“The Michael J. Fox Foundation has managed to become, in its short life, the most credible voice on Parkinson’s research in the world.”

— The New York Times

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**THE MICHAEL J. FOX FOUNDATION IS DEDICATED TO FINDING A CURE FOR PARKINSON’S DISEASE THROUGH AN AGGRESSIVELY FUNDED RESEARCH AGENDA AND TO ENSURING THE DEVELOPMENT OF IMPROVED THERAPIES FOR those LIVING WITH PARKINSON’S TODAY.**
The Michael J. Fox Foundation has set one clear and simple measure of success: accelerating the delivery of life-changing treatments — and ultimately, a cure — to people with Parkinson’s disease.

In 2008 we funded $32.8 million in Parkinson’s research, bringing our total investments since inception to over $140 million. But in our short history we have come to appreciate that ending Parkinson’s disease is not only about spending more money; it is about how we spend it. MJFF targets underfunded, high-risk, translational science, stepping in where government and industry players can’t or won’t, to drive PD therapies and address what’s broken in the broader medical research enterprise.

Our singular focus on developing new therapies requires a strategic approach. We review more Parkinson’s-specific grant proposals than any other private funder (nearly 800 in 2008), covering every phase of drug discovery and development through clinical studies. We strive to identify the most compelling ideas, then shepherd them through the vagaries of the therapeutic development process and toward the clinic. For most diseases, this purposeful view of how to drive research progress is absent. No one stakeholder exists to align the efforts of disparate players. No one is in charge of finding cures.

At MJFF, we’re shooting for nothing less than the cure for Parkinson’s. Our leadership, drawn from the worlds of both science and business, works tirelessly to increase impact by blending the best of those two worldviews. We proactively manage the largest PD portfolio in the world. We prioritize key studies, insist that researchers share their results early, and tee up academic/industry partnerships. We keep the most promising ideas on a strategic course forward. Our eye is on patients’ needs, clinical studies and better treatments.

The researchers we work with around the globe quickly come to appreciate how we streamline the research process by challenging them to overcome the “language barrier” common among biologists working in different disciplines — even if they study the same disease. Scientists will tell you that we are bridges and connectors, bringing together highly specialized researchers and clinicians who might not otherwise interact, let alone collaborate. In 2008 alone, we brought together more than 460 of them for meetings and workshops to set strategy and future direction. Never before have we had this level of discourse and enthusiasm, nor this much optimism that new, transformative treatments are within reach.

While we can never be satisfied until we’ve achieved a cure, we’ve named this report for the tangible progress we’re proud to have driven since we’ve come on the scene: More researchers working on Parkinson’s (in 2008 alone we funded nearly $6 million in research undertaken by 25 teams new to PD). More focus on relevance for patients. Industry getting involved earlier. And more scientific hits successfully passing to their next stage of development, whatever that might be.

Your generosity and support make this possible. Thank you for your commitment to ending Parkinson’s disease. Together we are speeding transformational therapies for PD — and in the process changing the paradigm for how medical research funders can impact the pace and nature of progress.

With gratitude,

Katie Hood
CEO

Michael J. Fox
Founder

Deborah W. Brooks
Co-Founder
DISCOVERIES ABOUT THE CELLULAR AND MOLECULAR CAUSES AND EFFECTS OF PARKINSON’S DISEASE ARE PUBLISHED IN SCIENTIFIC JOURNALS EVERY WEEK, BUT ONLY A TINY FRACTION STAND A CHANCE OF RESULTING IN BREAKTHROUGH THERAPEUTICS. Filtering through hits (some already decades old) and systematically evaluating their potential to impact patients’ lives — sooner, rather than later — is a job The Michael J. Fox Foundation tackles each day.

Reviewing as many as 800 grant applications a year, our staff PhDs and in-house research team, extensively trained in neuroscience and project management, continuously monitor and troubleshoot PD research developments. Then we aggressively apply financial and intellectual resources to push critical findings forward on the pipeline, assuring their steady advancement toward the clinic and patients.

In our short history, we’ve funded work on approximately 100 therapeutic targets for neuroprotective and symptomatic approaches to PD, and driven novel treatments to address complications of current therapies. Some targets have been validated, and work on them continues. But even when outcomes do not meet our hopes, taking ideas off the table allows us to redirect limited resources where they are more likely to lead to practical treatments.

The stories on these pages illustrate the MJFF impact: how we prioritize the projects where we believe our funding and expertise can make the greatest difference, then partner with researchers to speed their work toward relevance for patients.

When Proteins Misfold:
Driving Validation of a Novel Neuroprotective Target

In 2005, scientists working in tiny worms known as C.elegans demonstrated that the protein TorsinA, which occurs naturally in the brain, can protect dopamine neurons from death. While TorsinA’s normal function is not entirely understood, it is thought to be a “chaperone” — a molecule that helps cells repair damaged or misfolded proteins. Increasing TorsinA activity, researchers hypothesize, may improve cells’ ability to repair themselves.

Now MJFF is funding an academic-industry collaboration to validate the C.elegans results in a second pre-clinical model of Parkinson’s disease. The goal: establish enough evidence to compel an industry partner to launch a program that would fully flesh out the therapeutic potential of compounds targeting TorsinA function.

“The modulation of TorsinA points to a new direction for treating PD at what may be one of its root causes — the toxic effects of misfolded proteins that accumulate in critical brain cells,” says lead investigator David Standard, MD, PhD, of the University of Alabama at Birmingham. “If the protective effect of Torsin seen in C.elegans is also found in mammalian pre-clinical models of the disease, our work could spark meaningful investment in this promising new target.”

TARGETING THE SEROTONIN SYSTEM FOR TREATMENT OF LEVDOPA-INDUCED DYSKINESIAS

Anders Björklund, MD, PhD, of Lund University in Sweden and his colleagues are working to target the brain’s serotonin system as a way to lessen levodopa-induced dyskinesias. Dyskinesias are the uncontrollable, wavy or jerky disruptive movements that are a side effect of long-term dopamine replacement therapy. For many patients, they are among the most debilitating aspects of living with PD. The prospect of dyskinesias leads many patients to delay starting on levodopa, the gold-standard treatment for PD, or refuse it altogether.

Dr. Björklund hypothesizes that serotonin neurons, best known for their role in clinical depression and other mood disorders, also play a role in Parkinson’s. Over three years, with support from the Bachmann-Strauss Dystonia & Parkinson Foundation, MJFF has invested $725,000 in the Björklund team’s development of a serotonin-based treatment for dyskinesias, moving it several steps closer to the clinic than would otherwise be possible.

“We think that as Parkinson’s disease progresses and the dopamine system becomes more impaired, the serotonin system is called on to assist,” says Dr. Björklund. “Serotonin neurons are capable of converting levodopa to dopamine, and can store and release newly synthesized dopamine, as dopamine neurons do in a healthy brain.”

