

PROGRESS

ANNUAL REPORT 2009

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.





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Letter from the CEO, Founder and Co-Founder

In 2009, with the support of more than 56,000 individuals, corporations and foundations, The Michael J. Fox Foundation continued to invest where we saw potential to drive progress forward, pushing ourselves and our partners to ever-greater heights in pursuit of transformative treatments and a cure for Parkinson's disease.

Against an uncertain economic backdrop, we funded over \$39 million in targeted Parkinson's research — the most we've ever funded in one year — bringing our total research investments at year-end to nearly \$170 million. Yet those who know us know our core belief is that ending Parkinson's is not merely about spending more money, but about spending that money with impact. Last year we expanded our emphasis on critical research tools and patients' unmet needs while continuing to drive key next steps on top therapeutic targets. (Turn the page to read more about our high-priority research areas, the science we believe is closest or most critical to practical impact on patients' lives.)

Sitting at the hub of global PD research, our job is to act urgently and strategically to dismantle roadblocks and streamline the path to a cure. We talk — and listen — to the world's most prominent Parkinson's scientists from academic and industry labs about what they need and where new opportunities lie. Our staff, which includes both scientific PhDs and business-trained project managers, continually surveys a wide and complex field in order to prioritize the projects most needed to accelerate new therapies. We work to see the big picture, then invest our capital with one return in mind: speeding scientific solutions to the nearly five million people living with Parkinson's worldwide.

As Canada's *Globe and Mail* reported in September, our aggressive, entrepreneurial approach to science lies at the heart of our mission to find a cure for Parkinson's — and, in the process, to reshape the way medical research gets done. 2009 highlights include:

- Investing over \$11 million in biomarker development (bringing total funding in this area to over \$25 million) and laying the groundwork to sponsor the Parkinson's Progression Markers Initiative (PPMI), a landmark biomarker study launching in 2010. (While PPMI isn't covered in this report, you can learn more about it at michaeljfox.org/PPMI.)
- Allocating over \$3 million to pre-clinical models, including a grant to speed a cutting-edge gene knockout technology into Parkinson's therapeutic development within months of its advent. The technology was later named one of the top 10 scientific innovations of the year by *The Scientist*.
- Initiating a \$1-million clinical trial to establish a framework for the development of effective treatments for dyskinesia, the debilitating side effect of long-term dopamine replacement therapy.
- With lead support from The Edmond J. Safra Foundation, awarding \$2 million to drive development of treatment approaches for postural instability and gait disorder



(PIGD), a troubling constellation of symptoms that are poorly understood and respond inconsistently or not at all to dopamine replacement therapies.

- With lead support from the Brin Wojcicki Foundation, executing an integrated, multi-million-dollar strategy to advance biological understanding of LRRK2, the single greatest known genetic contributor to Parkinson's disease, while simultaneously laying the groundwork for effective LRRK2 clinical trials in the future.
- Launching PD Online Research (pdonlineresearch.org), a Web-based platform for research professionals to engage daily on key research hurdles and new findings. So far, nearly 2,000 Parkinson's researchers at all levels and from all over the world have become members.

We invite you to read more about these investments, and the potential we see in them to change the face of Parkinson's drug development, throughout this report and at michaeljfox.org.

Of course, effecting meaningful change in how new treatments are developed requires thoughtful strategies for engaging not only scientists but also patients and caregivers, policymakers and other research funders. That's why in 2009 we also focused on building and deepening our relationships and collaborations in every sector of the PD community. We chartered a Patient Council to provide input on our programmatic activities

from the critical perspective of those living with the disease. Our new Leadership Council is made up of generous advisors who provide leadership financial support and strategic insight about how we can more effectively engage new audiences to advance progress. And Team Fox, our grassroots fundraising network, continued to inspire and unite communities across the country in passionate pursuit of a cure.

Your dedication allows us to keep taking the risks that patients and their loved ones want taken in service of accelerating therapeutic breakthroughs. Our gratitude to you is as clear and strong as our vision of a world without PD.

Katie Hood

CE₀

Michael J. Fox Founder

Debi Brooks

Katie Hoose

Deborah W. Brooks Co-Founder

High-priority Research Areas: The Science We're Most Excited About

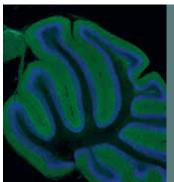


While MJFF's portfolio of investments includes up to 250 active grants spanning Parkinson's therapeutic development, to achieve our mission of speeding the cure, we must strategically evaluate research hits and prioritize limited resources. This section provides an overview of our top priorities for funding and intellectual leadership. All are currently believed by our in-house research team and expert advisors to be critical areas of focus in our pursuit of transformative treatments for Parkinson's in the shortest possible timeframe. You'll find detailed stories about our work in these areas throughout this report.

Top Therapeutic Targets: Alpha-synuclein, LRRK2, Trophic Factors

Genetic targets Alpha-Synuclein and LRRK2. Though only a small fraction of people with Parkinson's carry mutations in PD-implicated genes, findings from genetic studies open new avenues toward treatments that will benefit everyone with the disease. Two genetic targets, alpha-synuclein and LRRK2, have risen to prominence for their exceptional promise to provide new treatment approaches to Parkinson's.

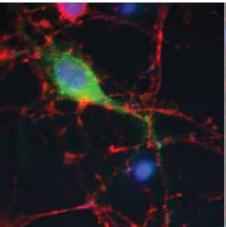
■ The gene known as alpha-synuclein produces a protein that aggregates to form Lewy bodies, microscopic clumps that are the pathological hallmark of PD. Though alphasynuclein's precise role in PD remains unclear, growing evidence supports the idea that decreasing its levels in the brain could be one way to slow or stop Parkinson's progression. MJFF has invested more than \$32 million in alpha-synuclein research to date.

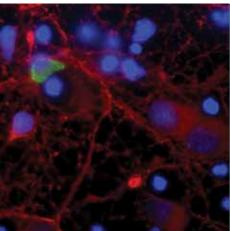


Cerebellum of a pre-clinical model created to overexpress the protein alphasynuclein (shown in green), helping scientists understand possible toxic effects of increased levels of the protein in the brain.

■ First linked to PD in 2004, mutations in the LRRK2 gene are now believed to be the most common genetic contribution to the disease. MJFF is driving a comprehensive strategy for advancing LRRK2 research. The goal is to shed light on the gene's biological role in PD while laying the groundwork for conclusive clinical trials. With lead support from The Brin Wojcicki Foundation, MJFF has invested over \$16 million in LRRK2 research to date.

Trophic factors. Trophic factors (also known as neurotrophic factors or growth factors) are specialized proteins that protect and nurture neurons, including the dopamine neurons that die in Parkinson's disease. While clinical trials involving trophic factors have not yielded hoped-for results, The Michael J. Fox Foundation continues to see great promise in trophic-based approaches to treating PD. The Foundation has invested over \$20 million in trophic factor research to date, and in 2009 earmarked another \$5 million under a 2010 *LEAPS* program to advance state-of-the-art trophic factor therapies into the clinic.





Life and death of a neuron: Fluorescently labeled neurons show degenerative changes after expressing the mutant LRRK2 protein, the dominant genetic mutation that causes Parkinson's in humans. Neurons are labeled red; their nuclei are blue; LRRK2 is green. At left is a cell expressing the normal version of LRRK2; the cell has a normal appearance. At right is a cell expressing the mutated form of LRRK2; it is shrunken and the nucleus is starting to die.

