achievements in our nation's progress… have been led by a combination of agitation and idealism." He wasn't talking about PD or even medical research. But to me, his description of the two core ingredients for great advances resonates with our mission to find the cure.

Our efforts, too, are one part agitation. We must highlight what's incomplete in the way medical research is currently funded, push for greater experimentation and risk-taking in the research we fund and the role private dollars can play, and refuse to accept the status quo. The second part of the equation, idealism, is just as crucial. We must believe in our hearts that we can and will identify the science leading to new and better treatments, and hold fast to that belief, no matter how challenging the quest can sometimes feel.

Your support is critical to both these core ingredients of progress. And I cannot thank you, our friends and contributors, enough for the enthusiasm, personal commitment and dedication you bring to our shared goal of finding the cure.

Warm regards,

Katie Hood

Katie Hood
CEO

IN THIS ISSUE

"Research 2.0"

Harnessing Web-based Technology to Change the Face of PD Clinical Research

There is little question that the Internet is changing the way we live. According to an April 2006 report from the Pew Internet & American Life Project, fully 73 percent of respondents (about 147 million adults) are Internet users, up from 66 percent (about 133 million adults) in a January 2005 survey. Over time, the report finds, Internet users have become more likely to note big improvements in their ability to shop and the way they pursue their hobbies and interests. A majority of Internet users also consistently report that the Internet helps them to do their job and improves the way they get information about health care.

Now two current Michael J. Fox Foundation initiatives seek to harness the power of the Internet to change — and potentially revolutionize — the way Parkinson's clinical research is conducted.

"Our Foundation sees vast potential in Internet and Web-based technologies to benefit people with Parkinson's by accelerating the development of diagnostic tools and transformative treatments for Parkinson's disease," said Katie Hood, MJFF CEO.

Historically, clinical research in Parkinson's (and other diseases) has required patients to travel, often several hours or more, for in-person interviews, examinations and tests. This is a burden for anyone living with a disease, and takes an incredible toll on people with PD, where unpredictable motor and non-motor effects, as well as the efficacy and side effects of medication, vary from day to day. Furthermore, the existing model for clinical research creates roadblocks to amassing a pool of study participants large enough to identify the cause(s) and early indicators of Parkinson's disease.

MJFF seeks to improve on this status quo by driving innovative, easy-to-use, scientifically validated Web-based tools that facilitate the gathering of reliable clinical and risk-factor information for Parkinson's disease research. A long-term aim is to increase the frequency and uniformity of patient data collection by allowing any interested Parkinson's patient to contribute to medical research from the convenience of home.

Support for 23andMe/Parkinson's Institute collaboration

In May 23andMe, a privately held personal genetics company, and The Parkinson's Institute and Clinical Center announced a research initiative, with financial support from MJFF, to support the development of advanced methods and tools for clinical and epidemiologic research for Parkinson's disease.

Together, 23andMe and The Parkinson's Institute will design and validate Web-based clinical assessment tools that can be administered to online communities. Additionally, 23andMe will establish a social networking platform to facilitate the development of communities and research projects based on common traits of Parkinson's disease patients.

Parkinson's Institute patients will provide specific information and insights including their individual environmental exposures, family history, disease progression and treatment response. Patients' risk factor and clinical data collected through the newly developed and validated Web-based tools will then be merged with their genetic data to conduct path-breaking research on Parkinson's disease.

Through the deployment of this innovative, Web-based approach, the initiative will help to expand the involvement of Parkinson's disease patients in clinical research and increase the frequency and uniformity of patient data collection.

J. William Langston, MD, CEO and chief scientific officer of The Parkinson's Institute and Clinical Center and a member of the MJFF Scientific Advisory Board, said, "The potential value stemming from a centralized database of Parkinson's patient information will help us investigate environmental factors correlated to genetic profiles and clinical outcomes in a way that has never been possible before. If successful, this work could dramatically accelerate our research on finding the cause and better treatments for the disease."

