THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

WINTER 2006 NEWSLETTER

GENE THERAPY: THE NEXT GENERATION

$4.2 MILLION *LEAPS* AWARD WILL JUMP-START DEVELOPMENT OF REGULATABLE GENE THERAPY

The Michael J. Fox Foundation for Parkinson's Research (MJFF) has committed $4.2 million to a team led by RheoGene Inc. to develop what could be the next generation of gene therapy: a delivery system that would provide clinicians a "switch" to control a gene implanted in a patient's brain. In collaboration with several academic institutions, RheoGene will develop, optimize and test its "RheoSwitch® Therapeutic System" (RTS) technology through Phase I clinical trials within four years. While Parkinson's disease is the first application, the work will have broad applicability to the safety and efficacy of gene therapies for many other diseases as well, and for their accelerated advancement into the clinic.

"This project has potential to revolutionize the clinical application of gene therapy," said Deborah W. Brooks, MJFF president and CEO. "It is a natural fit with the Foundation's commitment to drive innovative technology that will have a significant impact on patients' lives."

Gene therapy has been touted for years as a prospective cure-all for a wide range of health ailments. But its development as a widespread therapeutic technique has been hampered by the lack of any way to time or finely adjust doses or to "turn off" a gene once it has begun expressing a protein in the brain. The RheoGene-led team will work to establish RTS as a safe and effective means to regulate both the level (dose) and timing of gene expression using an orally administered activator drug, or "on switch." The advent of RTS would furnish an unprecedented safety mechanism by allowing gene expression to be completely shut off in the event of adverse side effects, simply through withdrawal of the activator drug.

The project will begin with a focus on two genes. One produces small molecule GDNF, a potent neurotrophic factor; the other produces large molecule AADC, an enzyme involved in dopamine synthesis. Both genes may have therapeutic merit, and different technologies may be required to regulate each. By working on both, the research team can widen the variety of genes to which the regulation switch they develop could ultimately be applicable. Like all *LEAPS* awards, the project hinges on specific milestones that will determine whether work on one or both of the genes ultimately goes forward.

The RheoGene award is also a reflection of the Foundation's increasing interest in neurotrophic factor research, to which MJFF's funding commitment to date totals about $8.5 million. Neurotrophic factors (also known as trophic or growth factors) have long been considered one of the most promising avenues of Parkinson's research, as they promote survival and improve function of neurons. *(For more information on trophic factors, see box, page 2.)*

"We are very excited that the Fox Foundation has recognized RheoGene's ability to create leading-edge technology," said Thomas Tillett, CEO of RheoGene. "This grant will enable us to continue to build on our successes with RTS to date in creating innovative solutions that provide safer and more effective gene therapies."

The award is made under the Foundation's *LEAPS (Linked Efforts to Accelerate Parkinson's Solutions)* initiative. *LEAPS* are multi-year, multi-million, multi-disciplinary projects to address questions that will have significant practical impact on the understanding and treatment of Parkinson's disease.

See Page 4 for Members of the RheoGene-led LEAPS Team

NEWS FROM THE PRESIDENT AND CEO

The thread that runs through all of the Foundation's work is the question we ask about every prospective research investment: What is the potential of this tool, study or trial to shorten patients' wait for improved Parkinson's treatments and, ultimately, a cure? Our driving goal is to propel scientific discoveries beyond academia, through the translational gap where promising ideas too often languish, and into the clinic for translation into meaningful therapies and interventions.

This issue highlights some major recent expressions of the Foundation's commitment to translational research. They include a *LEAPS* award that could spawn the next generation of gene therapy, a validation study of genes implicated in PD, and a project that builds on a promising Alzheimer's therapy to drive a potential new treatment for Parkinson's.

You'll also see, as a special insert, our 2005 Progress Report. As we enter our sixth year, we assess our progress and accomplishments to date, including driving the first dopaminergic human stem cell line and the first large-scale genetic map of Parkinson's — tools with potential to transform the way Parkinson's is diagnosed and treated.

We take pride in what we've achieved so far, but we won't rest until we reach our goal: a world where Parkinson's disease is only a memory.

Warm regards,

Debi Brooks

Deborah W. Brooks
President and CEO

IN THIS ISSUE

FOUNDATION SUPPORTS CEREGENE, INC. PHASE I GENE THERAPY CLINICAL TRIAL

The Michael J. Fox Foundation has committed $740,000 over three years to Ceregene, Inc., a San Diego-based biotechnology company focused on the development of gene therapies for neurodegenerative disorders. The grant, announced in November, will help fund Ceregene's Phase I clinical study of CERE-120, a new gene therapy product that has shown potential in pre-clinical testing to slow or stop the progression of Parkinson's disease by using a viral vector to deliver neurturin, a potent nervous system growth factor.