Patients' Unmet Needs

Available treatments for Parkinson's leave several troubling symptoms of the disease entirely unaddressed. These include cognitive deficits and mood disorders, problems with posture and gait, and gastrointestinal (GI) problems such as constipation. Complications of current treatments, including dyskinesia (the excessive, uncontrollable movements that result from long-term dopamine replacement therapy), also diminish quality of life.

The Michael J. Fox Foundation is committed to providing the financial and intellectual leadership required to drive treatments for patients' unmet needs. Since its founding, MJFF has invested over \$11 million in dyskinesia research, including a major clinical trial launched in December 2009 to validate vitally needed clinical scales (see page 15). We have also funded millions of dollars in research toward alleviating untreated symptoms of PD — including developing the first pre-clinical models to mimic GI symptoms in Parkinson's and, with lead support from The Edmond J. Safra Foundation, our 2009 \$2-million initiative to drive treatments for postural instability and gait disturbances.

Critical Research Tools, New Technologies and Data Sharing

Pre-clinical models. With about \$13 million in investments, MJFF is a field leader in the development of improved models of PD that accurately mimic the human condition, allowing researchers to test potential disease-modifying therapies. And to ensure that new and better models get into scientists' hands as quickly and efficiently as possible, we also are developing practical, low-cost channels for worldwide distribution of these critical tools.

Biomarkers and clinical scales. To date we've invested nearly \$29 million in biomarkers and clinical scales, tools necessary for researchers to definitively assess treatment effects in clinical studies. In 2009 we launched an initiative to validate clinical scales used to measure changes in dyskinesia severity. We also laid the groundwork to sponsor a game-changing longitudinal study, PPMI, launching in 2010, that will identify and verify PD biomarkers — molecular or physiological characteristics that can be objectively measured and evaluated to provide clearer outcomes from clinical trials and lower the hurdle to industry investment in PD.

Leveraging new technologies in PD. Research technologies emerge and evolve at a rapid pace. We monitor these developments and apply funding to strategically leverage those that could impact Parkinson's science. In 2009 one such technology was named to *The Scientist's* list of the top 10 scientific innovations of the year (see page 16).

Data sharing. New technologies and systems could revolutionize the way researchers communicate and share information. In addition to our ongoing activities to facilitate data exchange between and among academic and industry researchers, in 2009 we launched PD Online Research (PDOR) (www.pdonlineresearch.org). PDOR enables collaboration, instant communication and rapid problem-solving among scientists around the globe. Its goal is straightforward: enable quicker knowledge turns and faster progress toward therapeutic breakthroughs. By the end of the year, PD Online Research had almost 2,000 members from government, industry and academic sectors.

Transforming Basic Discoveries Into Therapeutic Targets



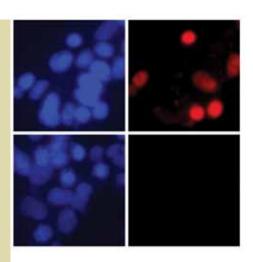
Basic discoveries about the biological mechanisms of Parkinson's disease are critical to the development of new therapies. Equally important, however, is a focused and deliberate effort to shepherd these discoveries through the complex process of therapeutic development and determine their real potential as breakthrough treatments. The stories on these pages illustrate MJFF's unique role in partnering with researchers to put the most promising results on a fast track toward practical relevance in patients' lives.

Going Viral: Could a Virus's RNA Help Protect Neurons?

Molecular virologist John Sinclair, PhD, of the University of Cambridge wasn't even thinking about Parkinson's when he discovered a previously unknown piece of viral RNA that keeps cells alive during infection. But his work on infectious disease elucidated an intriguing possibility: Could viral RNA protect the neurons that die in PD, thus modifying disease progression, something no current treatment has been proven to do?

MJFF quickly came on board to help him find out. With fast funding under MJFF's *Rapid Response Innovation Awards*, Dr. Sinclair successfully engineered a form of the viral RNA suitable for pre-clinical testing, and his team demonstrated its ability to protect neurons in parkinsonian models. The Foundation then provided follow-on funding for Dr. Sinclair's team to investigate the potential of the RNA complex to restore function to already-damaged neurons.

"PD patients have lost a substantial percentage of their dopaminergic neurons by the time of diagnosis," says Dr. Sinclair. "So the real question is whether this complex can stop that process, preventing the disease from progressing further." His group is also working to identify the specific region of the viral RNA responsible for the protective effects. "The more we can refine the RNA complex," he explains, "the quicker we'll be able to deliver a therapy from bench to bedside."



In the upper panels, the blue dopamine neurons at left are exposed to a toxin and die, as shown by the red marker for cell death at right. In the lower panels, the dopamine neurons at left have been treated with therapeutic RNA. As a result the cells do not die when exposed to the toxin, and no red cell death marker is visible at right.

"You don't gain much by keeping things under wraps. Actually getting different people with different viewpoints and different techniques to work together in an open fashion rapidly speeds up progress."

Patrick Lewis, University College London, MJFF LRRK2 Biology Consortium member

Sharing the Wealth (of Data): A Consortium Approach to Speed LRRK2-based Treatments

The LRRK2 gene holds tremendous promise as a therapeutic target for PD. Not only is it the single most common contributor to genetic cases of the disease, but it is a kinase — a type of cellular enzyme that is often highly druggable. Since LRRK2 was first linked to Parkinson's disease in 2004, it has reinvigorated the field of Parkinson's genetics and become the focus of intensive investigation by research teams all over the world.

MJFF's research staff, in concert with the world's leading experts in Parkinson's genetics, has moved quickly to integrate global LRRK2 efforts into a united and streamlined scientific movement that will help minimize the timeline to practical LRRK2-based therapies. In 2009 MJFF homed in on collaborative efforts to increase understanding of LRRK2 biology, including convening a major LRRK2 summit at the end of the year. The spirit of collaboration was also extended to MJFF's search for investigative teams to join a LRRK2 biology consortium aiming to fast-forward efforts to understand LRRK2 biology and target its vulnerabilities.

"This is a critical early moment in LRRK2 therapeutic development," says Brian Fiske, PhD, associate director, team leader, Research Programs. "MJFF recognized the opportunity to transcend the disparate, one-off efforts that all too often characterize scientific discovery and instead lead a strategic new approach that hits on multiple fronts simultaneously."

The journal *Nature Medicine* wrote: "To foster synergies moving forward, MJFF... established an international consortium to focus on one of the most promising candidate drug targets of the neurodegenerative disease. Under the terms of the two-year, \$3.5-million grant design, members of the consortium, which includes both academic and industry partners, will be compelled to share results and collaborate with one another on an ongoing basis to help accelerate therapeutic discoveries."

Nine different research teams are members of the LRRK2 biology consortium. They are working to help elucidate the functions of LRRK2 in the cell, identify other cellular proteins linked to LRRK2 (called substrates) and develop critical tools to drive further research. Several groups are using complementary approaches to investigate related questions around LRRK2. For example, three teams investigating substrates are using different types of tissues for each project, which will allow for faster and more efficient cross-validation of any findings.

"Getting people working together on LRRK2 research increases the pool of ideas and expertise to draw from, and it builds in a way to check your work with others, which is unfortunately rare in science," says Mark Cookson, PhD, a member of the MJFF Scientific Advisory Board and world-renowned expert on the cell biology of PD. "It will also help to keep people involved in the field, pushing forward to the next level that much faster. It's an approach grounded in common sense."