Web-based Clinical Assessments initiative

The second initiative driving Web technologies to improve clinical research for PD is the Foundation's new *Web-based Clinical Assessments* program, for which MJFF is currently reviewing proposals. Under this initiative, the Foundation seeks to drive the creation and testing of Web-based tools that would allow any patient with a personal computer and an Internet connection to participate in clinical research from the comfort of their own home.

"A Web-based clinical assessment can never entirely take the place of face-to-face interactions between patients and researchers," said Ms. Hood. "But as a supplemental measure it could heighten efficiency and help speed progress toward new treatments by increasing, for a given trial, the amount and breadth of information from which to draw conclusions."

Added Todd Sherer, PhD, the Foundation's vice president of research programs: "In addition to increasing the participation of individuals who might otherwise not realistically be able to take part due to travel, a Web-based clinical assessment could provide a more complete picture of symptoms by introducing the ability to test certain functions at home and throughout the day."

Grant applicants under this initiative must focus on three deliverables: the development of an assessment tool that will be available to patients through the Internet; the creation of a technological infrastructure through which patients will be able to access this tool; and the design and implementation of a pilot study to test efficacy.

The program will provide up to $1 million in funding for Web-based clinical assessments of various motor and/or non-motor symptoms of PD for up to two years. Funding is anticipated by October 2008.

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>
> — Katie Hood

Brush Up Your Biology:
Definitions of terms used in this story

Antioxidant: A chemical compound or substance that inhibits oxidation — damage to cells' membranes, proteins or genetic material by free radicals (the same chemical reaction that causes iron to rust). Some studies have linked oxidative damage to Parkinson's.

Epidemiology: The study of the patterns, causes, and control of disease in populations of people. Epidemiological studies help scientists identify potential causes of PD.

Metabolite: Any chemical product derived from breakdown (metabolism) of another chemical, for example through digestion.

Michael J. Fox Foundation Awards **$5.6 Million** for Phase 2 Clinical Trial of **Inosine/Urate** *(continued from page 1)*

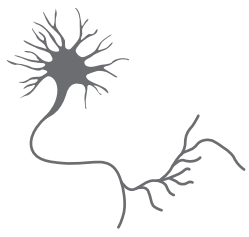
risks, only some of which have been definitively characterized to date. Kidney stones and gout are known risks; cardiovascular disease is a possible risk. (In the clinical trial, safety measures will be in place to help avoid these conditions, and to detect and treat them should they arise.)

Joining Drs. Schwarzschild and Ascherio as a third principal investigator of this *LEAPS* award is Karl Kieburtz, MD, MPH, of the University of Rochester School of Medicine and Dentistry. Dr. Kieburtz heads the Clinical Trial Coordinating Center there and is chair of the Parkinson Study Group, a network of top researchers conducting clinical research in PD.

LEAPS awards are multi-year, multi-million-dollar awards to teams of key experts who focus on answering major questions that can improve the diagnosis and treatment of Parkinson's disease. This third and final 2007 *LEAPS* award brings total funding under the 2007 *LEAPS* program to $13.8 million.

MJFF NEWS ANALYSIS

Fetal Cell Transplants Found to Develop Parkinson's-like Changes Over Time



Last April, news media around the world reverberated with highly unexpected Parkinson's disease research findings out of several labs in the United States and Lund, Sweden, published in the journal *Nature Medicine*. Through post-mortem analysis of the brains of PD patients who had undergone transplantation surgery to graft healthy fetal tissue into their brains in the late 1980s and early 1990s, it was revealed that some neurons in the grafts had developed Parkinson's-like pathology over the course of 11 to 16 years.

The work's most profound impact will likely be its potential to open entirely new experimental avenues for understanding the causes of Parkinson's onset and progression, and for the development of transformative new treatments that could stop the disease in its tracks. The findings may also hold implications for the future of neurotransplantation as a therapeutic approach to Parkinson's disease.