"The Phase I trial of CERE-120 brings several Foundation priorities to bear," said Deborah W. Brooks, MJFF president and CEO. "These include investigating the neurorestorative properties of neurotrophic factors *[see box]*, advancing translational research, and shortening the time it takes to turn basic research advances into meaningful therapies for patients."

While the primary goal of any Phase I clinical study is to demonstrate safety, Ceregene will also measure the efficacy of CERE-120 through brain imaging studies and standardized Parkinson's tests. MJFF support will significantly enhance the speed and depth of this data collection, allowing for more regular testing of a wider range of neurological functions than would otherwise be possible. Each patient will undergo a PET scan and a full battery of neurological tests every three months (in addition to regular visits to the clinic for more routine procedures such as blood tests). Assuming successful results, measurements from the Phase I study will lead to more efficient planning of a larger Phase II study that will gather more detailed data on both safety and efficacy.

"Extensive studies in animal models, including the most widely accepted models of Parkinson's disease, have consistently demonstrated that CERE-120 is safe and well tolerated in animals even at doses hundreds of times higher than the equivalent doses being tested in humans. These studies also demonstrate that CERE-120 may be able to improve symptoms as well as slow the progression of Parkinson's disease," said Raymond T. Bartus, PhD, Ceregene's COO and principal investigator on the grant.

The Foundation funding supplements Ceregene's own multi-million dollar investment in the study, which is under way at the University of California, San Francisco Medical Center and Rush University Medical Center in Chicago.

"We're pleased to have Fox Foundation support to optimize our clinical tests of CERE-120," said Jeffrey M. Ostrove, PhD, president and CEO of Ceregene. "This funding will allow us to gather, in the shortest time possible, the data needed to know if we are on to a safe therapy that might slow or stop the progression of the disease — something no treatment on today's market can do."

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Why trophic factors?

"Neurotrophic factors work in the brain the way fertilizer works in a field," says Todd Sherer, PhD, MJFF associate director of research programs. "As the fertilizer helps crops to thrive, neurotrophic factors promote survival and improve function of neurons." Also known as trophic or growth factors, these molecules have long been considered one of the most promising avenues for Parkinson's therapies and are a priority for MJFF, which has funded approximately $8.5 million in growth factor research to date.

Neurturin, the growth factor in the Ceregene trial, is a member of the same protein family as GDNF (glial-derived neurotrophic factor), which has previously been tested in people with Parkinson's. Both maintain survival of the dopamine-producing nerve cells that are required for normal bodily movement and that degenerate in people with Parkinson's.

Other MJFF investments in neurotrophic factors to date include two current *LEAPS (Linked Efforts to Accelerate Parkinson's Solutions)* projects and two *Community Fast Track* 2004 projects. Of the *LEAPS* projects, one seeks to develop a regulatable gene therapy delivery system (see page 1) and one investigates encapsulated cell technology as a delivery mechanism for GDNF. Under *Community Fast Track*, one team evaluated two proteins from the neuregulin family of growth factors as potential therapeutic agents in animal models, and another examined a molecule called pleiotrophin as a potential neuroprotective/restorative agent for dopamine neurons in animal models.

FOUNDATION DRIVES FIRST WHOLE-GENOME MAP OF PARKINSON'S DISEASE

FINDINGS HIGHLIGHT 12 SUSCEPTIBILITY GENES BUT NO "SMOKING GUN"; VALIDATION STUDY UNDER WAY

In fall 2005, researchers at the Mayo Clinic and Perlegen Sciences, Inc., funded under The Michael J. Fox Foundation's *LEAPS* (Linked Efforts to Accelerate Parkinson's Soliutions) initiative, produced the first large-scale whole-genome map of Parkinson's disease. The research, published in October in the *American Journal of Human Genetics*, highlights changes in 12 genes that may increase the risk for Parkinson's disease in some people. However, the comprehensive study found no genetic "smoking gun" — no strong single genetic determinant of Parkinson's.

As the field of "genomic medicine" expands at a rapid pace, the Perlegen/Mayo study represents the first large-scale attempt to assess the comprehensive role of genes in Parkinson's disease.