In intriguing pilot experiments in pre-clinical models, Dr. Björklund observed that manipulating the activity of certain serotonin neurons had a profound ability to reduce the severity of levodopa-induced dyskinesias. The researchers brought the data to MJFF for evaluation.

MJFF quickly approved Community Fast Track 2005 funding to validate the results in a larger study. When that study confirmed the pilot findings, MJFF sent more money to drive additional experiments. Within another year the scientists had identified two specific serotonin receptors, 5-HT1A and 5-HT1B, whose activation produced a near-complete suppression of levodopa-induced dyskinesias in pre-clinical Parkinson’s models. At the same time, they screened the scientific literature to identify known candidate drugs that activate both receptors and may be suitable for clinical use. In December 2008, Manolo Carta, PhD, a member of the Björklund lab, received funding for another round of experiments, which could be the final pre-clinical work required before a Phase 1 clinical trial.

“We’ll pay particular attention to the long-term effects of these drug candidate compounds,” says Dr. Carta. “The results will be highly relevant for the design of a proof-of-concept clinical study investigating the efficacy of this approach to treat dyskinesia in people with PD.”

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Anders Björklund and Manolo Carta
Targeting Glutamate Receptors for Sustained Symptomatic Relief

MIFF is partnering with P. Jeffrey Conn, PhD, to jump-start a new class of symptomatic PD treatment targeting the glutamate system. (To learn more about glutamate’s potential therapeutic role in PD, see “Anatomy of a Novel Target” below.)

Dr. Conn, Vanderbilt University’s Lee E. Linnard Professor of Pharmacology and Director of the Program in Drug Discovery, came to MIFF with evidence that increasing the activity of certain glutamate receptors could alleviate symptoms in pre-clinical models of PD. He received Target Validation 2005 funding to home in on the right receptors for further study, and to identify molecules capable of boosting the activity of these receptors. That work substantiated the mGlu4 receptor as an especially promising target for a new symptomatic therapy.

Typically, once promising drug leads are identified, they must be engineered into a compound suitable for clinical testing. This phase of work requires an interdisciplinary team with expertise spanning medicinal chemistry, molecular biology and in vivo studies. Late in 2007, with support from The Edmond J. Safra Foundation, MIFF granted Dr. Conn a $4.4 million LEAPS (Linked Efforts to Accelerate Parkinson’s Solutions) award to assemble and lead such a team for further work on the mGlu4 receptor. The LEAPS’ team spent 2008 more thoroughly characterizing mGlu4’s therapeutic potential while simultaneously generating a viable drug candidate to target it. Further optimization is ongoing in the first half of 2009, with pre-clinical testing of the most promising candidate on deck for the latter part of the year.

Anatomy of a Novel Target: Exploring Glutamate

While the dopamine system has long been the primary interest of PD researchers, recent evidence supports the potential of glutamate, another neurotransmitter, as a therapeutic target for PD.

Like dopamine, glutamate is a signaling molecule that plays a role in transporting brain messages and controlling body functions. Early findings suggest that manipulating specific parts of the glutamate system could alleviate Parkinson’s symptoms and complications while bypassing the dopamine system altogether. Alternatively, it may be possible to develop a dual or complementary treatment approach, in which glutamate-based therapies lessen patients’ needs for dopamine-based therapies — in turn reducing the debilitating side effects of long-term dopamine replacement.

“Dopamine replacement therapies lose effectiveness over time and bring serious side effects. And many disruptive symptoms of Parkinson’s don’t respond to dopamine replacement at all,” says MIFF awardee Stephen Traynelis, PhD, of Emory University. “My lab is exploring whether decreasing the activity of a particular glutamate receptor may lower the known overactivation of three different sets of neurons in Parkinson’s.”

MIFF has funded 11 researchers in six separate labs, including Dr. Traynelis, to advance novel treatment paradigms based on glutamate.

“A great deal of Parkinson’s disease research, including the validation of glutamate as a therapeutic target, is at a stage where scientists have not yet identified the precise tactic that will yield the greatest therapeutic benefit,” says Katie Hool, CEO. “Throughout our portfolio, MIFF identifies multiple promising approaches and funds them simultaneously. Even if one strategy fails, another may still be making strides toward practical relevance for patients.”

Targeting Inflammation in PD

For decades researchers have worked to understand the role of chronic inflammation in the death of dopamine neurons in PD. MIFF is exploring multiple approaches to characterize the relationship between inflammation and Parkinson’s, and to validate therapeutic targets that could slow or reverse inflammation-related pathology.

In 2003 Kalipada Pahan, PhD (then a faculty member at the University of Nebraska Medical Center), received funding to study the role of naturally occurring protein NF-κB in the production of various inflammatory molecules. Working in pre-clinical PD models, Dr. Pahan’s team demonstrated that chains of amino acids known as NBD peptides, which control inflammation and protect neurons, can rescue dopamine neurons from death. In 2008 MIFF brought Dr. Pahan (now at the Rush University Medical Center) one step closer to the clinic by funding him to test the efficacy of NBD peptides in more predictive models of PD. If the results show promise at this stage, NBD peptides could enter the clinic and become the basis of a novel drug to modify the progression of PD.

Maú Tansey, PhD, of the UT Southwestern Medical Center at Dallas is pioneering a separate inflammation-based therapeutic approach to PD. Dr. Tansey was first funded in 2003 to investigate a pre-inflammatory protein called Tumor Necrosis Factor (TNF). Based on exciting progress from that project, MIFF staff elected to provide supplemental funding to Dr. Tansey in 2004 and 2005. She went on to demonstrate in pre-clinical models of PD that dopamine neurons can be rescued from death by inhibiting the activity of TNF. In 2008 the Foundation funded Dr. Tansey’s current investigation of a gene therapy approach selectively targeted at soluble TNF that could inhibit inflammation, potentially slowing or stopping the progressive loss of dopamine neurons in Parkinson’s disease.

“Teaching microglia: Image of glutamate receptor immunoprecipitation.”

Electron micrograph: Image of glutamate receptor immunoprecipitation.

“I’m enthusiastic about partnering with The Michael J. Fox Foundation because they share my team’s commitment to push promising therapeutics toward the clinic and patients. MIFF understands and provides the kind of support — financial and intellectual — required to speed the translation of research discoveries into new treatments.”

— Jeff Conn

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SPEEDING CLINICAL TESTING
OF NEW INTERVENTIONS

Clinical research for any disease is expensive and requires unique and distinct expertise. No matter how promising a new treatment strategy, shepherding it through trials and regulatory approval is a lengthy and costly process. An entire team must be assembled with the skill and experience to conduct research in humans. Individuals who fit the study’s needs must be found and agree to enroll. Once the intervention begins, tests must be performed at regular intervals, often requiring multiple visits to a clinical center. Results must be scrupulously assessed and reported to the appropriate regulatory bureau with compelling evidence that the new treatment represents a marked improvement over existing ones.