Healthy young cells get sick

The primary change observed by researchers in the grafted fetal tissue was the emergence of Lewy bodies, the classic pathological sign of Parkinson's disease. Lewy bodies are protein clumps, or aggregates, primarily made up of the protein alpha-synuclein. Alpha-synuclein is normally present in healthy neurons, though researchers do not know what its job is.

"The observation of Lewy bodies in the grafts gives us a hint about what is going on in the pathology of a person with Parkinson's disease: it progresses slowly and is capable of spreading from an affected site to a new, healthy site," said Patrik Brundin, MD, PhD, professor of neuroscience in the Neuronal Survival Unit at Lund University in Sweden and senior author on one of the papers describing the results.

In addition to developing Lewy bodies, some of the cell bodies of the dopamine neurons in the transplants showed an increased level of the alpha-synuclein protein that had not formed aggregates. In young individuals, this protein is normally found only in nerve cell terminals, at the opposite end from the cell body. In the cell bodies themselves, its levels are usually at such low levels that it cannot be seen (even with a microscope). With normal aging, the protein starts to appear in the cell bodies.

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.

"In the grafts we studied, we saw a progressive increase of alpha-synuclein levels inside the transplanted cell bodies," said Dr. Brundin. "We can tell it was progressive because one of our patients was grafted on two occasions — one side of the brain in 1989, and the other in 1993. This meant we were able to examine the same brain with two different ages of transplants. In the younger graft, 40 percent of the dopamine cells had increased levels of alpha-synuclein in the cell body. On the other side, 80 percent had it. In cells of this age — that is, between 12 and 16 years old — one would not expect to see alpha-synuclein in any of the cell bodies. That's fascinating, although we do not know why it happens."

A clue about the cause

Researchers do not yet know the cause or causes of Parkinson's disease. For this reason, a key debate in the field revolves around what brings on the disease. One possibility is that it begins with a one-time insult, or "hit," of some sort (environmental, or perhaps a combined gene-environment interaction), which is present in the brain only for a short time but leads to a self-sustaining process continually "sickening" brain cells with Parkinson's. Alternatively, the disease may be caused by a molecule or process that is always present and active in the brains of those affected.

"At the time of the fetal cell transplant surgeries, we thought: If an earlier hit had somehow set something in motion in the host dopamine cells, then the transplanted cells should be spared, because they're fresh, they weren't present when that hit took place," said MJFF Scientific Advisory Board member Jeffrey Kordower, PhD, Jean-Schweppe Armour Professor of Neurological Sciences and director of the Research Center for Brain Repair at Rush University, and senior author of another of the new papers. "On the other hand, if whatever is causing the disease is still present and active, it might turn right around and attack these new cells."

Added J. William Langston, MD, CEO and chief scientific officer of The Parkinson's Institute and Clinical Center and member of the MJFF Scientific Advisory Board: "To me, the first and most profound observation from the new results is that whatever is in the Parkinson's brain can attack these cells. The fact that even a few of these cells would get PD is extremely scientifically important. It tells us that the cause of Parkinson's is probably not a single trigger earlier in life that continues to affect the cells years later."

Transplantation as a viable PD treatment

As is often the case when a major finding is still very new, there is a great deal of variance in what scientists believe the news may mean for therapeutic and clinical application of transplantation technology — and, more broadly, cell replacement strategies — in the near term.

"While these grafts offered some patients an extended period of symptomatic benefit, the fact remains that the grafted cells may be vulnerable to PD pathology," said Todd Sherer, PhD, vice president of research programs for MJFF. "This news is generating a careful assessment of the therapeutic potential of cell transplants. For now, it is too soon to draw conclusions about the overall risk/benefit ratio of neurotransplantation."

"It is definitely not a 'stop sign' in terms of continued work to better understand and refine transplantation as a therapy," said Dr. Brundin. "From a clinical outcome perspective, it is encouraging that these grafts can function more than a decade after transplantation surgery. The patients we examined had 100,000 or so surviving dopamine neurons on each side of the brain. It's good news that the grafts could live and function as long as 16 years."