"If validated," said MJFF president and CEO Deborah W. Brooks, "the discovery of these 12 potential susceptibility genes — genes that don't cause a disease outright, but might make a person more or less likely to develop it — could provide new insights into what causes Parkinson's. *(See box, right, for more information on validation.)*

In one of the most comprehensive genetic studies of any disease to date, researchers studied the association of about 200,000 single-letter variations in the genome known as single nucleotide polymorphisms, or "SNPs" (pronounced "snips"), in people with Parkinson's disease. The study examined DNA from 1,550 people — 775 with, and 775 without, Parkinson's disease. Although 13 SNPs — found within 12 genes — were statistically more common in PD patients than in healthy individuals, the size of any single SNP's effect was small. This indicates that these single gene variants contribute only slightly to whether someone has PD or not. These results may support the theory that rather than single genes, combinations of genes or gene-environment interactions may be necessary to develop most common forms of Parkinson's disease.

Other noteworthy findings include confirmation that variation in two previously known regions of the genome, PARK10 and PARK11, are likely associated with Parkinson's disease susceptibility. Some of the other SNPs found to be associated with susceptibility were in or near genes with direct biological relevance to the disease.

"This is something we've wanted to do for years, and now we finally had the technology and fund-

Continued on Page 8

EPIDEMIOLOGICAL STUDIES OF PARKINSON'S: WHAT DO THEY MEAN FOR YOU?

Preliminary results of epidemiological studies conducted by MJFF scientific advisor Alberto Ascherio, MD, PhD, recently led to media reports that the regular use of ibuprofen may delay or prevent the onset of Parkinson's disease. But while the study is important and intriguing, researchers emphasize that it is too soon for people with Parkinson's to draw the conclusion that they should begin an ibuprofen regimen.

"It would be premature for people with Parkinson's to start taking ibuprofen or other anti-inflammatory drugs," Dr. Ascherio cautioned. "A single epidemiological study's results do not directly translate into prevention or treatment actions."

To validate substances associated with increased risk, he explained, multiple epidemiological (or epi) studies must be done. To validate the treatment potential of substances associated with decreased risk (as in the case of ibuprofen), randomized trials are needed.

"Epi studies play a crucial role in the research cycle," said Katie Hood, MJFF vice president of research programs, "by pointing up promising directions for future research." She noted that other epi studies have demonstrated a link to reduced Parkinson's risk for behaviors including increasing caffeine intake and smoking — generally considered a bête noire of human health.

"A smaller risk of Parkinson's is not a good trade-off for severely compromised cardiovascular health and a vastly increased risk of cancer," said Ms. Hood. "No physician can in good conscience recommend that her patients take up smoking." But further research into potentially neuroprotective compounds found in cigarettes could eventually lead to a new Parkinson's therapy.

As always, Ms. Hood added, the best way for people with PD to optimize their treatment is to establish and maintain a good relationship with their primary care physician and movement disorder specialist.

Validating the results of the Perlegen/Mayo study

To determine whether the initial Perlegen/Mayo findings hold in the broader population and to home in on which if any of the SNPs may merit additional scrutiny, the Foundation has quickly pushed forward with a validation study of major speed, size and scope.

Using genetic resources available through the Edmond J. Safra Global Genetics Consortia — MJFF's network of geneticists committed to sharing their population data on Parkinson's disease — the Foundation assembled three large consortia of research teams that worked in tandem to validate the initial findings. The consortia aggregated DNA samples from some 10,000 Parkinson's patients and control subjects. For each DNA sample, the researchers determined the SNP variant (also known as a genotype) for all 13 SNPs identified in the Perlegen/Mayo study. The resulting data sets are now being analyzed. Once results of the analysis are available, later this spring, the Foundation will coordinate with the investigators to publish the findings in a peer-reviewed journal.

"Our goals for the validation study were twofold," said Brian Fiske, PhD, MJFF associate director of research programs. "Naturally, it was of primary importance to better understand the initial findings and whether they hold in a larger set of patient populations worldwide. Our secondary goal was to proceed in a way that would help unify the field of Parkinson's genetics by clearly outlining and prioritizing the next stages of this work."

The research consortia for the validation study were led by Lorene Nelson, PhD, of Stanford University; Haydeh Payami, PhD, of the Wadsworth Center/New York State Department of Health; and Alexis Elbaz, PhD, of INSERM in France. Meta-analysis of the resulting genotype data they generated is being conducted by John Ioannidis, PhD, of the University of Ioannina (Greece), an expert in large-scale studies of this kind.