In addition to these standard hurdles, Parkinson’s disease trial sponsors lack objective tools and scales for measuring the effects of disease-modifying interventions. This represents a serious challenge in PD clinical research. Biotech and pharmaceutical companies, whose resources are needed to carry new therapeutics over the finish line, are unlikely to risk investing in trials where the likelihood of clear and marketable outcomes is low.

MJFF shares patients’ urgency to overcome these challenges and bring new therapies to market as fast as possible. In prioritizing clinical trials, we emphasize proof-of-principle and first-in-human studies that can alter the risk profile of a given treatment. We also step in as needed to help assemble and organize the right teams, lend expertise to biotech and pharmaceutical companies testing the PD waters, and vet the Parkinson’s potential of drugs approved for other diseases, and sponsor trials where intellectual property or patent issues reduce companies’ incentive to get involved.

Why Test Other Diseases’ Drugs for Parkinson’s?

Over the 10 to 15 years it takes to turn a target into a marketable drug, a pharmaceutical company typically spends $800 million or more. One reason it takes so long and costs so much is that the safety of every new candidate drug for human use must be carefully established. That’s why MJFF pays close attention when a drug already approved by a regulatory body shows potential to benefit Parkinson’s. If MJFF funding can help demonstrate efficacy against PD, the drug can advance much more rapidly to clinical testing in Parkinson’s patients.

In addition to the projects described on these pages, the Foundation is funding Erwan Beazar, PhD, of the University of Bordeaux, France, to investigate statin (high cholesterol) drugs to alleviate levodopa-induced dyskinesias. And Marina Emborg, MD, PhD, of the University of Wisconsin, Madison, is exploring the diabetes drug pioglitazone as a neuroprotective treatment for Parkinson’s disease. Her work, funded by MJFF since 2005, has demonstrated that pioglitazone causes functional benefits in pre-clinical models of PD. “Pioglitazone already has FDA approval and a well-established safety profile,” says Dr. Emborg. “With further promising pre-clinical outcomes, it could be ready for clinical studies in Parkinson’s patients as soon as 2010.”

COULD A HIGH-BLOOD-PRESSURE DRUG SLOW THE PROGRESSION OF PD?

In December 2008 MJFF announced a three-year award of $2 million to fund a Phase 2 clinical trial investigating isradipine, an FDA-approved high blood pressure drug. Isradipine is in a class of high-blood pressure medications that work by blocking the activity of calcium channels, which help cells fire electrically. D. James Surmeier, PhD, a noted Parkinson’s researcher at Northwestern University in Chicago, developed a theory that hyperactive calcium channels may stress dopamine neurons, leading them to shut down or die. He hypothesized that drugs like isradipine might reduce this stress, thereby slowing or stopping the progression of Parkinson’s disease. In 2007 he published this hypothesis in the prestigious scientific journal Nature.

No current Parkinson’s treatment has been definitively proven to modify the progression of PD. Available therapies mask symptoms while the underlying pathology continues to worsen. A neuroprotective treatment is the ultimate goal of Parkinson’s research. Dr. Surmeier’s article suggested a potential new research path to such a treatment. MJFF research staff encouraged him to apply for immediate Foundation funding. Within weeks of his first conversation with MJFF, Dr. Surmeier had a $75,000 Rapid Response Innovation Award in hand to expand pre-clinical testing of his hypothesis. Dr. Surmeier’s experiments quickly demonstrated considerable promise for isradipine in slowing Parkinson’s progression. In October 2008 the results were met with excitement at the Foundation’s second PD Therapeutics Conference in Chicago.

The next steps were clear: determine requirements to take these findings to a clinical trial and see whether the promising pre-clinical data carried through to people with PD. Safety would be a particular concern: Many people with Parkinson’s already have low blood pressure, so lowering blood pressure further could prove dangerous. Working closely with Dr. Surmeier and his Northwestern colleague Tanya Simuni, MD, the Foundation mapped the route to a pilot Phase 2 clinical trial to establish optimal dosage and possible side effects.

Potential disease-modifying effects of isradipine in a pre-clinical model of PD

Following enthusiastic peer review, and with support from the Mann Family Foundation in memory of its founder, Fred Mann, MJFF awarded the investigators a $2-million Clinical Investigation Award. The award allowed the researchers to begin the trial in 2009 in 100 patients with early idiopathic PD. If the trial yields a critical mass of data on isradipine’s efficacy in Parkinson’s disease, other funders will have a strong incentive to expand the Phase 2 trial and continue into Phase 3 — helping speed this potential breakthrough to PD patients.

An important cautionary note: While MJFF is funding clinical trials on supplements and drugs already available for purchase or prescription, people with Parkinson’s (other than those who ultimately enroll in these trials) should not begin taking these agents as part of a Parkinson’s disease treatment regimen without the explicit recommendation of their doctor. Evidence to date has not yet definitively proved a benefit to PD, and these substances carry potential health risks, which doctors will carefully monitor in trial participants. It is crucial that all 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.
CERE-120 AND THE FUTURE OF TROPHIC-BASED APPROACHES TO PD

In November 2008 the Parkinson’s community was disappointed to learn that Ceregene Inc.’s CERE-120, a gene therapy approach to treat Parkinson’s patients with trophic factor neurinurin, had not demonstrated greater benefit than a placebo in a double-blind, controlled Phase 2 clinical trial. Trophic factors (also known as neurotrophic factors or growth factors) are the specialized proteins that protect and nurture neurons, including the dopamine neurons that die in Parkinson’s disease. Ceregene’s Phase 2 trial of neurinurin was partially supported by The Michael J. Fox Foundation with leadership funding from the family of Board member Daniel E. Spitzer, MD. A successful Phase 1 trial also was funded by MJFF with principal support from The Pioneer Fund, a private family foundation that supports endeavors including medical research.

Phase 2 trial participants, all Parkinson’s patients, were split into two groups — one group received active CERE-120 and one received inactive placebo. In both groups, 70 percent of participants showed a five-point or greater improvement in their UPDRS motor off scores. This made it a challenge to demonstrate that CERE-120 had exerted a therapeutic effect. The problem was exacerbated, as always in PD clinical trials, by the lack of a biomarker that could objectively measure treatment effects.

Nonetheless, The Michael J. Fox Foundation continues to see real promise in trophic-based approaches to treating PD — even, potentially, in CERE-120 itself. Lessons learned from this trial will be of great value in refining future attempts to treat PD with trophic factors, noted Todd Sherer, PhD, vice president of research programs at MJFF. “Going forward, the data from the Phase 2 CERE-120 trial will help researchers make critical adjustments in how and where they attempt to deliver trophic factors to the Parkinson’s brain. This could be the key to future trials’ success.”