Yet others note that the development of pathology in the grafted cells is only the most recent complicating factor in the increasingly complex story of cell replacement strategies for PD. While there is little doubt that this science holds unprecedented potential to yield new therapeutics, major hurdles remain to be solved before cell replacement approaches can practically be deployed as Parkinson's treatments. Scientists have had limited success in engineering dopamine neurons from stem cells, but there is still a great deal of work to do to get the engineered neurons to survive and thrive after transplantation. Researchers still do not know with certainty the best location for transplantation in the brain. Issues may arise from low-grade inflammation resulting from the surgery itself. And now, there is an open question as to how long and how well transplanted cells can function before succumbing to disease pathology.

"The whole story, when looked at in perspective, doesn't mean we should give up," said Dr. Langston. "We're going to conquer a lot of these things someday. But it's a resource issue at this

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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, research bios and supplemental grant information (where applicable) — please search the Funded Grants Database located in the Research section of our Web site at www.michaeljfox.org/research.cfm.

Second Annual **PD Therapeutics Conference** Announced

Registration is now open for researchers wishing to attend the Foundation's second annual PD Therapeutics Conference, the only scientific symposium exclusively focused on drug development for Parkinson's disease. Chaired by Jeffrey Kordower, PhD, The Jean-Schweppe Armour Professor of Neurological Sciences and Director of the Research Center for Brain Repair at Rush University, the conference will highlight drug discovery and development for Parkinson's disease. Select MJFF-funded investigators will present research on novel neuroprotective agents, innovative mechanisms to address disease symptoms and improvements in relevant animal models and biomarker discovery/development. The conference takes place in Chicago, Illinois, on Monday, September 15, 2008.

MJFF Commits Up to **$3 Million for Clinical Trials** to Improve Treatment of Parkinson's Disease

In February the Foundation announced the 2008 launch of its annual *Clinical Intervention Awards*. The program, formerly known as *Clinical Discovery Awards*, has been revamped with an even greater focus on clinical testing of promising therapies with potential to fundamentally improve the treatment of Parkinson's disease symptoms and even impact disease progression. Ideal proposals will be rooted in well-designed and rigorous clinical trials that test potentially high-impact treatment approaches. Applicants may seek full support for a trial, if feasible within the program budgetary constraints, or may request funding to supplement a clinical testing effort supported by other funding sources. Funding is anticipated by September 2008.

$2 Million Awarded to Shed Light on **PD-implicated Genes LRRK2 and Alpha-Synuclein**

In January MJFF 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 — that play a major, but still only partially understood, role in Parkinson's disease. The genes were selected for study under the first funding round of MJFF's *Critical Challenges in Parkinson's Disease* program following a survey of the field by the Foundation's research staff and advisors. Investigators awarded under the alpha-synuclein challenge will look at various ways in which disease-related modifications of alpha-synuclein might lead to toxic effects. The four investigators awarded under the LRRK2 challenge all seek to test whether an abnormal increase in LRRK2's enzymatic function triggers toxicity.

Therapeutics Development Initiative 2008 Includes Special Funding Track for Academic Drug Development Researchers

In April the Foundation launched its $10-million 2008 *Therapeutics Development Initiative (TDI)*, designed to stimulate pre-clinical drug development research to keep potential new therapies moving toward clinical testing. While *TDI* funding originally was available only to biotech and pharmaceutical companies, under the 2008 funding round MJFF has included a special funding track for academic researchers. "The Foundation recognizes the strengths beyond target identification that academic scientists bring to therapeutics discovery and development," said P. Jeffrey Conn, PhD, a member of the MJFF Scientific Advisory Board and head of the Program in Translational Neuropharmacology and Drug Discovery at Vanderbilt University in Nashville, Tennessee. "The drug development process is a constantly changing ecosystem, one in which a for-profit's risk appetite necessarily rises and falls with access to capital. Academic institutions, being less subject to these kinds of economic shifts, often have latitude to advance discovery efforts for early and high-risk targets that industry would generally pass up until a later stage of development." The first two rounds of *TDI* were enthusiastically received by industry researchers and the scientific community at large. To date the Foundation has awarded nearly $8 million total under the initiative for 14 projects.