"The consortium approach brings a consistency that would not be possible if multiple groups tried to validate findings on their own," concluded Dr. Fiske. "And our compressed timeline allows the validation results to follow closely on the preliminary findings, maximizing their relevance and utility to the field."

MEMBERS OF THE PROTEOTECH-LED LEAPS TEAM

ProteoTech, Inc.
Alan Snow, PhD

Boston College
Daniel Kirschner, PhD
Professor of Biology

University of California, San Diego
Eliezer Masliah, MD
Professor, Neurosciences and Pathology

Consultant
Manfred Weigele, PhD
Former Director of Chemistry, Hoffman-LaRoche U.S.

Advanced Pharmaceutical Research, Inc.
Anil Kumar, PhD
CEO and Lead Chemist

Boston University
Benjamin Wolozin, MD, PhD
Professor of Pharmacology

MEMBERS OF THE RHEOGENE-LED LEAPS TEAM

RheoGene Inc.
(a wholly owned affiliate of the University of Pittsburgh Medical Center)
Dean Cress, PhD
Mark Braughler, PhD

University of California, San Francisco
Krys Bankiewicz, MD, PhD
Professor, Neurological Surgery and Principal Investigator, Movement Disorders Research Program

Northwestern University
Martha C. Bohn, PhD
Medical Research Council Professor and Director, Neurobiology Program, Children's Memorial Research Center

For more information, see story, page 1

PROTEOTECH AWARDED $3.1 MILLION FOR DEVELOPMENT OF NEW THERAPY WITH POTENTIAL TO STOP PARKINSON'S PROGRESSION

The Michael J. Fox Foundation for Parkinson's Research (MJFF) has committed a *LEAPS* award of $3.1 million over three years to a team led by ProteoTech Inc. to develop a treatment for Parkinson's that can disrupt or inhibit clumping of the protein alpha-synuclein. This clumping is associated with the loss of dopamine-producing cells in the brains of people with Parkinson's. The researchers theorize that blocking it could prevent further cell loss and stop Parkinson's disease progression.

Compounds already shown by ProteoTech to be effective in the test tube will be tested in cellular and animal models of Parkinson's disease. By the end of the three-year project, the team hopes to identify a compound and perform the preclinical testing needed to file an application with the FDA for a Phase I clinical trial.

"Researchers have focused a great deal of attention on alpha-synuclein, but many questions about its role in Parkinson's remain unresolved," said Deborah W. Brooks, MJFF president and CEO. "A chief goal of this project is to move the debate out of the lab and into the clinic. If successful, the work could speed the discovery of a groundbreaking therapy to slow or stop the progression of Parkinson's disease."

Many neurodegenerative diseases share the trait of clumping of various proteins, although there is considerable debate over whether the protein clumps in PD are a cause or effect, damaging or protective. Validating alpha-synuclein is therefore a high priority for the field, and the Foundation funded three *Target Validation* projects targeting alpha-synuclein in 2005 — one targets cellular pathways hypothesized to block the toxic effects of a form of alpha-synuclein, and the other two look at ways to lower alpha-synuclein levels or prevent its ability to aggregate. The *LEAPS* project, however, aims to potentially leapfrog over the harmful/helpful debate about alpha-synuclein by testing the hypothesis that protein clumps in Parkinson's are harmful through the development of a therapy to disrupt and prevent their formation.

ProteoTech is a leader in research and development of new therapeutics derived from proteoglycan and amyloid technologies for the treatment of major human diseases. This project leverages the company's prior experience with protein clumping in Alzheimer's disease. In the past five years Proteo-Tech has developed a small molecule compound, Exebryl™-1, that in preclinical testing has been shown to markedly reduce brain beta-amyloid deposits in animal models of Alzheimer's disease as well as to result in notable improvements in and reversal of memory impairments in these animals.

"We're excited that The Michael J. Fox Foundation has recognized ProteoTech's work in Alzheimer's as a significant base to build on in Parkinson's disease," said Alan Snow, PhD, president and chief scientific officer of ProteoTech. "I look forward working with this stellar team of researchers to develop a disease-modifying small molecule therapy that we anticipate will help slow or even, reverse the progression of Parkinson's disease.

For information on the other award under this round of LEAPS funding, see page 1.

CLINICAL DISCOVERY TO BE ANNUAL INITIATIVE

MJFF has announced that it will make *Clinical Discovery* an annual initiative, earmarking up to $3 million for the program in 2006. The program supports small-to-medium clinical research projects that apply cutting-edge Parkinson's science directly to patients and patient care.