“There’s no question that outcomes of trophic-based trials have been frustrating so far,” added Katie Hood. “Our Foundation shares that frustration with patients. But far from giving up, we’re working aggressively to learn from past outcomes in order to solve the problems that have hindered these treatments to date. MJFF believes it is possible to obtain the same beneficial response in PD patients that has been observed time and again in pre-clinical studies.”

Exercise and PD: Getting to the Bottom of the Connection

There is some scientific evidence that exercise holds specific benefits for people with Parkinson’s disease.

“Personally, I believe it’s quite likely that exercise may prove to be more beneficial than some of the pharmaceutical agents available to PD patients,” says Lisa Shulman, MD, of the University of Maryland. “With MJFF funding, my team is working to definitively show that exercise can be a beneficial addition to overall management of the disease. And exercise is something that can restore a sense of control and reduce feelings of helplessness. Having a chronic disorder doesn’t mean you need to be a ‘passive patient’, you don’t have to throw in the towel.”

MJFF has invested over $2.7 million in exercise studies to date. Our priorities: establishing concrete evidence of how exercise may alleviate PD symptoms, or even slow or stop disease progression; and accelerating identification of the most effective forms of exercise for people with PD.

INVESTIGATING INOSINE

In April 2008 the Journal of Neurology published an epidemiological study showing that people with early PD who had elevated blood levels of urate — a natural antioxidant in the blood — were able to forgo dopamine replacement therapy longer than people with lower urate levels. Those with higher urate levels also showed less severe changes on brain scans.

“Our findings, combined with prior knowledge of urate’s protective properties in laboratory studies, raised the possibility that urate-elevating strategies could be used to slow the neurodegeneration of Parkinson’s disease,” says the study’s lead author, Michael Schwarzschild, MD, PhD, of Harvard Medical School.

Epidemiological findings are intriguing, but must be tested clinically. Dr. Schwarzschild and his colleagues wanted to take the next logical step: determining whether raising urate levels in PD patients might slow the progression of Parkinson’s. They immediately began designing a Phase 2 clinical trial to investigate the potential of a naturally occurring chemical, inosine, which is converted by our bodies into urate.

As inosine is widely available to consumers at health food and vitamin stores, no corporate entity had the incentive to sponsor clinical research to definitively assess its potential in Parkinson’s. “When we thought about potential funders, it was clear that finding funding for this trial might take years,” Dr. Schwarzschild said. “Only MJFF would have the incentive and flexibility to fund a trial like ours in a matter of months.” He and his colleagues decided to approach the Foundation.

“Dr. Schwarzschild and his team brought their results to us knowing that we were the only organization likely to jump on inosine as a strategy for PD because of its promise as a new treatment, regardless of IP value or profit margin considerations,” says Katie Hood. “This is just the kind of gap between the bench and the clinic that our Foundation exists to bridge.”

With support from The Edmond J. Safra Foundation, MJFF awarded the team a LEAPS award of up to $5.5 million to undertake the Phase 2 study. The goals are to assess the safety of using inosine to raise blood urate levels, and to determine optimal dosage. The researchers plan to begin patient enrollment in mid-2009 and are applying for NIH funding for a larger trial.

Despite the promising findings so far, Dr. Schwarzschild cautioned, people with Parkinson’s (other than those who enroll in this trial) should not start taking inosine.

“The potential benefits of urate must be tempered against the risks of elevated urate levels, which include gout and kidney stones. 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.”
**MOBILIZING NEW TECHNOLOGIES AND TOOLS IN PD THERAPEUTIC DEVELOPMENT**

While new genetic and cellular targets have invigorated pre-clinical and clinical Parkinson’s research over the last 10 years, converting these discoveries into practical treatments requires deliberate and strategic investment in the development of new research technologies and tools.

In 2008 MJFF worked to apply novel concepts to PD at every stage of development. RNAi technology could bring relief by silencing molecules whose overexpression is implicated in PD. New methods ranging from a nasal spray to gene therapy might allow for practical and non-invasive delivery of therapies that do not naturally cross the blood-brain barrier.

Acceleration also arises because we facilitate and lead the development of research tools that could shift paradigms across the board for pre-clinical and clinical research. Since 2002 MJFF has led the hunt for biomarkers to diagnose and measure the progression of Parkinson’s disease, vital tools for the development of disease-modifying therapies. And in our quest to create pre-clinical tools that can help researchers better understand PD as well as screen new therapies, our portfolio includes the development of new genetic models and an exploration of induced pluripotent stem cell technology to develop personalized models of Parkinson’s disease. We are also exploring how the Internet may change the way research gets done — as it has changed so much else in the past decade.

**Nanotechnology for Parkinson’s Disease**

In December 2004 Cephalic Therapeutics, Inc., of Cleveland, Ohio, first published results of a human clinical trial for cysctic fibrosis showing that nanotechnology — condensing molecules of DNA into particles tiny enough to penetrate the membrane surrounding a cell’s nucleus — can be used as a novel approach to gene therapy. Now, MJFF is working to determine the feasibility of a nanotechnology gene therapy approach for Parkinson’s disease.

Under the Foundation’s 2007 Rapid Response Innovation Awards, which provide fast funding for high-risk, high-reward concepts that could kick-start new treatment approaches to Parkinson’s, David Yurek, PhD, successfully introduced condensed DNA coding for trophic factor GDNF. These nanoparticles are small enough to enter brain cells. These particles were safely injected into the brains of pre-clinical models of PD and successfully caused the cells of interest to begin manufacturing GDNF.

In 2008 MJFF approved supplemental funding for Dr. Yurek, a faculty member at the University of Kentucky, to partner with Cephalic Therapeutics, the provider of condensed DNA, to compare several different formulations of DNA coding GDNF. The goal is to optimize a particular formulation for long-term expression in pre-clinical models and determine whether the treatment results in improved motor function. If the project is successful, it could help lead to an entirely new strategy for treating PD.

**ALPHA-SYNUCLEIN: SILENCE MAY BE GOLDEN**

The naturally occurring brain protein alpha-synuclein is a major constituent of Lewy bodies, protein clumps that are the pathological hallmark of PD. Recent studies (including some funded by MJFF as early as 2002) have shown that alpha-synuclein may play a role in the development of rare familial cases of PD, as well as the more common sporadic form of the disease. Though its precise role in PD remains veiled, growing evidence supports the hypothesis that decreasing alpha-synuclein in the brain could be one way to slow or stop Parkinson’s progression.

While aggressive work is ongoing toward a traditional small-molecule pharmacological approach to regulating alpha-synuclein, to date no drugs that can lower the protein’s levels in the brain have advanced to clinical trials. MJFF believes that other approaches are worth exploring. Since 2005, MJFF has been funding investigation of RNA interference (RNAi), also known as gene silencing, as a strategy for reducing alpha-synuclein in the Parkinson’s brain.

RNAi is a mechanism naturally present in all body cells. “Small interfering RNA” (siRNA) molecules are able to silence a gene’s expression of a particular protein through the destruction of messenger RNA, the molecule that contains the instructions for protein synthesis. Since the discovery of RNAi in the 1990s, researchers have worked to harness this natural capability of small RNA molecules to silence genes’ expression of proteins linked to disease — such as alpha-synuclein in PD.