Bringing FDA to the Table

By Michael J. Fox and Donna E. Shalala

On April 28 in Arlington, Virginia, more than 150 academic and industry neuroscientists met to take targeted steps toward overcoming a challenge with life-altering consequences for the nearly five million Parkinson's patients worldwide and countless additional millions living with other central nervous system disorders.

The goal of the meeting — co-sponsored by The Michael J. Fox Foundation, the U.S. Food and Drug Administration, the American Association of Pharmaceutical Scientists and the Parkinson Study Group — was to make inroads into one of the thorniest problems facing Parkinson's disease and all disorders of the brain: the fundamental lack of defined clinical trial outcomes that could help scientists establish whether a given candidate drug is exerting a so-called "disease-modifying effect."

In layman's terms, today's drugs for Parkinson's disease are Band-Aids. They mask symptoms — less and less well over time — while the underlying disease continues to progress. In spite of the new scientific findings that continually accrue from public and private research spending worldwide, we've got no treatment that can actually slow or stop the disease from getting worse.

Financier and philanthropist Mike Milken is fond of saying that even a train capable of going 300 miles an hour is of little value if the tracks are built for a top speed of 55. The Michael J. Fox Foundation is working urgently to help build the train. To us that means driving the advancement of basic science discoveries forward on the drug development pipeline, to turn them into validated drug targets for clinical trials. We don't know what causes Parkinson's disease, so we can't leave any promising stone unturned. To date we've prioritized work on more than 100 possible targets for Parkinson's disease in the hope of vetting their potential and getting them to patients faster. It's no easy task in a wide field of seemingly equally worthy research opportunities.

Yet we think this is only half of the job at best. The train will never get us to our destination unless we work equally urgently to build new tracks. That means forging new techniques and brainstorming tomorrow's infrastructure today — the goal of the meeting in Arlington — to meet the formidable challenges of testing potential new drugs in the clinic and shepherding them through the regulatory process. It means fostering creative and strategic collaborations to help overcome the inherent challenges of developing life-changing treatments for disease in what is by definition an imperfect system for testing and regulating new therapies.

The vast majority of candidate drugs, even those that advance as far as pre-clinical testing in animal models, never make it to clinical testing in humans, let alone regulatory review. For the relative few that do, FDA is charged with a task vexing enough to inspire any Greek playwright or Russian novelist: striking a perfect balance between two critical and opposing imperatives — the need for safety and the need to make genuinely innovative treatments available to people living with catastrophic illness or injury. What we have to strive for is an FDA indication based on the strongest data available. That requires designing cost-effective trials that can overcome a lack of information and yield results conclusive enough to keep new trains speeding out of the station and down the tracks.

It goes without saying that we'd all prefer ironclad assurances. But even if that were theoretically possible, it would bring the system to a screeching halt. And from the vantage point of patients and their families, it's already moving far too slowly.

According to the Tufts Center for the Study of Drug Development, it takes 10 to 15 years, and more than $800 million, to shuttle any given drug from lab bench to FDA approval to U.S. market. Clinical research is too often carried out in isolation; few to no natural handoffs exist to help academic and industry researchers, or basic scientists and clinicians, connect and communicate in ways that advance treatments. For central nervous system disorders (including our Foundation's exclusive province, Parkinson's disease), where a lack of standard methods used by researchers makes data mining across studies difficult, the process is only longer and costlier.

It is incumbent on interested parties to work now to solve these problems. We must optimize our ability to work with incomplete information. We must precisely define the results we are seeking, and determine the best way to analyze outcomes to see how close we've actually come to our desired results. There is no question that these are daunting challenges. But until we meet them, clinical trials for disease-modifying drugs for Parkinson's and every central nervous system disorder will be hampered by exorbitantly high costs and inconclusive data. And patients' quality of life will continue to hang in the balance.