"Our goal is to drive novel therapies to patients," said Deborah W. Brooks, MJFF president and CEO. "The lack of adequate funding for small-to-medium clinical research projects sets up a major roadblock to new treatment options."

The Foundation launched *Clinical Discovery* in 2004 to significant response from the scientific community. Four grants were awarded totaling about $2 million: an investigation in China of the potential neuroprotective effects of green tea; a trial of a novel strength training technique for dysphagia, which occurs when the muscles involved in swallowing weaken or do not work properly; and two investigations of novel uses of Positron Emission Tomography (PET) imaging to quantify changes in the brain associated with Parkinson's onset.

LAUGHTER IS THE BEST MEDICINE

"FUNNY THING" RAISES MILLIONS FOR PARKINSON'S RESEARCH

The Michael J. Fox Foundation raised nearly $4 million at the fifth installment of its gala event, "A Funny Thing Happened on the Way to Cure Parkinson's," held Saturday, November 19, 2005, at the Waldorf-Astoria hotel in New York City. The evening's costs were entirely covered by the Foundation's Board of Directors, meaning that every penny raised goes straight to cutting-edge Parkinson's research.

Wanda Sykes

The event was hosted by comic Jimmy Kimmel, who welcomed the evening's approximately 750 guests — including supermodels Elaine Irwin Mellencamp and Maggie Rizer, candy impresario Dylan Lauren, business leader Ronald O. Perelman and advertising mogul Donny Deutsch — as they entered the Waldorf-Astoria's striking Grand Ballroom and took their seats. The crowd was then warmly welcomed once again by actress Amanda Peet, who told guests that she was personally grateful for their support of the Foundation because her own family has been touched by Parkinson's.

(L-R) Jimmy Kimmel, Sarah Silverman, Colin Quinn, Michael J. Fox, Sam Fox and Tracy Pollan

As guests dined on sumptuous courses of grilled shrimp with mango-cilantro salad, tournedos of beef with roasted garlic confit, and a citrus medley garnished with gold leaf chocolate and passionfruit, appetites for laughs were sated with rollicking stand-up performances by Colin Quinn, Sarah Silverman and Wanda Sykes. In between stand-up sets, guests rocked out to music performed by the versatile and talented all-star house band under leader Simon Kirke. Band members included Rob Arthur, Tommy Burns, John Conte, Domino Kirke, Paulette McDaniel and Mark Rivera.

As the evening drew toward its close, Michael J. Fox took the stage to thank everyone who contributed to the evening's success — including event co-chairs Karen Finerman and Barry Cohen, the Foundation's Board of Directors (with a shout-out to his "favorite Board member," wife Tracy Pollan), and especially the loyal supporters whose generosity and continued commitment have made the Foundation a leading funder of Parkinson's research.

John Mellencamp

With that, Fox introduced the evening's closing act: a musical set by American icon John Mellencamp, who thrilled the crowd with some of the biggest hits of his 30-year career, including "Little Pink Houses," "Small Town" and "Scarecrow."

The Foundation joins Michael J. Fox in thanking everyone whose immense contributions made the event such a success.

FOR INFORMATION ABOUT UPCOMING FOUNDATION EVENTS, PLEASE VISIT US AT WWW.MICHAELJFOX.ORG

(L-R) Taylor Phinney, Connie Carpenter and Kelsey Phinney with Michael J. Fox. They were among more than 130 Foundation supporters from across the country who came to New York City on Saturday, November 19, 2005, for a special Research Roundtable and brunch at the Waldorf-Astoria hotel. Guests met Michael J. Fox and MJFF president and CEO Debi Brooks, and learned about the latest advances in Parkinson's research from three of the Foundation's scientific advisors. Alberto Ascherio, MD, PhD, spoke on the importance of epidemiology studies in understanding PD; Anders Björklund, MD, PhD, talked about current strategies for restoring and replacing dopamine neurons; and Susan Bressman, MD, discussed how to optimize current PD treatment options. The Roundtable was made possible by a generous gift from GE Healthcare.

GOLFERS TEE UP FOR PARKINSON'S

Michael J. Fox's fivesome: (L-R) Vincent Tese, Jimmy Cayne, Michael J. Fox, Ed Levy, and Lee Mikles

The BREAKING PARkinson's Fifth Annual Golf Outing to benefit The Michael J. Fox Foundation for Parkinson's Research, held on September 19, 2005, raised more than $1.7 million for Parkinson's research. The Foundation's guests and 98 golfers — including Michael J. Fox, whose five-some finished in second place — enjoyed a fantastic day of sport and camaraderie, followed by cocktails, dinner and an auction.