Number of labs funded by MJFF in 2009 that had never worked in PD before

\$6.6 million

Amount of 2009 research funded by MJFF in those labs

Leverage: MJFF's Industry Strategy Bears Fruit

\$28.7 million

2009 MJFF funding to academic/ nonprofit teams

\$10.2 million

2009 MJFF funding to industry teams With over 55 currently active industry collaborations and more than 85 since MJFF's inception, there is little doubt of the Foundation's commitment to partnering with biotech and pharmaceutical companies to speed treatments toward clinical testing and patients. But the greater goal of the Foundation's "de-risking" strategy is to create momentum and induce industry players to commit their own significant resources to pre-clinical and clinical Parkinson's therapeutic development programs.

"We look for leverage everywhere," says Debi Brooks, MJFF co-founder. "That means identifying the projects where it's a good bet that our investment of, say, a few hundred thousand dollars can create a tipping point and increase the odds of a company investing millions down the line."

Throughout 2009, mounting evidence suggested that MJFF has made several good bets on industry so far.

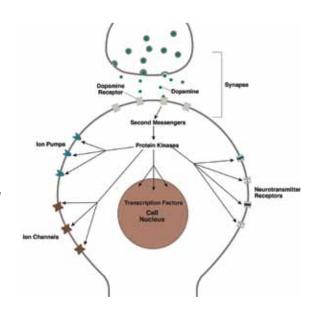
For example, Intra-Cellular Therapies, Inc. has been funded by the Foundation since 2006 to develop a small-molecule drug to increase the potency of levodopa, enabling relief of motor symptoms

at lower doses and reducing dyskinesias. With positive outcomes in several relevant models of PD, principal investigator Gretchen Snyder, PhD, received supplemental funding in 2009 for what will likely be the final pre-clinical work required before a Phase 1 clinical trial.

Amicus Therapeutics of New Jersey also received MJFF funding in 2006 to test an orally administered small molecule with promise to decrease alphasynuclein clumping, a hallmark of PD pathology. When the MJFF-funded test of a chaperone in a preclinical model of PD resulted in intriguing efficacy and dosing data, Amicus launched an internal PD drug development program. The company now expects to complete advanced pre-clinical proof-of-concept studies in Parkinson's disease during the course of 2010 and to report additional data in the second half of the year.

"The support we received from The Michael J. Fox Foundation was a key factor in our decision to commit to a Parkinson's program," says John F. Crowley, chairman and CEO of Amicus. "In 2010 we expect to make significant progress in our preclinical programs in Parkinson's disease."

With funding from The Michael J. Fox Foundation, Intra-Cellular Therapies Inc (ITI) is developing therapeutics to promote the intracellular response of brain cells to dopamine and restore the functions of dopamine that are lost in Parkinson's disease. In the schematic at right, dopamine, released from nerve terminals, interacts with receptor proteins to produce intracellular changes in second messengers and protein kinases that control the activity of brain cells through effects on different classes of proteins, including neurotransmitter receptors, ion pumps, ion channels and transcription factors. Based on the work of Paul Greengard, Nobel Laureate in Physiology & Medicine (2000).





UPDATE

A Major Milestone for Glutamate and PD

MJFF's 2008 annual report highlighted the work of *LEAPS* awardee P. Jeffrey Conn, PhD, who is pursuing an entirely new kind of symptomatic treatment for PD that would target glutamate — a molecule that, like dopamine, helps the brain send messages to the body. In 2009 Dr. Conn's team at Vanderbilt University hit a major scientific milestone. "We discovered systemically active molecules and verified that they were beneficial in a pre-clinical model of PD," says Dr. Conn. His team is now examining the effects of chronic dosing with these agents, testing their effects on subtle aspects of motor function in less severely parkinsonian models, and optimizing their drug-like characteristics. While there are no guarantees, if all goes well, the researchers could launch a clinical study in Parkinson's patients by 2013.

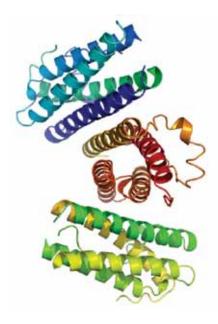
Jeff Conn and Colleen Niswender

G-CSF: A New Trophic Factor Approaches the Clinic

In 2006 researchers Mathias Baehr, MD, and Jochen Weishaupt, MD, of University Hospital Goettingen in Germany approached MJFF to discuss a growth factor called G-CSF (granulocyte-colony stimulating factor). G-CSF, already approved by the U.S. Food and Drug Administration to treat complications of chemotherapy in cancer patients, was believed to reduce cell death in a pre-clinical model of Parkinson's disease. The researchers were awarded funding under MJFF's *Target Validation* program to gather additional data critical for advancing to clinical trials in PD patients, such as an effective dose range.

In results published in the *Journal of Neurochemistry* and *BMC Neuroscience*, and presented at the Foundation's third annual PD Therapeutics Conference in September 2009, the researchers conclusively demonstrated that G-CSF was protecting neurons in a PD model; they also shed light on how it was achieving this beneficial effect. The researchers then ran extensive pre-clinical studies on an enhanced form of G-CSF called pegfilgrastim, which minimizes side effects and remains in the system longer.

Within months, MJFF granted follow-on funding for final pre-clinical studies in another relevant Parkinson's model. "We will monitor the effects of pegfilgrastim over time, look for any side effects and precisely measure its ability to reduce cell loss and improve motor symptoms in pre-clinical models," says Dr. Weishaupt. "If all goes well, this will be the final step before a clinical study to test safety in Parkinson's patients."

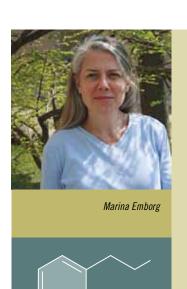


Protein structure of G-CSF

Speeding Clinical Testing of New Interventions



MJFF shares patients' urgency to bring new and better Parkinson's 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 help assemble and organize teams, lend expertise to biotech and pharmaceutical companies testing or going deeper into PD waters, 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.



Chemical structure of pioglitazone

How Sweet It Is: A Diabetes Drug that Could Modify Progression of PD

When reports of the anti-inflammatory properties of the diabetes drug pioglitazone began to surface in the early 2000s, scientists saw an opportunity to translate these findings into therapies for multiple diseases where inflammation is a contributing factor, including Parkinson's disease. In 2002, this promising avenue of research was given a boost when pioglitazone was shown to prevent the death of dopamine neurons in pre-clinical models of PD.

In 2005, Marina Emborg, MD, PhD, director of the Preclinical Parkinson's Research Program at the University of Wisconsin, received an MJFF *Community Fast Track* award to test the neuroprotective properties of orally administered pioglitazone in more relevant pre-clinical models of PD.

"We knew that pioglitazone might one day provide an innovative, simple and non-invasive strategy to prevent Parkinson's progression," says Dr. Emborg. "Furthermore, since pioglitazone is already known to be safe, it could be quickly translated into clinical trials in PD patients. MJFF funding was vital to our efforts to provide proof-of-principle for a new class of compounds to treat PD and other neurodegenerative disorders."

When Dr. Emborg's preliminary data suggested that the active compounds of pioglitazone were neuroprotective, MJFF provided supplemental funding to determine whether the doses used in pre-clinical models could be translated to humans. This work will provide critical data on optimal dosage to inform a clinical trial in PD patients slated to launch in 2010 with significant funding from NINDS, the National Institute of Neurodegenerative Disease and Stroke (NIH).

"Repurposing existing drugs for Parkinson's could be a key approach to creating new and better treatment options for patients," says Todd Sherer,"but it's difficult for scientists to get funding for this kind of work. MJFF is committed to driving such efforts for the benefit of people living with the disease, and uniquely poised to do so."

"I know a lot of foundations, and [MJFF is] amazingly well-organized, and they care. They really care what happens. I've never experienced this before. It's a unique situation. That is why they are so successful."