“Michael J. Fox Foundation is optimistic about aggressively pursuing RNAi therapeutics for PD,” says CEO Katie Hoood. “It’s a completely novel approach, but one that could lead to a major scientific leap forward in terms of improving patients’ quality of life.”

In 2005 work funded under Target Validation, researchers at Alnylam Pharmaceuticals and Mayo Clinic Jacksonville (Florida) demonstrated that siRNAs reduced alpha-synuclein levels in pre-clinical models of Parkinson’s disease. Now a $3.5 million award under the Foundation’s LEAPS (Linked Efforts to Accelerate Parkinson’s Solutions) initiative, granted with support from The Edmond J. Safra Foundation, is funding an interdisciplinary consortium of scientists to push this work toward clinical relevance.

The LEAPS team, led by Mayo Clinic’s Matt Farrer, PhD, with collaborators at Alnylam and The Parkinson’s Institute and Clinical Center, is working to identify an optimal alpha-synuclein siRNA drug candidate, then establish efficacy and the “therapeutic window” for optimal alpha-synuclein siRNA drug candidate, then establish efficacy and the “therapeutic window” for RNAi technology could be tested in PD patients in Phase 1 clinical trials. If successful, this project could ultimately lead to the development of an alpha-synuclein siRNA candidate drug that, in the future, could be tested in PD patients in Phase 1 clinical trials.

**Structure of the alpha-synuclein protein as it may look inside a neuron. The portion colored reddish orange in this representation seems to be the critical part for forming clumps, as found in Lewy bodies, whereas the “tail” section (paral) normally helps prevent clumping.**

**Schematic representation of the therapeutic mechanism of RNAi. Left to rights: A short interfering RNA (siRNA) is designed to correspond to a gene target of interest. The siRNA is then synthesized with drug-like properties. The modified siRNA penetrates the cell membrane and harnesses the RNAi mechanism for gene silencing to achieve a therapeutic effect.**

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Outsmarting the Blood-Brain Barrier

The blood-brain barrier (BBB) is critical to human health. It surrounds the brain and keeps out agents that could do us harm. Unfortunately, this thin membrane of tightly packed cells is an overachiever. In addition to putting up a velvet rope for viruses and other pathogens, it prevents many potentially beneficial therapies for neurodegenerative diseases, including Parkinson’s, from entering as well.

So-called large- and small-molecule treatments work by causing therapeutic molecules to enter the bloodstream. From the blood, these molecules are taken up by the appropriate body cells to bring about the desired beneficial effect. Small-molecule treatments make up the majority of orally administered treatments on today’s market. Large-molecule treatments typically involve the use of specialized proteins. To rescue dopamine neurons from death, small or large therapeutic molecules must find their way into the brain. But the BBB prevents them from doing so.

The Foundation is committed to driving new and novel approaches to drug delivery throughout its portfolio of PD research investments. And in 2008 MJFF and The Kinetics Foundation co-launched a $2-million initiative, Improving Delivery of Parkinson’s Disease Therapeutics to the Brain, dedicated to improving therapeutics delivery across the BBB as well as refining surgical approaches that today represent the only option for getting many therapeutics of interest into the brain.

Ancient History Meets Science Fiction: A “Trojan Horse” That Can Sneak GDNF across the Blood-Brain Barrier

In 2006 William M. Pardridge, MD, of the University of California, Los Angeles, was funded by MJFF to vet the potential of “Trojan horse” technology to overcome the challenge of getting trophic factors across the blood-brain barrier (BBB). Trojan Horse technology aims to fuse a large molecule, which normally cannot cross the BBB, to an antibody that naturally can. The antibody hides the large molecule from the BBB’s sentry — as the Trojan horse of Homer’s Iliad hid Greek soldiers, allowing them to enter Troy — and ferries the attached protein from the blood to the target site in brain.

“Prior attempts to treat PD may have failed because of problems with drug delivery,” says Dr. Pardridge. “Trojan Horse technology provides a new approach to target therapeutic agents of interest to the proper areas of the Parkinson’s brain.”

Dr. Pardridge demonstrated in pre-clinical models that a single intravenous injection transported the GDNF gene to the desired areas of the brain, resulting in lasting improvement in motor function and brain biochemistry. Building on these promising early results, in 2008 MJFF awarded $1 million to Santa Monica-based biotech ArmaGen Technologies, Inc., for a project using Trojan horse technology to re-engineer the GDNF protein to cross the blood-brain barrier. The end goal is to create a safe and effective treatment in which the GDNF protein, fused to a genetically engineered antibody naturally capable of crossing the blood-brain barrier, can simply be injected into the blood.

“Trojan horse technology has intrigued P. Johnson, Ph.D., chief scientific advisor to MJFF. “The Foundation’s goal is to speed the timetable for determining just how real the potential here is.”

Nasal Spray: An On-the-Nose Approach to Delivering GDNF?

Barbara Waszczak, PhD, a professor at Northeastern University, is focusing on the potential of a nasal spray to treat much more than the common cold. In 2007 Dr. Waszczak approached MJFF with her idea to use an intranasal method to deliver GDNF to the brain and quickly received a Rapid Response Innovation Award to investigate the efficacy of delivering the protein through the nose. She found that when given intranasally, GDNF reached the brains of pre-clinical models in sufficient quantities to protect dopamine neurons from an experimental neurotoxin.

Now, with funding under the Foundation’s 2008 Improving Delivery of Parkinson’s Disease Therapeutics to the Brain, Dr. Waszczak’s team is using GDNF provided by Agen to determine if this delivery method results in nasal toxicity and how much GDNF actually reaches the target area of the brain.

Using Reprogrammed Cells to Develop a New Model of LRRK2-associated PD

U.K. researchers Patrick A. Lewis, PhD, of the Institute of Neurology and John Hardy, PhD, of University College London, have received MJFF funding to use induced pluripotent stem cells (iPS cells) to develop an entirely new cellular model of Parkinson’s disease. iPS cells are created when scientists “reprogram” skin cells into an embryonic-like state. Dr. Lewis will engineer iPS cells from the skin cells of people with a form of Parkinson’s linked to a mutation in the LRRK2 gene. The cells will then be converted into the specific dopamine-producing cells within the substantia nigra that die in PD. By comparing these engineered cells to those from individuals who do not have a genetic disposition to Parkinson’s disease, the investigators hope to discover what makes the LRRK2 cells different and more susceptible to a premature demise. This, in turn, could help uncover new molecular and cellular pathways involved in PD as well as new targets for drug treatment.

“If this project succeeds, we will have developed a new PD model from which we can learn more about the mechanisms underlying the disease — knowledge essential to developing better treatments,” says Dr. Lewis. “In addition to providing a valuable resource for basic discovery research into Parkinson’s, such a model would also provide an important testing ground for therapies to reverse any deficits that we uncover.”