Guests bid on an array of rare and wonderful donated prizes that included a ride in the Goodyear Blimp, a summer internship at Deutsch Advertising and, of course, more golf, including rounds on two spectacular courses: the esteemed National Golf Links of America in Southampton, NY, and Merion Golf Club in Ardmore, PA.

Held in honor of Robert Klein, the outing was co-chaired by Foundation Board members Holly Andersen and Edwin A. Levy with Gene Gurkoff, Robert R. Greenberg, R.J. Nemer and Eric Rothfeld. An anonymous donor matched all 2005 donations in honor of Stanko Stojkovic. The event took place at Deepdale Golf Club in Manhasset, New York.

FLUX CAPACITATOR SHOWS PROMISE AS FUNDRAISING DEVICE

Uday Sehgal (right) and his brother Niraj pose in front of Doc Brown's DeLorean

On November 5, 1955 — as fans of Michael J. Fox and his iconic turn as Marty McFly in the "Back to the Future" trilogy are aware — Doc Brown (played by the vibrant Christopher Lloyd) fell and hit his head. When he came to, he had the idea for history's greatest invention: the flux capacitor, that marvel of modern science that would make time travel a reality (in the movies, at least).

One great idea often begets another. And so it was that Uday Sehgal of Los Angeles and his creative group of friends were inspired with another stroke of genius. Realizing that November 5, 2005, marked 50 years since the invention of time travel, this merry band set out to celebrate in a manner befitting such an epic anniversary: with a screening of "Back to the Future," drinks and dinner to benefit The Michael J. Fox Foundation.

The "50-Year Flux Party" was a great success. Tickets were $50 to attend the screening, dinner and party, or $20 just for the party. The event raised more than $4,000 for Parkinson's research from ticket sales, donations and a raffle. Proceeds were donated in honor of Daniel and Michele Walker and family in memory of their father, who suffered from Parkinson's disease.

Says Uday: "We had a wonderful time and felt very good about the results, both monetarily and with regard to advocacy for the cause."

FUTURE HOLLYWOOD LEADERS RAISE THOUSANDS FOR PARKINSON'S

For the third year running, the Junior Hollywood Radio and Television Society (JHRTS) made its annual holiday party a benefit for The Michael J. Fox Foundation. This year's event raised close to $45,000 for Parkinson's research, more than doubling the proceeds from the previous year's event.

Jacob Fenton and Kiersten Robinson, JHRTS co-presidents

The idea to dedicate the annual event to raising funds for the Foundation came from JHRTS Board members with a driving desire to find a cure. One had lost her father to PD; the other, Justin Sternberg, worked for Michael J. Fox at his production company, Lottery Hill, for almost two years in New York during the "Spin City" years. "It seemed like a natural choice," said Andrea Kavoosi, JHRTS vice president, "to raise money to cure a disease that affects millions of people, including one of young Hollywood's idols — Michael himself."

The party, attended by about 800 society members and guests, was held at Privilege, a West Hollywood hotspot. Tickets cost $25 in advance and $40 at the door, and a raffle included prizes from Dell Computer and Coach.

JHRTS is a membership organization exclusive to the assistant through coordinator levels from any area in the entertainment industry — especially assistants from television studios, networks, agencies and production companies.

"It is amazing," concluded Ms. Kavoosi, "that most of the group organizing this event don't make $40,000 a year themselves, but come together once a year to raise that much to help the millions who live with Parkinson's. Our success, as always, was a result of the energy and motivation of our committee and board who worked tirelessly. The majority of members and board members of JHRTS are in the television business and Michael is as close to the hearts of people in the television industry as you can get. We love him."

The 2005 VFW Poker Run raised a celebration-worthy $17,000 for The Michael J. Fox Foundation. The annual event is sponsored by VFW Post 9362, Victory Riders Association (VRA) (Sun Prairie Chapter) and the Hanley Company. This year's total matched the proceeds from last year's event – "I guess there are worse ruts to be in!" quipped Dan Clavette of VFW Post 9362, who snapped this shot of poker sharks (L-R) Tom Gannon, Commander VFWPost 9362; Phil Gerg, Quartermaster VFWPost 9362; Tammy Coker, Manager VFWPost 9362; Larry Danielson Past VFW State Quartermaster/Adjutant and "Parkinson's Poster Boy"; Sue Manthe, Secretary, VRA; Jean Manthe, Treasurer, VRA; and Don Klein, President, VRA.