Wolfgang Oertel

\$29.4 million

2009 MJFF funding to U.S.-based research teams

\$9.5 million

2009 MJFF funding to international research teams



Lighting Up the Connection between Tobacco and Parkinson's Disease

Researchers and patients have long been intrigued by the link between tobacco and Parkinson's disease. "There have been numerous compelling observations to suggest that tobacco exposure may hold multiple benefits for PD patients," says Carlie Tanner, MD, one of the world's leading experts on environmental factors in PD and a member of the MJFF Scientific Advisory Board. "Epidemiological studies consistently demonstrate that tobacco use lowers the risk of developing Parkinson's disease, and experiments in pre-clinical models have shown that nicotine may protect dopaminergic cells from death. Several studies also suggest a symptomatic effect, though small and somewhat variable. And recent data shows that nicotine may reduce levodopa-induced dyskinesias."

Yet key questions about the relationship among smoking, nicotine and Parkinson's — including whether the protection seemingly conferred by smoking tobacco products stems from the nicotine in those products, other components of tobacco, or metabolic aspects related to smoking itself — remain unanswered.

In 2009 The Michael J. Fox Foundation awarded \$1.1 million for NIC-PD, an international clinical trial vetting the effects of nicotine skin patches on Parkinson's disease. It is the first long-term clinical trial expressly designed to test whether nicotine may in fact modify the progression of PD.

The double-blind, placebo-controlled trial — the first-ever multisite, investigator-initiated collaboration between Parkinson's research groups in Germany and the United States — will be conducted over three years in 150 newly diagnosed

Parkinson's patients. (Study participants will be treated and observed for one year.) Principal investigators Wolfgang H. Oertel, MD, and Marcus M. Unger, MD, of Phillipps University Marburg, Germany, and Karl Kieburtz, MPH, of the University of Rochester, New York, will evaluate the disease-modifying potential of transdermal nicotine using standard nicotine skin patches of the type used by millions of smokers as a quitting aid.

Speaking to the journal *CenterWatch Monthly*, which reported on NIC-PD in its story "Michael J. Fox Foundation Gives German Investigator-initiated Trial New Life," Dr. Oertel said: "I know a lot of foundations, and [MJFF is] amazingly well-organized, and they care. They really care what happens. They go to the advisory board meetings. [Usually,] the advisors meet without the scientists and then they are called in and either their head is chopped off or they get the check. But, at Michael J. Fox, you meet for two days with the advisors and they go with you through all the topics. It's amazing. I've never experienced this before. It's a unique situation. That is why they are so successful."

"There's no doubt that the epidemiological data on smoking and PD is intriguing," says Katie Hood, CEO. "Our priority is on taking action to validate this data clinically in order to potentially translate it into a practical, patient-relevant therapy."

Targeting Glutamate to Treat Levodopa-induced Dyskinesias



Warning

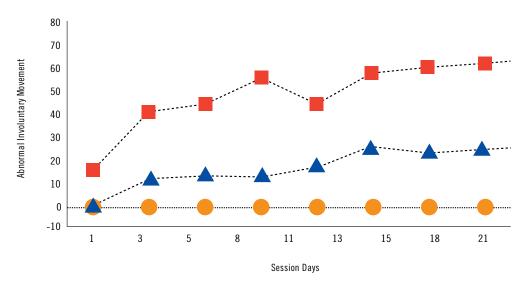
An important cautionary note: While MJFF is funding clinical trials on supplements and drugs already available for purchase or prescription, people with Parkinson's (other than those who ultimately enroll in these trials) should not begin taking these agents as part of a Parkinson's disease treatment regimen without the explicit recommendation of their doctor. Evidence to date has not yet definitively proved a benefit in 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.

Developing effective treatments to alleviate dyskinesias — the disruptive, involuntary movements that are a side effect of long-term dopamine replacement therapy — is a high-priority research area for MJFF. In 2009 one promising approach involving glutamate — a neurotransmitter of increasing interest to PD researchers — moved forward to the early stages of clinical research. MJFF has been a champion of an approach targeting a specific glutamate receptor, mGluR5, since 2005. The Foundation's de-risking efforts have now chaperoned mGluR5 from basic discovery to clinical testing and attracted industry interest in the target.

"Finding new and safe treatments that can prevent dyskinesias would allow patients to continue on levodopa, benefiting from its full symptomatic efficacy even in advanced stages of the disease," says Todd Sherer, PhD, vice president, Research Programs. "This would lead to an enormous improvement in patients' quality of life."

The initial data on mGluR5 and dyskinesia came from Angela Cenci-Nilsson, MD, PhD, of Lund University in Sweden. In 2005 Dr. Cenci-Nilsson received a *Target Validation* award to demonstrate that blocking the action of one particular receptor, mGluR5, prevented levodopa-induced dyskinesias in rodent models of PD.

The Foundation quickly provided follow-on funding for Dr. Cenci-Nilsson to partner with Erwan Bezard, PhD, of the University of Bordeaux in France. Their goal: take preliminary results to the next level in a more relevant model of PD. The pair worked closely with MJFF research staff to identify a compound capable of reducing mGluR5 activity. Finding one already in human clinical testing for another disease, they adapted their studies to this compound to accelerate development toward the clinic.



Abnormal involuntary movement scores, a measure of dyskinesia severity, increase over time in parkinsonian models treated with levodopa (represented by red squares). This increase is blunted in models receiving treatment with an mGluR5 antagonist as an add-on to levodopa (represented by blue triangles). The mGluR5 antagonist alone does not induce any abnormal involuntary movements (represented by yellow circles). Each data point represents the average value from eight to 10 models in each group.

"The Michael J. Fox Foundation's staff are highly committed, truly capable people. They monitor your progress; they're extremely aware of where Parkinson's research is going and where it needs to go. They won't fund a project just because it's trendy, or because of a scientist's famous name. Their goal is to promote quality research with high translational value, and they do everything to achieve that goal."

Angela Cenci-Nilsson

MJFF is now partnering with Danna Jennings, MD, of The Institute for Neurodegenerative Disorders in New Haven, Connecticut, to verify the action of this compound and determine a safe and effective dose for use in future clinical trials. Using PET scans and a fluorescent imaging molecule that binds to mGluR5, Dr. Jennings images PD patients' brains before and after treatment. "An important step before investing in a large clinical trial is to make sure that the drug is in fact getting to the brain and binding to the expected targets," says Dr. Jennings. "Is the drug reaching the brain at appropriate levels?

What is the dose most likely to provide meaningful clinical benefit? Our research aims to answer these questions."

MJFF's commitment has galvanized the field, prompting industry scientists to conduct clinical testing of other compounds targeting mGluR5. "By driving pre-clinical development of promising drug targets, MJFF is providing tangible incentives for industry to increase its involvement in Parkinson's research," concludes Dr. Sherer. "The development of dyskinesia therapies based on mGluR5 activity is a perfect example of this strategy."

\$10.1 million

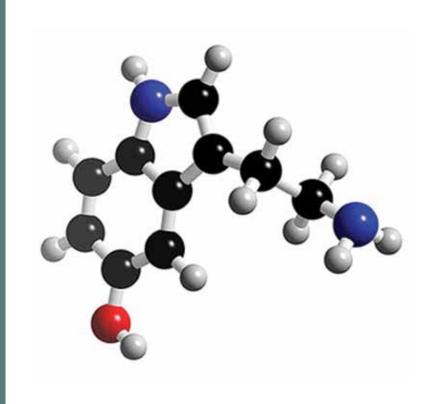
Amount of research funded by MJFF in 2009 to address patients' unmet needs including dyskinesia

UPDATE

Serotonin and Dyskinesia: MJFF Support Leads to Pilot Clinical Trial

Progress 2008 featured the efforts of Anders Björklund, PhD, and his colleague, Manolo Carta, PhD, of Lund University in Sweden to develop a new treatment for dyskinesia targeting the brain's serotonin system, better known for its role in clinical depression. With Foundation funding, the researchers have now demonstrated that abnormal, dyskinesia-inducing dopamine release can be effectively blocked by drugs that act on two specific receptors, known as 5-HT1A and 5-HT1B, located on the serotonin neurons. They have also shown that this technique is particularly effective when the two receptors are activated simultaneously.