Structure of a fragment of a LRRK2-related protein from a bacterial equivalent of the PD-related kinase LRRK2. One of the proteins in the bacteria has an evolutionarily conserved version in humans. This structure is therefore a basis for understanding how mutations in human LRRK2 cause PD — and how we might modify this.
“Our partnership with MJFF has allowed us to upgrade the infrastructure of our Brain and Body Donation Program and collect data that will identify new predictors of cognitive dysfunction, early parkinsonian pathology in non-symptomatic subjects, and PD-like pathology in body tissue not previously implicated in PD.” — Charles H. Adler, MD, PhD, Professor of Neurology, Mayo Clinic College of Medicine, and Co-Principal Investigator of MJFF’s Prescott Family Initiative at The Arizona Parkinson’s Disease Consortium

Selected List of 2008 MJFF Meetings

The Power to Convene
Driving research toward transformative treatments requires not only better communication, but also cooperation and multidisciplinary thinking. In 2008 MJFF brought together more than 460 top researchers from academic and industry labs all over the world for formal and informal face-to-face conferences, summit meetings and workshops. These activities are not ends in themselves, but rather catalysts for concrete action steps — new grant programs, funding for critical tools and resources, novel collaborations and other tactical interventions to move promising ideas forward faster.

Following are highlights of approximately 60 scientific sessions, grant reviews and assessments that we sponsored or co-sponsored in 2008 to help set strategy and future direction for the entire field. In addition to these meetings, our full Scientific Advisory Board convened in Fort Lauderdale in March, and our Executive Scientific Advisory Board met in June and November.

Drug Delivery Workshop, January 16
(Convened with The Kinetics Foundation)
Experts in drug delivery worked to improve understanding of challenges in delivering therapeutics to the brain.

Demonstrating Disease-modifying Effects for the Treatment of Parkinson’s Disease: Drug Development and Regulatory Issues, April 28-29
(Convened with the United States Food and Drug Administration, the American Association of Pharmaceutical Scientists and the Parkinson Study Group)
Experts in Parkinson’s disease, drug development, quantitative clinical pharmacology and statistics worked toward a consensus on objective endpoints for clinical trials of neuroprotective therapies.

MJFF Research Strategy Assessment, August 6
External experts objectively assessed MJFF activities to date and provided recommendations for future programmatic activities.

Fetal Tissue Transplants and PD Pathology Summit, September 4
Experts discussed new findings on long-term survival and status of fetal transplant tissue in Parkinsonian patients and implications for cell replacement strategies in PD.

Second Annual PD Therapeutics Conference, September 15
More than 120 academic and industry researchers and business development professionals attended the only major scientific symposium exclusively focused on speeding PD therapeutics development.

LRBK2 Biology, November 5
Leading experts set priorities for investigation into the biology and pathology of the Parkinson’s disease-associated gene LRBK2.

LRBK2 Cohort Meetings, December 4 and 12
PD scientists discussed the unique data or information that could be provided by cohorts of Ashkenazi Jewish and North African Arab-Berber individuals with PD-implicated LRBK2 mutations.

In 2008 MJFF applications for funding and number of grant applications increased by 23% over 2007. MJFF funded five projects to develop Web-based tools — that could enable Parkinson’s patients to work with; and, ultimately, faster progress toward a cure.

In May MJFF announced that it would support a partnership between personal genetics company 23andMe and The Parkinson's Institute and Cure Parkinson’s Project to fund research to help identify new treatments to combat Parkinson’s.

Could the Internet Change the Way Research Gets Done?

What if it were possible for any interested individual to switch on their personal computer and participate in clinical research — without ever needing to leave their home? The Michael J. Fox Foundation thinks such a development would lead to increased participation in clinical research at lower cost; amplification of patients’ voices in the research process; more data for researchers to work with; and, ultimately, faster progress toward a cure.

With acceleration of new treatments MJFF’s chief goal, the appeal of technology-enabled approaches to PD research is clear. In 2008 the Foundation funded five projects to develop Web-based tools — such as online questionnaires, or motion-sensor devices — that could enable scientifically valid PD research to be conducted outside the confines of the clinic.

In May MJFF announced that it would support a partnership between personal genetics company 23andMe and The Parkinson’s Institute and Clinical Center to develop Web-based tools and surveys to gather information from people with Parkinson’s in a scientifically meaningful way. That project is still in progress, with validation studies under way for the use of Web technologies to gather epidemiological data. Additionally, in September four research teams were awarded $3 million under the Foundation’s Developing and Validating Web-based Clinical Assessments for Parkinson’s Disease initiative. Teams will test different methods of remotely gathering data on aspects of Parkinson’s ranging from cognitive and motor function to visual and spatial symptoms, as well as develop Spanish-language Web-based assessments.

“The Internet has changed so much of what we do in our lives over the last 10 years — how we buy, how we communicate, how we find information, how we do business,” says CEO Katie Hood. “It’s hard to believe it can’t have a similar impact on how we do research.”
The most promising projects, undertaken by the best teams, at the right times.

Each year The Michael J. Fox Foundation receives hundreds of grant proposals from scientists based at medical research institutes, universities and biotech and pharmaceutical companies all over the world. In reviewing these applications, our research staff and expert advisors are always seeking the same thing — ideas ready to be translated into new treatments, teams with the expertise to execute those ideas, thoughtful and realistic work plans, and outcomes that will take us closer to breakthrough treatments and a cure for PD. MJFF had active research projects with the following institutions and companies in 2008.