The Michael J. Fox Foundation is interested in only one thing: impacting the lives of people with Parkinson's disease. But other stakeholders would be wise to consider the tremendous return on financial investment that will come with feasible solutions to the problems that currently hinder development of genuinely innovative treatments.

Our four groups came together out of a shared determination to do whatever it takes to speed scientific solutions that will impact untold millions of lives, now and in the future. We salute the FDA, the American Association of Pharmaceutical Scientists and the Parkinson Study Group for joining us in thinking big — and for recognizing that now is the time to do it.

Michael J. Fox, the actor, established The Michael J. Fox Foundation for Parkinson's Research in 2000. Donna E. Shalala, president of the University of Miami and former secretary of the U.S. Department of Health and Human Services, sits on the Foundation's Board of Directors.

SAB Member **Mark Cookson** Receives 2007–2008 Langston Award

At the 2008 full meeting of its Scientific Advisory Board (SAB), held in March, The Michael J. Fox Foundation announced Mark R. Cookson, PhD, as the recipient of the 2007-2008 Langston Award. Dr. Cookson is an investigator in the Cell Biology and Gene Expression Unit of the Laboratory of Neurogenetics, National Institute of Aging (NIA), Bethesda, Maryland. He is a cell biologist whose laboratory efforts are directed at finding the underlying pathways that lead to Parkinson's disease.

The Langston Award is an annual $25,000 unrestricted research grant recognizing an SAB member whose commitment to the Foundation goes "above and beyond" the expected. It was created by The Michael J. Fox Foundation in 2005 in recognition of the exemplary dedication and leadership of J. William Langston, MD, CEO and chief scientific officer of The Parkinson's Institute and Clinical Center. Dr. Langston served as the Foundation's first chief scientific advisor and was founding chairman of its Scientific Advisory Board. As the architect and head of this first group, he set the course for the Foundation's scientific efforts, helping to establish what is today recognized as a model for driving high-impact research.

"I was shocked to receive such a prestigious award," said Dr. Cookson. "It's a great honor to be held in the same regard as people I look up to enormously."

Dr. Cookson has served on the Foundation's SAB since December 2005 and has made outstanding contributions across the board including assessing grant applications under the *LEAPS* and *Target Validation* programs. He served as a reviewer for the *Critical Challenges* program in its inaugural year, helping to ensure that the Foundation fulfilled its objectives for the new program. He chaired the *Community Fast Track* committee and now reviews applications on an ongoing basis for the *Rapid Response Innovation Awards* program. His experience and expertise also came to the forefront as a "hot topics" speaker on the PD-implicated gene LRRK2 at the inaugural PD Therapeutics Conference co-hosted by the Foundation in fall 2007.

Dr. Cookson also has spoken extensively to lay audiences at the Foundation's Research Roundtable events, designed to communicate front-line research advances to people with Parkinson's and their loved ones, and has served as a commenter for the Foundation's "News in Context" features that offer perspective and a neutral point of view on breaking Parkinson's news.

"It has been so important to me to work with the Foundation over the past few years," Dr. Cookson noted. "To be able to do something positive, to challenge ideas about not just what science should be prioritized but also how we should identify and support the best ideas. I hope to continue helping MJFF however I can, and that eventually none of us will be needed."

Todd Sherer, PhD, the Foundation's vice president of Research Programs, said, "Whenever called upon, Mark has given generously of his time and energy, with great enthusiasm for our efforts. We are thrilled to recognize his dedication with the Langston Award."

TEAMFOX
FOR PARKINSON'S RESEARCH

5K Closer to a Cure

Rik and Laura Spiers in Wyoming

Seven years ago, Indianapolis resident Rik Spiers, then 50, was diagnosed with Parkinson's disease. Researching Parkinson's online in 2006, he discovered Team Fox and quickly made the decision to become a member. "I didn't waste any time," Rik chuckles now. Just days before he and his wife were scheduled to leave for a Wyoming vacation, he took the opportunity to ask friends and family to sponsor him on a hike he planned to take while out west. He raised $1,000 on that trip and knew he wouldn't stop there.