Based on these results, Dr. Björklund's team is now conducting an MJFF-funded pilot clinical trial in 24 Parkinson's patients at Lund University Hospital and Karolinska Hospital Huddinge (both in Sweden). The trial is being carried out in collaboration with the U.S. biotech company PsychoGenics, using their proprietary drug Eltoprazine, which activates both 5-HT1A and 5-HT1B and has shown promising results in pre-clinical trials to date.



Structure of the neurotransmitter serotonin

Mobilizing New Technologies and Tools in PD Therapeutic Development



To advance the rapeutic targets toward the clinic requires highly specialized tools and technologies, whose development in itself requires significant financial and intellectual investment. But there is no financial incentive for any single stakeholder to allocate major funding to this critical need. MJFF, with its singular focus on patient-relevant outcomes, is uniquely positioned to marshal the resources and partners that can propel development of tools and technologies with potential to move the entire field forward.

Using Virtual Reality to Address Freezing of Gait

An MJFF-funded team in Sydney, Australia, is using functional magnetic resonance imaging (fMRI) in a virtual environment to visualize patients' brains while safely triggering freezing of gait episodes. The project is part of a \$2-million MJFF commitment to therapeutic development for postural instability and gait disturbances in Parkinson's disease, made possible with lead funding from The Edmond J. Safra Foundation.

While lying in the MRI scanner, patients will use foot pedals to 'walk' through a realistic three-dimensional environment they see on a small screen. The virtual environment task will probe cognitive processes that often provoke freezing episodes (such as sliding doors) or alleviate them (such as striped floors).

"We hypothesize that rather than simply reflecting a process related to gait, freezing episodes are in fact related to a breakdown in the circuitry that coordinates different functions such as movement and thinking," says principal investigator Simon Lewis, MD. "We want to identify the abnormal pattern of brain activation hopefully increasing understanding of freezing and opening new directions for targeting therapy."



Simon Lewis

"Throughout all my experiences with MJFF I've been impressed with the rigor and accountability of the Foundation's process, and with the creative and competent way that the staff goes about its mission of finding better treatments and a cure for Parkinson's disease. I'm willing to dedicate as much time and effort to the Foundation as I do because I truly believe this organization is going to make a difference."

Gene Johnson, PhD, Chief Scientific Advisor, MJFF

Maximizing Learning from At-risk Populations: MJFF Drives LRRK2 Cohort Studies in New York, Tel Aviv and Tunisia

On page 7 you read about the LRRK2 biology consortium, part of MJFF's strategy to increase understanding of the LRRK2 gene that is believed to be the single most common contributor to genetic cases of Parkinson's disease. The Foundation is simultaneously working to define the clinical impact of LRRK2 on PD — that is, how LRRK2 may cause or prevent specific symptoms, impact rate of progression, or otherwise affect disease severity and trajectory.

The Foundation is funding two research teams to study PD in cohorts of Ashkenazi Jews and North African Arab-Berbers, two populations with a significantly elevated incidence of the PD-implicated LRRK2 mutation known as G2019S. What they learn will not only provide answers about what it means to have a LRRK2 mutation, but also open new avenues of therapeutic development for people with the far more common sporadic form of the disease.

A team of investigators from Mayo Clinic, Jacksonville, and the Institute of Neurology in Tunis is following an Arab-Berber cohort in Tunisia. A second group comprising investigators at Beth Israel Medical Center, Columbia University, Tel Aviv Sourasky Medical Center and the Institute for Neurodegenerative Disorders is tracking Ashkenazi Jews in New York and in Tel Aviv, Israel.

"Not all people with LRRK2 mutations get PD, and for those who do develop the disease, there is great variability in symptoms," says Susan Bressman, MD, of Beth Israel Medical Center, coordinating principal investigator for the New York/Tel Aviv cohort. "By studying large numbers of people with the same mutation, we can start to understand its implications for risk and disease course in individuals."

To ensure that all data collected can be analyzed, shared and compared as efficiently and meaningfully as possible, MJFF worked with the investigators to set up collection methods standardized across both cohorts. This will improve the ability of the researchers to compare

results and link clinical features to underlying biological and genetic processes.

"By studying these uniquely affected populations, our goal is to make drug development efforts centered on LRRK2 more efficient and ultimately speed patient-relevant outcomes from this work," says Katie Hood, CEO.

A Critical Step toward Controlling Dyskinesia

The drug levodopa is the gold-standard treatment for relieving the stiffness, tremors and rigidity of PD. But patients are forced to weigh symptomatic relief against the knowledge that, at some point, levodopa will very likely cause dyskinesia. Patients wait as long as possible to begin levodopa; even after starting, many limit dosage to reduce the risk of dyskinesia. If dyskinesia develops, patients often reduce their levodopa dose and settle for a lesser benefit from the best medical therapy available for their disease.

Dyskinesia is a moving target in every sense of the phrase. It takes different forms and varies widely from day to day and even hour to hour. Partly for this reason, the development of accurate clinical scales to detect type, severity, duration, and impact on the patient has been elusive. While several scales exist, their effectiveness has never been rigorously compared. Without scales the scientific community has confidence in, there is no framework for clinical testing of possible new treatments. This in turn creates a hurdle to biotech and pharmaceutical companies investing in the development of potential new dyskinesia therapies.

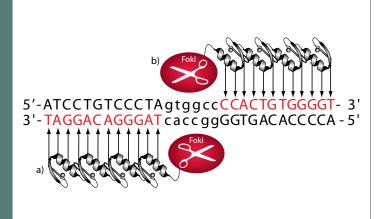
In 2009, as part of its ongoing efforts to drive new dyskinesia treatments, The Michael J. Fox Foundation announced a \$1-million clinical study to validate effective dyskinesia scales. The multi-site study, led by Christopher Goetz, MD, at Rush University Medical Center in Chicago, will aim to conclusively identify the scales that most accurately measure dyskinesia.

The experimental design involves amantadine, a current, albeit inadequate, drug frequently used off-label to treat dyskinesia. Patients will be treated with amantadine or placebo, and then have their dyskinesia rated over the course of several weeks using numerous dyskinesia measurement scales. (The researchers will examine the response to placebo as well, in order to favor scales that maximally separate placebo-associated changes from amantadine-associated changes.) The results will establish a path for clinical testing of future promising novel dyskinesia treatments, increasing the likelihood of industry investment in future clinical trials.

Model Techniques for Speeding PD Drug Development

Pre-clinical models are vital tools for drug development. Researchers require good models to increase understanding of cellular, molecular and behavioral aspects of disease, as well as to screen potential new therapies before they move forward to testing in humans. Parkinson's therapeutic development is held back by the lack of any pre-clinical model that accurately recapitulates both the underlying processes, and the symptoms, of the human condition. Even when good models are developed, better distribution channels are required to quickly get them into researchers' hands.

Zinc Finger Nuclease
(ZFN) must be
delivered as a pair
to be functional.
When all ZFN
components are
properly assembled,
a highly specific pair
of 'genomic scissors'
is created.