**Organizations with Active MJFF Awards in 2008**

**United States**
- 23&Me, Inc.
- Acadia Pharmaceuticals
- Alica Therapeutics
- Amgen, Inc.
- Beth Israel Deaconess Medical Center
- Harvard Medical School
- Beth Israel Medical Center
- Biodesy, LLC
- Boston University
- Brandeis University
- CIN Diagnostics
- California Institute of Technology
- Caliper Life Sciences (Kexegen)
- Case Western Reserve University
- Carnegie, Inc.
- Clemson University
- Cleveland Clinic
- Columbia University
- Copenicus Therapeutics, Inc.
- Covance
- Depomed, Inc.
- Emory University
- Faldéh Pharmaceuticals, Inc.
- Harvard University
- The Institute for Neurodegenerative Disorders
- Intracellular Therapies, Inc.
- Intrexus Corporation
- Johns Hopkins University
- Kaiser Permanente
- Link Medicine Corporation
- Massachusetts General Hospital (Harvard Medical School)
- Massachusetts Institute of Technology
- Mayo Clinic
- McLean Hospital (Harvard Medical School)
- Memorial Hospital of Rhode Island
- MGEXIN Corporation
- Mount Sinai School of Medicine
- National Institute of Neurodegenerative Disease and Stroke, NIH
- Nebraska Health and Human Services System
- Neuroscience Biosciences
- Neurelaxing Pharmaceuticals, Inc.
- Northeastern University
- Northern California Institute for Research and Education
- Northwestern University
- Omeros Corporation
- Oregon Health and Science University
- PPD, Inc.
- Parkinson’s and Movement Disorders Center of Maryland
- The Parkinson’s Institute and Clinical Center
- Philadelphia VA Medical Center
- Protech, Inc.
- Purdue University
- Rush University
- Sangamo Biotechnologies, Inc.
- Shanghai, Inc.
- Spaulding Rehabilitation Hospital
- State University of New York at Buffalo
- Sun Health Research Institute
- SUNY Downstate Medical Center
- Temple University
- The Salk Institute for Biological Studies
- Theragene, Inc.
- Thomas Jefferson University
- Tufts University
- UNDIN—Robert Wood Johnson Medical School
- University of Alabama
- University of Alberta at Birmingham
- University of California, Berkeley
- University of California, Los Angeles
- University of California, San Diego
- University of California, San Francisco
- University of Cincinnati
- University of Florida
- University of Kentucky
- University of Maryland
- University of Miami
- University of Michigan
- University of Nebraska
- University of Pennsylvania
- University of Pittsburgh
- University of Rochester
- University of South Florida
- University of Tennessee
- University of Texas at Houston
- University of Texas Health Science Center, San Antonio
- University of Texas Southwestern Medical Center at Dallas
- University of Virginia
- University of Washington
- University of Wisconsin, Madison
- Vanderbilt University
- Washington University in St. Louis
- Weill Medical College of Cornell University
- Wyeth Pharmaceuticals
- Yale University
- ZenoBio Therapeutics, Inc.

**Australia**
- University of Melbourne

**Canada**
- Aiden Therapeutics
- Molecular Diagnostics
- Toronto Western Hospital
- University of Ottawa

**China**
- University of Chile
- University of China
- Capital University of Medical Sciences

**Denmark**
- Lundbeck A/S

**Finland**
- University of Helsinki
- University of Aarhus

**France**
- École Normale Supérieure
- INSERM
- Salpétrière Hospital
- Joseph Fourier University
- University of Bordeaux
- Tours

**Germany**
- Johann Wolfgang Goethe University
- Paracelsus Elena Klinic
- Philipps University Marburg
- Rheinisch Biotechnologie GmbH
- University of Innsbruck
- University of Ulm
- University of Tubingen
- University Hospital Göttingen

**Greece**
- Biomedical Research Foundation
- Academy of Athens

**Iceland**
- deCode

**Israel**
- CellHere Neurosciences Ltd.
- Hebrew University of Jerusalem NeuroDerm Ltd.
- ProMeloc Biotherapeutics
- Tel Aviv Sourasky Medical Center

**Italy**
- San Raffaele Institute

**Netherlands**
- Academic Medical Center
- Leiden University Medical Center
- Maastricht University Hospital
- Nijmegen University Medical Center
- University of Aarhus

**New Zealand**
- University of Auckland (New)

**Norway**
- DiaSentis U.S. Inc.

**Portugal**
- Institute for Molecular Medicine

**Spain**
- Hospital General Vagac

**Sweden**
- Karolinska Institute
- Lund University Sweden

**Switzerland**
- Swiss Federal Institute of Technology Lausanne

**United Arab Emirates**
- United Arab Emirates University

**United Kingdom**
- Imperial College London
- The Institute of Neurology
- Phystopharm
- Pronigma Neuroscience Ltd.
- ReNeuron Group Plc.
- University of Cambridge
- University of Glasgow
- University of London
2008 IN PHOTOS

Top Row, clockwise from left:
MJFF Board Chair George Prescott (left) and a member of his foursome get ready to hit the green at Breaking Parkinson’s, which in 2008 raised over $830,000 for Parkinson’s research.

MJFF staffers Alison Ukenetz (left) and Vanessa Fuss at the Parkinson’s Unity Walk.

Middle Row (l–r):
MJFF Co-Founder Debi Brooks and CEO Katie Hood address 870 “Funny Thing” guests.

Michael J. Fox and Tracy Pollan.

Bottom Row:
The 2008 Team Fox ING NYC Marathon runners visit The Rachael Ray Show with Board member Woody Shackleton and his wife, Denise.
The Michael J. Fox Foundation is humbled by, and deeply grateful for, the incredible dedication of our friends and supporters. Your generosity allows us to continue doing whatever it takes to make Parkinson’s a thing of the past.

**The Edmond J. Safra Core Programs for PD Research** In 2008, recognizing the Edmond J. Safra Foundation’s extraordinary commitment to our shared search for revolutionary treatments for Parkinson’s disease, MJFF named its core scientific programs in honor of the late philanthropist and humanitarian Edmond J. Safra. Mr. Safra’s devotion to this cause lives on with his beloved wife, Lily, a member of the Board of The Michael J. Fox Foundation and, since her husband’s passing, Chairwoman of The Edmond J. Safra Foundation.

**Rapid Response Innovation Awards** — supporting groundbreaking Parkinson’s disease research in real-time.

**Target Validation** — supporting rigorous testing of early-stage discoveries to determine whether they are true targets for PD therapeutic development.

**Clinical Intervention Awards** — supporting clinical research toward new neuroprotective treatments, improvements on existing therapies and treatments for unmet symptoms.

This report lists those who supported us with significant contributions in 2008. Also listed are the many friends and family members they honored or memorialized through their donations. Their names remind us that finding a cure has never been more urgent.

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<th>Amount</th>
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<td>Breaking Parkinson’s/Edwin A. Levy</td>
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<td>$500,000 or more</td>
<td>Great Investors’ Best Ideas Foundation/Michele and Shad Rowe</td>
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*Recognizes multi-year commitment
**Recognizes one-time multi-year award

**MJFF Board Appeal: Catalyzing Industry Investment in Parkinson’s Disease** Speeding transformative treatments requires a creative strategy that goes beyond funding isolated projects in academic research labs. Increasing industry engagement in pre-clinical therapeutic development is essential to bridging the gap between discovery and the clinic. In 2008 the Foundation launched a three-year targeted initiative to deepen industry involvement in our efforts.