INTERESTED IN ORGANIZING A FUNDRAISER FOR MJFF?

LEARN MORE ABOUT OUR GUIDELINES AND GET SOME IDEAS BY VISITING WWW.TEAMFOX.ORG

Michael J. Fox at the *2006 AARP The Magazine's Impact Awards Luncheon*, held in New York City in December, with (L-R) host Paula Zahn and fellow honorees Jane Kaczmarek and Harry Belafonte. The Impact Awards are given annually to 10 individuals whose "innovative thinking, wisdom, and leadership have improved the world we live in." Fox was also featured on the cover of the January/February issue of the *AARP The Magazine*, which profiled all 10 honorees.

TEAMFOX
FOR PARKINSON'S RESEARCH

TEAM FOX MARATHONERS RAISE MORE THAN $70,000 FOR PARKINSON'S RESEARCH

(Front row, L–R:) Susie Rosenthal, Chris Busbee, Dorrie Harris (Middle row, L–R:) Jennifer Abrams, Heather Allerdice-Gerow, Martha Ruest, Natalia Daniel, Pam Presser (Back row, L–R:) Mike Kloepfer, Seth Degarmo, Heath Tohara, Eric Birnbaum (Not pictured:) David Sack, Dean Spignola, Becky Decker, Jennifer Shaw, Ryan Roelle, Ray Camono, Derek Yan, Poonam Khanna, Abbi Gleeson, Jerry Costello, Colleen Reagan

Team Fox, the Fox Foundation's new grassroots community fundraising initiative, hit the ground running on Sunday, November 6 — the date of the 2005 ING New York City Marathon. Some 22 runners came from as far away as California and Florida and ran one of the nation's most challenging courses to raise an astounding $70,000-plus for The Michael J. Fox Foundation. Team Fox supporters joined spectators from the Parkinson's Disease Society of the United Kingdom along the route, cheering on all the athletes racing for the fight to end Parkinson's.

Every Team Fox member finished the 26.2-mile race, including New York's Abbi Gleason, the 37th woman to finish (in 2:57:07). And of course, in addition to their impressive athletic and fundraising feats, the Team Fox marathoners helped raise awareness of Parkinson's disease and the ongoing need for research dollars.

Team Fox provides community fundraisers with helpful resources, Web-based tools, and a logo to "brand" events as helping to find a cure for Parkinson's disease. Anyone can join the team, and there are innumerable creative ways to have a great time while supporting the Foundation's mission to find a cure for Parkinson's. Supporters have organized golf tournaments, dedicated birthday and anniversary celebrations to finding a cure, competed in walks, runs and triathlons, held tag sales and block parties, flipped pancakes, and found so many other ways to involve their friends, family and community in this meaningful cause.

For more information on how you can get in the game, visit www.teamfox.org or contact Amanda McDorman, the Foundation's special gifts officer, at amcdorman@michaeljfox.org.

How can I get involved?

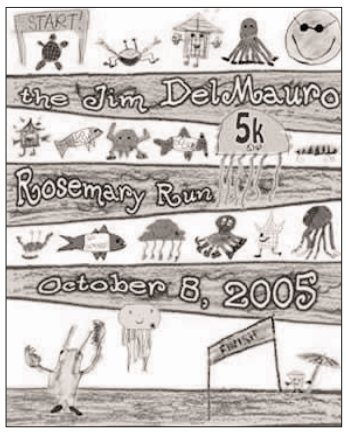
Everyone is invited to join Team Fox, and there are so many ways you and your community can make a difference in the fight against Parkinson's. An initial contribution entitles Team Fox members to download materials that make it fun to plan and stage an event. These include:

- **The Team Fox logo;**
- **Customizable form letters for enlisting sponsors and thanking donors;**
- **"How to"guides to event planning;**
- **Sample press releases to publicize the event and the cause.**

Team Fox members are also invited to attend an annual spring recognition event in New York City.

For more information on how you can get in the game, visit www.teamfox.org or contact Amanda McDorman, the Foundation's special gifts officer, at amcdorman@michaeljfox.org

ROSEMARY BEACH 5K RAISES $14K FOR MJFF



The second Jim DelMauro Rosemary Run, a 5K organized by the Rosemary Beach (FL) Property Owners Association in honor of Jim DelMauro, raised nearly $14,000 for Parkinson's research on October 8, 2005.