The development and distribution of improved models is a major priority for MJFF, and in 2009 the Foundation's efforts bore significant fruit.

Knocking out PD

A laboratory technique known as gene knockout lets scientists working in pre-clinical models remove a specific gene of interest, effectively turning it off ("knocking it out"), allowing them to study genes' effects on cellular disease processes. Gene knockout has been used for decades in laboratory mice, but never successfully in rats until July 2009, when biotech Sigma-Aldrich published proof-of-principle for the first knockout rats.

"Rats offer numerous advantages as models for Parkinson's drug development," says Todd Sherer, PhD, vice president, Research Programs. "They more closely mimic many behavioral aspects of human Parkinson's disease, offer a greater amount and wider range of tissue for testing and allow scientists to conduct certain tests that are impossible in mice or non-mammalian models."

Sigma-Aldrich used a novel technology called Zinc Finger Nuclease (ZFN). It causes targeted breaks in double-stranded DNA that can snip out specific genes of interest. ZFN was developed by Sangamo BioSciences and licensed to Sigma-Aldrich in 2007. Its application in rats would later be named one of the top 10 scientific innovations of 2009 by *The Scientist*.

By August MJFF had awarded a Sigma-Aldrich team led by Edward Weinstein, PhD, a one-year grant to develop five Parkinson's knockout models, each lacking one gene known to play a role in PD: alphasynuclein, LRRK2, DJ-1, Parkin and PINK1. The creation of knockout rat models of PD will provide new opportunities for understanding the functions of different PD-implicated genes. The researchers expect to report back to MJFF on the creation and characterization of their models by mid-2010.

A pre-clinical model shows the effects of a human LRRK2 mutation

In 2009, with funding from MJFF under the *Development of Progressive Pre-clinical Models of PD* initiative, CJ Li, PhD, of Weill Cornell Medical College published the first reported mouse model for the study of LRRK2 gene mutations. (Read more about LRRK2 on page 4). Unlike the knockout rats, Dr. Li's mouse models express the human LRRK2 gene, allowing scientists for the first time to evaluate the progressive effects of these gene mutations — a critical step in the process of converting genetic discoveries into patient-relevant therapies and a vital need for biotech and pharmaceutical companies working to develop new treatments for Parkinson's.

"Dr. Li's models represent a much-needed preclinical tool to screen and validate potential new therapies for Parkinson's disease," says

"The Michael J. Fox Foundation for Parkinson's Research didn't waste any time putting recently published knockout rat technology to work." Science-Business eXchange (cover story), October 22, 2009

MJFF Scientific Advisory Board member Kalpana Merchant, PhD, of Eli Lilly and Co. "They also can be used to study the underlying mechanisms of LRRK2 mutations and how they contribute to PD."

MJFF has quickly provided supplemental funding to Dr. Li and collaborator J. Timothy Greenamyre, MD, PhD, of the University of Pittsburgh to further characterize neurobehavioral deficits, neurochemical irregularities, dopamine cell loss, neuropathology, and molecular features in models of different ages.

"We anticipate that these models of PD will recapitulate various components of the human disease," says Dr. Li. "This increases the potential that meaningful comparisons can be made between what we find in the models and what is seen in PD patients."

Practical distribution channels for widespread access to the best tools

To reduce the costs and improve the speed and efficiency of producing and distributing research

models, in 2009 MJFF partnered with The Jackson Laboratory (JAX) in Bar Harbor, Maine, to strengthen JAX's existing Parkinson's Disease Mouse Model Repository.

The repository will house and distribute valuable MJFF-funded mouse models for use by the entire PD research community, removing a significant barrier to access. The mouse models created by Dr. Li and his colleagues, as well as other pre-clinical models developed with funding from MJFF, are already at JAX and ready for distribution.

"Working with JAX is one example of how MJFF is doing whatever it takes to speed drug development by getting the best research tools into as many scientists' hands as possible," says Sohini Chowdhury, associate director, team leader, Research Programs. "We can't stand by and watch access issues slow down research progress."



CJ Li (right)

MJFF partner Sigma-Aldrich's position in *The Scientist*'s Top 10 scientific innovations of 2009 for its novel knockout-gene technology

Our Global Reach: Select List of Organizations with Active MJFF Awards in 2009

Mayo Clinic

Medtronic Neuromodulation

Montana State University

With up to 250 active awards in our portfolio at any given time, The Michael J. Fox Foundation is continuously engaging with Parkinson's disease researchers and thought leaders across the globe. Below are the organizations, companies and institutes that initiated new MJFF-funded PD research projects in 2009.

United States

Acadia Pharmaceuticals **Adolor Corporation** Alzheimer Research Forum Amylin Pharmaceuticals, Inc. ArmaGen Technologies, Inc. Beth Israel Deaconess Medical Center Biodesy, LLC **Brandeis University** Brigham & Women's Hospital **Brown University** Caliper Life Sciences (Xenogen) Carmot Therapeutics, Inc. Case Western Reserve University Ceregene, Inc. Chaperone Therapeutics, Inc. Codman and Shurtleff, Inc. Colorado State University Columbia University Coriell Institute for Medical Research Covance Creative Commons **Duke University Envivo Pharmaceuticals Epitomics**

Emory University FoldRx Pharmaceuticals. Inc. Foundation for the National Institutes Harvard University Henry Ford Health System In Silico Biosciences Indiana University Intra-Cellular Therapies, Inc. Invitrogen Corporation Isis Pharmaceuticals, Inc. Life Technologies Louisiana State University Health Sciences Center-Shreveport Massachusetts General Hospital

Mount Sinai School of Medicine National Institute on Aging (NIA)/NIH Northern California Institute for Research & Education Northwestern University Oregon Health & Science University Parexel Pfizer Global Research and Development **Purdue University** Retrotope, Inc. Rockefeller University Rush University Saint Jude Children's Research Hospital Satoris Inc. Sigma-Aldrich Sign Path Pharma. Inc. SRI International Stanford University Sun Health Research Institute Targacept, Inc. The Burnham Institute for Medical Research The Institute for Neurodegenerative Disorders The Jackson Laboratory The Parkinson's Institute

Canada University of Alberta NeurAxon. Inc. The Salk Institute for **Biological Studies** Neurodyn Inc. Thomas Jefferson University University of Alabama at Birmingham Denmark University of California, Los Angeles University of Aarhus University of California, San Francisco France University of Chicago

University of Cincinnati

Health Sciences Center

University of Colorado at Denver &

University of Colorado Denver

University of Florida University of Illinois at Chicago University of Iowa University of Pennsylvania University of Pittsburgh University of Rochester University of South Florida University of Southern California University of Texas University of Texas Southwestern Medical Center at Dallas University of Washington Virginia College of Osteopathic

Weill Medical College

University of Sydney University of Melbourne

Wayne State University

Austria

Australia

University of Innsbruck

University of Liege

Belgium

Katholieke Universiteit Leuven reMYND NV

University of Ottawa Toronto Western Hospital

University of Bordeaux University of Nantes INSERM Toulouse University Hospital

Germany

InterMed Discovery GmbH Max Planck Institute for **Biophysical Chemistry** NextPharma University Hospital Goettingen Philipps University Marburg

Greece

Foundation for Biomedical Research of the Academy of Athens

Ireland

Opsona Therapeutics LTD

Hebrew University-Hadassah Medical School

Tel Aviv Sourasky Medical Center

University of Brescia University of Padova

Spain

Universidad Autonoma de Madrid

Sweden

Lund University

Switzerland

Swiss Federal Institute of Technology Lausanne

National Institute of Neurologyy

United Kingdom

University of Dundee University of Cambridge GlaxoSmithKline Imperial College London Institute of Neurology University of Newcastle upon Tyne

761

Number of grant applications reviewed by **MJFF** in 2009

Our Power to Convene: Select List of **2009 MJFF Workshops and Summit Meetings**

In 2009, MJFF brought together more than 500 top researchers from academic and industry labs all over the world for approximately 40 conferences, summit meetings and workshops. These sessions catalyzed concrete action steps — new grant programs, funding for critical tools and resources, novel collaborations and other tactical interventions to move the best ideas forward faster.