MJFF is grateful for the remarkable dedication of our Board of Directors in helping us achieve this goal. With characteristic generosity and enthusiasm, members of the Board pledged over $10 million in seed funding. MJFF extends its heartfelt thanks to the following Board members, whose personal leadership, both financial and intellectual, continued to be vital to our success in 2008 industry efforts:

- Holly Anderson, MD, and Douglas Hirsch
- Shanna and Joe Brooks
- Joyce and Barry Cohen
- Dovetail Deutsch
- Einhorn Family Charitable Trust
- Karen Fireman and Lawrence Golub
- Neda and John Forrester
- Judy and Al Glickman
- Lisa Piazza and David B. Golah
- Julie and Amy Griffee Foundation
- Ann and Sky Irving
- Margarita and Michael M. Kondrath
- Cynthia and Edmund A. Levy
- Julie and Doug Ostrowsky
- Tracy Pollan and Michael J. Fox
- Judith and George Prescott and Family
- Michele and Shad Rowe
- Edmond J. Safra Foundation
- Carolyn and Curtis Schenker
- The Shackleton Family Fund
- Heidi and Daniel Spitzer
- Amy and Fred Weiss

**2008 DONOR LISTING**
Donor listing continued from page 23

**Recognizes existing multi-year commitment**

Catherine and John T. Morse

Fred and Marcia Cohn

**Recognizes new multi-year commitment**

Matthew Perry

The Phoenix Foundation

Havenly Foundation

Bartlett and Richard Regan

The Robertson Foundation

Canary and Marc Pena

Paul and Jan Fonfara

Elizabeth and Scott Schaaf

Mark Siger

Jane and Malcolm Snow Foundation, Inc.

David Thomas

Chris and Jill Sibbery

Sokei Pharmaceuticals, Inc.

Sokos Capital Advisors, LLC

Sara-Cocci and Rob Speyer

The Jenny and Elyse Spiggen Foundation

Swepery Foundation*

Melinda E. Swan Foundation

Victor Two

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Amy and Fred Weisz

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Victor Two

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Vaccon Inc., Inc.

Amy and Fred Weisz

The Peter Mark Family

Kathleen Kennedy and

Frank Marshall

Soazoa and Anan Mathur

Wavick Newpath Capital

Cynthia and Michael McDermott

Michelle McElroy

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Cheryl and Robert McRae

Dennis M. Michaelis

Janet and Kelly McRae

Brendan and David Schimenti

Schloordijk Foundation

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Mary and Robert Slaughter

Janet and Frank Sweeney Trust

Shields and Tanya Smith

Wendy Smith

Dana and Paul Stнесен

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The Simmons Family Foundation, Inc.

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Kaiser and Donald Wisniewski

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Match Entertainment, Inc.

Meloy and Barbara Weoss

The Flanwylln Foundation, Inc.

Art Meltz

Sarah and Bill Wishnow

Jean B. Wilson

Daniel Wolf

Barbara and Stanley Zin

Robert Zweig

Jay Zalokar

$5,000 or more

Anonymous (3)

Elle and Ron Ackerman

Nico and Laura Ann Aker

of the Community Foundation

For the National Capital Region

Aiko and Alan Altman

Nancy Hassanou

Steve Alexander

Mr. and Mrs. Robert A. Altizer

Sue and Charles Anderson

Urban Kerney

Linda and Frank Abe

Melba Y. Bareham

Mr. B. B. Beams

Holly Herman, MD, and

Ed Bernard

The Boston Foundation

Broads Foundation

The Fireman Foundation, Inc.

Cathy and Marcell Le Blanche

Rodway Bridge Associates, Inc.

Ryan Birt

Dave Berghaus

Mr. Valerie A. Dilhoff and

Mr. James D. Byline

Robert T. Chang

Steven Chronis

Paula Crain

Molly and Victor Coleman

Colorado Parkinson Foundation

The Dows杜兰特 Foundation

Nahal and John Daly

Linda Daly

Dark Trick Films

Katharine and Costa Darras

Jim Dowdewicz

ADP

Danae and Brian Donahue

Gavin Dhingra

Mark Finkenbiner

Dr. Michele Farina, Incorporated

If you have made estate plans that include MIFF and would like to be a member of The Grocer Circle, please call Karen Jenkins at (212) 589-6895 ext. 269.
We are grateful to these companies for their generosity in matching employee gifts to MJFF.


We demand the same accountability and transparency of ourselves as of our awardees, and we keep a tight rein on expenses. Fiscal accountability and transparency are core elements of our organizational values, particularly in how we spend supporters’ contributions. While we believe that a quality enterprise requires investment, we are proud that, since inception, 85 percent of our funds have gone directly to research program efforts.

We deliberately have no endowment, instead seeking to deploy funds raised as quickly and wisely as possible. This is an unusual strategic position for a nonprofit. But we believe that to find a cure for PD as quickly as possible, our capital needs to push research forward today—not sit in an endowment or reserve. In 2008 this philosophy proved especially prescient. With no investment portfolio, MJFF suffered no investment losses.

We are outcomes-focused, incorporating milestones and tying grant payments to achievement of those milestones. We fund promising, high-potential research projects as long as they remain on track. We work with awardees to troubleshoot and tackle problems as they arise, but if the science stalls, we halt funding so that limited resources can be reallocated to other efforts.

We proactively measure the impact of our dollars on the pace of Parkinson’s research progress. Our in-house research team scores the outcomes of every grant we make, in the interest of assessing impact and maximizing learning to inform future efforts. In 2008 we also conducted an external audit of our research program, asking unbiased advisors to help evaluate our efforts.

We measure our impact not by input — dollars raised — but by output — scientific advances achieved. We’re proud of what we’ve accomplished to date. But ultimately we have only one definition of success: Scientific solutions that produce tangible improvements in patients’ lives.

2008 financial highlights follow. Full audited financials and our most recent IRS Form 990s are available at www.michaeljfox.org.
Year Ended December 31, 2008  2007

ASSETS
Cash, cash equivalents and investments $30,962,536 $32,185,002
Contributions receivable, net 26,762,424 15,566,497
Prepaid expenses and other current assets 162,958 37,015
Security deposits 33,061 33,061
Property and equipment, net 388,610 518,718
Total assets $58,309,589 $48,340,293

LIABILITIES AND NET ASSETS
Liabilities:
Accounts payable and accrued expenses $1,066,594 $957,787
Grants payable, net 38,882,706 31,311,041
Deferred rent 367,192 270
Loan payable 1,013,285 —
Total liabilities $41,329,777 $32,665,098

Net Assets:
Unrestricted (deficit) (5,516,236) 6,766,811
Temporarily restricted 22,496,048 8,908,384
Total net assets $16,979,812 $15,675,195

Net assets, end of year $16,979,812 $15,675,195

Research Program Activities 85%
Administration 3%
Fundraising 12%

Research, Translational Research 66%
Understanding Disease 7%
Clinical Research 27%
New Tools and Technologies

Translational Research 66%
Understanding Disease 7%
Clinical Research 27%
New Tools and Technologies

GROWING INVESTMENTS IN PD RESEARCH 2001-2008

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<th>Year</th>
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Note: Investments are in highly liquid U.S. government securities.

Katie Rees
CEO
Michael J. Fox
Founder
Deborah W. Brooks
Co-Founder

Sandy Drayton:
Vice President, Communications

Without Editor: Holly Bunkery
Associate Director, Communications
Contributor: Diana Iri
Communications Officer/Team Fox Officer

Design: Susan Shaw
Susan Shaw Design

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