On May 3 of this year, Rik hosted a 5K race/walk in conjunction with the Indianapolis 500 Mini-Marathon. He again reached out to friends and family, asking them to walk or run. He also contacted local press to help publicize his efforts. His neighborhood newspaper ran a story, not only informing the community of the fundraiser, but also raising awareness of Parkinson's and the critical need for funds to drive research toward transformative treatments.

On the day of the event, participants crossed the finish line wearing Team Fox t-shirts and raised close to $2,300 for Parkinson's research. Rik now plans to make his 5K an annual event, one he terms a 'counter-competitive race': "There will be no cure through competition alone," he says. "Defeating Parkinson's disease will take cooperation and team work."

CHECK OUT THE NEW TEAMFOX.ORG!

The redesigned Team Fox Web site went live on April 1. In addition to a great new look and easy-to-navigate layout, the site now features a map to search by state for members and events, a photo gallery, Team Foxers' personal stories, running routes, downloadable logos and banners, how-to guides, and a bulletin board/discussion forum for members.

Check out **www.teamfox.org** today. Every team needs a hero — Team Fox needs you!

Ready to Take on the Challenge

Though Evan Schumacher, 39, of Boston, has always been physically active, he never thought he would run a marathon. That changed in January, when his father was diagnosed with Parkinson's disease. Familiar with The Michael J. Fox Foundation and supportive of its mission to fund results, Evan quickly discovered Team Fox.

"I had never dreamed of running 26.2 miles," Evan says, "but I felt incredibly motivated by Team Fox." Eager to get started, he signed up to run the legendary Boston Marathon in his hometown on Patriot's Day, April 21.

In exchange for guaranteed entries in the world's most prestigious races, Team Fox Athletes commit to raise a minimum of $5,000 for Parkinson's research. Evan began by sending e-mails to all of his friends to ask for their support. They not only rallied to his cause, but assisted by spreading news of his marathon plans to their friends and family. With the help of his network, Evan has far exceeded his initial goal, raising over $26,000 for Parkinson's research to date — a figure that has boosted him to the position of the second-highest 2008 fundraiser for Team Fox.

"Running the marathon wasn't easy, and I'm still debating taking on the same challenge again next year," Evan says. "But even if I retire as a marathon runner, I know I'll keep working with Team Fox to host events and raise money for research. It's my personal mission to raise awareness and funds for the research needed to help my dad and others like him in the battle against PD."

Evan Schumacher

Cocktails for the Cure

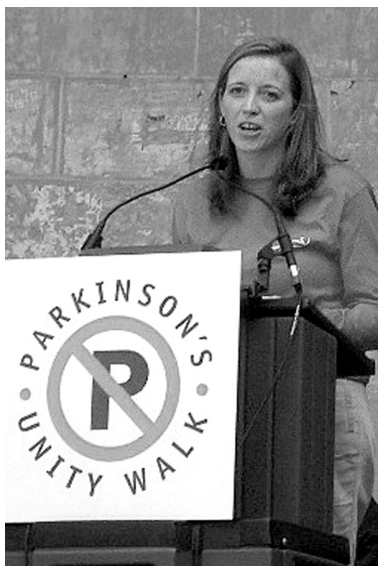
Karen, Andy, Rick and Matt Bechtel

In 1998, Rick Bechtel of Lexington, Massachusetts, was diagnosed with Parkinson's disease at age 46. As time passed, his wife, Karen, and sons, Andy, 28, and Matt, 24, began to see how the disease was slowing Rick down — affecting his ability to work and taking him away from the things he loved, like playing golf. In 2006, they joined Team Fox to begin fundraising for high-impact Parkinson's research toward a cure.