"MJFF's PD Therapeutics Conference is an essential meeting for PD drug development because of its focus on what really matters: presenting the highestimpact research ideas and compelling data. The goal is to streamline the process of aligning suitable partners and forging effective new

Franz Hefti, PhD. Chief Scientific Officer, Chair, PD Therapeutics

collaborations."

Avid Radiopharmaceuticals: Conference 2010

535

Number of researchers convened by MJFF for 40 strategic meetings in 2009

ADDF Drug Discovery for Neurodegeneration. February 2–3

(Sponsored by the Alzheimer's Drug Development Foundation)

Todd Sherer, PhD, vice president Research Programs, chaired a session on drug discovery and development for neurodegenerative diseases. Participants brainstormed potential solutions to issues including selection of research models, target validation and pre-clinical development.

Placebo Response Workshop, March 30

(Co-funded by The Davis Phinney Foundation) Leading experts prioritized strategies for gaining a greater understanding of placebo effects in Parkinson's to improve the design and testing of future therapeutics. The placebo effect — in which patients who receive an inert substance nonetheless experience some or all benefits of active treatment — has increasingly complicated the interpretation of outcomes from PD clinical trials, creating a significant hurdle to the development of new treatments.

Next Steps on Dyskinesia, June 3

World-leading experts on dyskinesia, including members of the Foundation's Dyskinesia Working Group, assessed the status of various therapeutic approaches to alleviating this debilitating complication of long-term dopamine replacement therapy, and prioritized strategic next steps for MJFF and the field.

Third Annual PD Therapeutics Conference, September 30

Nearly 200 academic and industry researchers and business development professionals attended the only major scientific symposium exclusively focused on speeding PD therapeutic development.

Industry Strategy Session, October 8

Global leaders of biotech and pharmaceutical firms provided crucial feedback on MJFF's efforts to engage industry to date. Participants also suggested next steps on de-risking Parkinson's drug targets and explored additional ways that the Foundation could partner with industry to speed the development of transformative treatments and a cure for PD.

Partnering for Cures. December 1-3

(Sponsored by FasterCures)

Katie Hood, CEO, Debi Brooks, co-founder, and senior MJFF staff members participated in this first-of-its-kind meeting that brought together philanthropies, medical research foundations, and the biopharmaceutical industry in an effort to forge strategic collaborations key to the timely development of new medical treatments.

LRRK2 Summit, December 9

Global experts in PD genetics assessed the state of the field in LRRK2 biology and therapeutic development, evaluated MJFF and field-wide activities, and recommended actions for MJFF and the field to accelerate understanding of the role of LRRK2 and its translation into meaningful therapies for people with Parkinson's disease.



2009 in Photos

- 1. Julianne Moore and Bart Freundlich.
- 2. Gregg Allman, Denis Leary, Sam Fox, Elvis Costello, Roger Daltry, Michael J. Fox, John Popper and Steven Tyler backstage at "A Funny Thing Happened on the Way to Cure Parkinson's Disease."
- 3. Board member David Einhorn and his wife, Cheryl.
- 4. Amar Kuchinad, the top Team Fox fundraiser of 2009, after the NYC Half Marathon.
- 5. Board member Ryan Reynolds.
- 6. Twins Drew and Kyle Shackleton run the Chicago Marathon for Team Fox, qualifying for the Olympic trials in the process.
- 7. Michael J. Fox and Stevie Wonder at "A Sunny Thing Happened on the Way to Cure Parkinson's Disease."
- 8. Allison Maguire and Brian Grant (formerly of the Portland Trailblazers).
- 9. Rachael Ray and John Cusimano.



- 10. MJFF Board Chair George Prescott and his daughter, Cheri.
- 11. Board member Al Glickman with his wife, Judy, and Michael J. Fox.
- 12. MJFF Co-Founder Debi Brooks and Patient Council member Eugenia Brin.
- 13. David and Paige Glickman, hosts of "Sunny Thing" 2009, greet guests from the stage.
- 14. Tracy Pollan and Michael J. Fox.
- 15. Michael J. Fox, Martin and Helen Scorsese and Ronald O. Perelman.
- 16. Scott Fahey, Board member Doug Ostrover, MJFF CEO Katie Hood, Scott Williams and Board member Curtis Schenker.

2009 Donor Listing

In 2009, with the help of more than 56,000 individuals, corporations and foundations, The Michael J. Fox Foundation funded over \$39 million in Parkinson's research. We are deeply grateful for our donors' ongoing commitment to our mission to discover breakthrough treatments for Parkinson's disease.

This report lists those who honored us with significant contributions last year. Also listed are the many friends and family members to whom they paid tribute with their donations. It is in their name and spirit that we work with continued urgency toward a cure.

\$25,000,000 or more

The Brin Wojcicki Foundation

\$10,000,000 or more

Chris Sullivan*

\$2,000,000 or more

EMD Serono*
Kinetics Foundation*
Judith and George Prescott and Family*
The Edmond J. Safra Foundation*
The Dotha S. Welbourn
Charities Trust

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Margaret C. Glosser Trust Judy and Al Glickman/ Albert Glickman Family Foundation Anne and Burt Kaplan* Shackleton Family*

\$500,000 or more

Benaroya Foundation
Donny Deutsch*
Elan Pharmaceuticals, Inc.*
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^{*}recognizes multi-year commitment

\$250,000 or more

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Karen Pritzker and Michael Vlock

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Robert Pritzker

The Pumpkin Foundation/Joe and Carol Reich

Mrs. Edmond J. Safra

Carl and Ruth Shapiro Family Foundation

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Anonymous (3)

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Valerie Feigen and Steven Eisman

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Marjorie and Robert Hirschhorn

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\$10,000 or more

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The Robert Wood Johnson Foundation Eleanor Francis Nelson Jordan JP Morgan Chase Foundation Ellen Francesca Judge

Drs. Julie and Scott Kalniz

continued on page 25

*recognizes multi-year commitment

MJFF Becomes a Registered Canadian Charity

In 2009, The Michael J. Fox Foundation became a registered, tax-exempt charity in Canada, making all donations to MJFF from Canadian residents tax-deductible to the full extent of the law. Said MJFF founder and Canada native Michael J. Fox, "We have always been fortunate to be on the receiving end of a steady outpouring of Canadian support for our efforts to speed a cure for Parkinson's. Canadian researchers have also been actively involved in our scientific agenda since our earliest days. It's tremendously meaningful to me that our Foundation is now an officially registered charity in my home country." The Foundation is grateful to these Canadian friends for their generosity in 2009.

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G. Wesley Voorheis
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Robert D. Wortzman



\$10,000 or more (continued from page 23)

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In 2009, over 1,000 dedicated Team Fox members collectively raised nearly \$3 million to support The Michael J. Fox Foundation's high-impact research programs. Whether they flip pancakes, start a golf tournament, hold a yard sale or run a marathon, these passionate and creative people all over the world form an unstoppable team that keeps finding more ways to help advance the Foundation's vital work — bringing us all closer to new treatments and a cure for Parkinson's disease.