The annual run/walk was inaugurated in 2004 and in its first year raised about $7,900. It honors Jim DelMauro, first president of the Rosemary Beach Property Owners Association. The event not only raises money for MJFF but is a natural tribute to the active lifestyle of DelMauro, a former marathoner now living with Parkinson's.

About 140 runners and walkers — including DelMauro — completed the 2005 race, whose course goes through the center of town. Event organizers Lori Bradley and Kathy Kemp raised funds by approaching local businesses and individuals for sponsorships, garnering a total of 40 sponsors whose logos were featured on the official event T-shirt. Runners also paid entry fees of $15 in advance or $20 on event day.

In spite of a nearly 100-percent fundraising increase over their first time out, the organizers are hardly resting on their laurels. They are working to continue building the annual event into a time-honored Rosemary Beach tradition, aiming to increase the total amount raised by 20 percent each year. MJFF is deeply grateful for their commitment, which is crucial if the Foundation is to cross its own finish line and find a cure for Parkinson's.

Jim DelMauro (center) crosses the finish line

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

Grand Central Station, P.O. Box 4777
New York, New York 10163
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WINTER 2006 NEWSLETTER

FOUNDATION ANNOUNCES NEW RFAS FOR DRUG DISCOVERY, MAMMALIAN MODELS OF PD

MJFF is currently reviewing proposals submitted in response to two new Requests for Applications (RFAs):

"De-risking" pharma investment in Parkinson's — *PD Drug Discovery and Development* is designed to validate the therapeutic potential of scientific discoveries and push them one step closer to the clinic. MJFF will provide up to $1.5 million in funding to validate therapeutic targets involved in aspects of Parkinson's including both motor and non-motor symptoms.

The translation of basic science findings into therapeutic interventions requires additional applied work in the form of validation studies. These studies determine whether altering the biological function of a target or pathway provides a beneficial effect in a relevant PD model. This essential step is one to which neither academia nor industry has consistently devoted the necessary resources.

The initiative is part of the Foundation's commitment to draw increased industry attention to Parkinson's disease and 'de-risk' the investment of R&D dollars for new PD therapies.

Building a better mouse model of PD — The $2-million *Progressive Predictive Animal Models of Parkinson's* initiative aims to catalyze the creation of progressive, predictive mammalian models of Parkinson's disease — crucial research tools for testing neuroprotective and neuroregenerative therapeutic strategies in clinical studies.

While existing models can be useful for studying the pathology of specific mechanisms and pathways implicated in Parkinson's, it is generally recognized that no validated model in standard use currently mimics the disorder's gradual progression in humans.

An ideal model would reproduce as many features of Parkinson's disease as possible, including progressive dopaminergic degeneration and dysfunction and evidence for relevant protein aggregation.

"PHASE 1 TRIAL" CONT'D

The Ceregene grant was funded in its entirety by the Pioneer Fund, a private family foundation that supports endeavors including medical research, under the Foundation's Clinical Discovery program. Clinical Discovery is designed to stimulate well-designed clinical research projects focused on potentially high-impact approaches to Parkinson's disease. "We committed to funding the CERE-120 trial because of its great potential benefit for people with Parkinson's," said Scott Hamilton, Olympic gold medalist and Pioneer Fund Board member. "We are pleased to work together with The Michael J. Fox Foundation to drive the kind of cutting-edge science that can lead to meaningful advances for the millions touched by this disease."

"GENETIC MAP OF PARKINSON'S" CONT'D

ing to make it happen," said the study's first author, Mayo Clinic neurologist Demetrius Maraganore, MD.

"In one year, The Michael J. Fox Foundation and the Mayo Clinic have generated results that will greatly focus future research efforts in Parkinson's disease," added David Cox, MD, PhD, chief scientific officer and co-founder of Perlegen Sciences. "If replication of only one of these findings leads to a better understanding of the causes of the disease or improvements in early detection or treatment, we will have made significant progress."

The Mayo Clinic/Perlegen Sciences study was funded by a one-year, $2.8 million *LEAPS* grant, with funding provided by prominent Wisconsin businessman George Prescott and his family and matched by the Foundation's Board of Directors. The work also benefited from longstanding funding from the National Institute of Environmental Health Sciences (NIEHS), which supports the study of humans.

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH IS DEDICATED TO ACCELERATING THE DEVELOPMENT OF A CURE FOR PARKINSON'S DISEASE THROUGH AN AGGRESSIVELY FUNDED RESEARCH AGENDA.

For questions or comments regarding the MJFF newsletter or Web site, please contact editor Holly Barkhymer at hbarkhymer@michaeljfox.org