In 2007 Andy and Matt organized their first event, a cocktail party. To publicize the event, they sent an Evite to friends and family and directed invitees to their personalized Team Fox Web page. The party attracted close to 120 guests and raised an amazing $8,000.

With one success already under their belt, the brothers decided to plan a 2008 event. This time Karen joined in the planning process, and Rick served as guest of honor. The family held their second annual cocktail party at Ned Devine's, a bar in Boston's historic Faneuil Hall, on April 19. In addition to a suggested donation of $20 at the door, they held a raffle for Red Sox tickets, which alone raised $800. This event was even bigger and better than the last, raising more than $11,000 and hosting more than 150 friends from all over the country. Fresh from this triumph, Matt and Andy have already launched into planning next year's event.

"It's awesome to be raising money for Parkinson's research," said Matt of his Team Fox experience, "and it's overwhelming to see so much support from our friends and family."



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Parkinson's Unity Walk

1 MJFF CEO Katie Hood addresses the crowd

2 MJFF staffers Alison Urkowitz *(left)* and Veronique Enos

3 The crowd, 10,000 strong

4 Jennifer Hagel of MJFF with former Attorney General Janet Reno

4

5

Spring 2008 was a whirlwind of activity for The Michael J. Fox Foundation. The 14th Annual Parkinson's Unity Walk (pictures 1–4) attracted over 10,000 members of the PD community to New York City's Central Park on April 26 to raise awareness of the disease and over $1.6 million for research. On May 2 MJFF hosted its second "MVP Awards" dinner (pictures 5–9) to thank the dedicated Team Fox members who have raised an astonishing $3 million for Parkinson's research to date. And the Foundation set out for the West Coast to host its star-studded "Playing to Win the Fight against Parkinson's" poker night benefit (pictures 10–14), which raised $600,000 for PD research on May 8 in Los Angeles.

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MVP Awards Dinner

5 Michael J. Fox with Micki Kitchell *(left)* and Team Fox member Caroline Maguire

6 Team Fox members Barbara *(left)* and Laura Roche take in the event video

7 Michael J. Fox with top 2007 Team Fox fundraisers Linda and Paul Ruby

8 Michael J. Fox with Team Fox members Ann and Ken Glowienke

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"Playing to Win the Fight Against Parkinson's"

9 Guests Holly Robinson Peete and Rodney Peete, founders of the HollyRod Foundation

10 Michael J. Fox and Tracy Pollan with "Scrubs" castmates Zach Braff and Sarah Chalke

11 Guests Tara Fowler and Montel Williams

12 Michael J. Fox with MJFF CEO Katie Hood

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Fetal Cell Transplants Found to Develop Parkinson's-like Changes Over Time (CONTINUED FROM PAGE 3)

point. Neurotransplantation focuses on only one aspect of Parkinson's disease: its effects on the dopamine system. Yet today there is an increasing recognition that to effectively treat PD, we must target the dopamine-non-responsive symptoms as well as the dopamine system."

Next steps

For Parkinson's researchers, the obvious next question is how best to take advantage of this unexpected finding and use it to learn more about the disease in a way that will ultimately lead to a true cure, or even prevention.

In September, The Michael J. Fox Foundation will host a summit meeting in New York City to convene the world's top cell replacement experts for a goal-oriented discussion of how to move the work forward in animal models and in living cells. Meeting participants will brainstorm experimental design and come up with a "short list" of questions that must be answered in animal models in order to determine what mechanisms caused the PD pathology to "spread" in the brains of the patients who received fetal cell transplants. Drs. Brundin and Kordower will be there.

"If we can recreate in Parkinson's disease models what occurred in the patients, we can get closer to truly understanding what's going on at the cellular level," said Dr. Brundin. "This in turn would give us a much better chance of creating new drugs that slow or stop disease progression. This could be very important for everyone with Parkinson's."

Dr. Langston agreed. "This could be concept-changing in terms of our understanding of what goes on in triggering the evolution of this disease."

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.