\$50,000 or more

Susan Bilotta Tips for Parkinson's

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5th Annual Pancakes for Parkinson's

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\$5,000 or more

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ING NYC Marathon

Team Fox's growing marathon program was honored to be included again as an official charity partner in the 2009 ING NYC Marathon. 220 runners from four countries and 21 U.S. states put one foot in front of the other for 26.2 miles to raise over \$857,000 for The Michael J. Fox Foundation's research toward a cure.

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Eileen Werndorfer Brookfield Parkinson Run/Walk

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\$2,500 or more

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Jason Mang Laura Manofsky Joseph McDonnell Pamela McIlvaine Andrew McLean Mike McPartland Deborah Meyer Kristine Miller Gwen Miller Brian Monk Annick Mullen Kristin Murray Keith Nelson Mariel O'Brien Daniel O'Reilly Lauren Ostendorf Caitlin Peters Gail Peters Gina Pham Rebecca Philps Nancy Polstein Pat Price Andy Renton Siobhan Roberts Joao Rodrigues Paul Roer Maren Rosen Susie Rosenthal JP Rutigliano Susan Ryan Lauren Rybas **Emily Sarokhan** Karin Sawyer **Rob Scheifley** Gwen Schroeder Karen Segall Jennifer Senske Jennifer Shea Nicole Sieffert-Fink Corrin Silver Phil Sosnow

Stephen Stowe

Frank Stramiello

Jacquelyn Strycker

John and Susie Teal

The Sauder School of

Michael Sunwoo

Jennifer Szpila

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Amberleigh Thetford
Lucy Evans Ulmer
David Weber
Abby White
Margaret Whiting
Peter Wilson
Murray John Wilson
Ronald Wong
Aileen Wong
Jean Yee
Patti Yoon
John Zainea

\$1,000 or more

Danielle Andreasi Daryl Austin Jason Bennett The Coffee Bean & Tea Leaf Jennifer D'Aoust **Jamin Davies** Joey Davis Steve Day Timothy Diamond Thomas Donahue Phil Evans Bruce Fina **Daniel Gercke** Andrew Gordon Wendy Grider Jeremy Heckerling Karen Janos Christine Leslie Alissa Lifshitz Matthew MacGregor Leslie McBeth Katherine McDonald Brian McManus Patty O'Connell Kevin O'Connor Joanna Pedersen Jason Roer Daniela Rosello Alex Rosello Erin Sheard **Neil Thomson**

David Wilburn

Patrick Hatton Chicago Marathon

Lori Hes More Marathon

Jeffrey Joseph Fireworks for Fox

Natalie Karp Canyon Ranch Group Trips

Mount Allison University Pancakes for Parkinson's

Jillian Libenson 1st Annual Nona Libenson 5K/10K

Linda Lyle

Pay Forward for Parkinson's

Chaya Mallavaram Memorial Gifts

Jason Matter Triple Bypass Bike Ride

lill Matter

Triple Bypass Bike Ride

Dustin Matthews Hacker's Cup Golf Tournament

Robin Maxcy Boston Marathon

Clent Mericle

Hit the Road Jack 5K Run/Walk

Amy Miller Twin Cities Marathon

The Monusky Family 2009 "60 for 60" Campaign for Parkinson's Disease Research

Kevin Moss South Florida Team Fox Scuba Dive

Rosemary Pepe Party to End Parkinson's

Jennifer Porter Popcorn for Parkinson's

Colette Porcelli Lettieri Inn at Quogue Fashion Show

Kim Ready Cowtown Ultra Marathon

Samuel Ross Marine Corps Marathon

Running for Papa Nashville Country Music Marathon

Lori Saviers 10 Mountains 10 Years: A Quest for the Cure

Trey Sebus Chicago Marathon

Play Proceeds

Steve Spencer "You Can't Take It With You"

Brian Thorne 2nd Annual Friends of Team Fox Holiday Party Kari Travis Boston Marathon

Colleen Wuebben Wuebben Family Skate-a-Thon

\$1,000 or more

Maureen Ashdown Pocket Change 4 Parkinson's

Berkeley County Parkinson's Support Group Bonanza and Softball Tournament

Richard Broughton The Annual OBX CruZ for the Cure of Parkinson's Disease

Jessica Brown

Capital of Texas Triathlon

Sarah Bunn "Detoxify Your Life" Seminar

Lou Bushinsky Chicago Marathon

Grainne Byrne NYC Half Marathon

Bonnie Cha NYC Half Marathon

Vicky Clark Sale for a Cure

Ken Clary WhistleStop Marathon

Jennifer Cogan Philadelphia Marathon

Eileen Colon The Army of Change

Katie Congdon Willow Tree Half Marathon

John Cuccinello Jarden Westchester Triathlon

Laura Dalle Pazze Warrior Dash

Stella Darby Liversedge Half Marathon

Jeffrey Davis Team Fox Athlete

Michelle De Luca NYC Half Marathon

Robert Denlow Boston Marathon

Meghann Dials Illinois Marathon

The Dobrez Family Team Fox Fundraiser

Greg Drumheller The Jerry G. Barnhart Memorial Poker Tournament

Martin Eldred Humpy's Classic Marathon

Elaine Ellis Premier Jewelry Show Inci Ertan Dinner & Cooking Class

Ian Fagan NYC Half Marathon Brandy Fain Netzer

ING Half Marathon Dani Farber NYC Half Marathon

Miranda Feldmann Silly Spooky Movie Nights

Christine Finan NYC Half Marathon

Morgan Fixel Team Fox Fundraiser

Hailey Flynn and Robin Lee NYC Half Marathon

Linda Foresha Pirouettes for Parkinson's

Sheldon Garfinkle NYC Half Marathon

Helen Gerry Purse Sales

Alan Gettis Philadelphia Marathon

Mark Gherty American Birkebeiner

Jacqueline Gibbons Hartford Half Marathon

Jill Goldenziel Boston Half Marathon Eugene Gurkoff

Team Fox Fundraiser Sandra Haas

NYC Half Marathon Diana Hadden Cincinnati Flying Pig Marathon

The Hanna Family Hanna Family Legacy

Gerard Hayes NYC Half Marathon

Adam Hegge Pull for Parkinson's

Chad Henson Dallas White Rock Marathon

Kieran Hughes Special Occasion Gifts

Larry Ice

Parkinson's Awareness **Building Events**

Lenore Imhof Jarden Westchester Triathlon

Jordan Isenstadt NYC Half Marathon

Karen Janos Team Fox Fundraiser Lisa Jay

Spectrum- Fall Dance Concert at Laguna Beach High School

Jennifer Johns Boston Marathon

Tara Jay Johnson The Richard L. Johnson Memorial Golf Tournament

Brad Kear Multiple Marathons

Mary Kelly Team Fox Athlete James Knuckles Chicago Marathon

Jeffrey LaGrange Board of Education Dress Down Day

Tracy Lehnecker Medicus Foundation Fundraising

Brian Levy NYC Half Marathon

Michael Lewis Honor Gifts

Nate Lukas

Peter Liberto Friends Helping Friends

Jennifer Love Pancakes for Parkinson's

More than Words: A Benefit Concert Madison Lyleroehr Vocal Performances and CD Proceeds

Edward Macdonald and Nikita Romanoff NYC Half Marathon

Chris Magoon and Katie Magoon Providence Rhode Race Lisa and Branko Maric

Joint Birthday Party Theresa Marran Team Fox Dessert Buffet

Mark Mason Kona Ironman

Cassandra Mastrianni Pizza for Parkinson's and Day of Enchantment

Soania Mathur Team Fox Fundraiser

Sean McDonald Cedar Springs Circle Annual

Crawfish Boil

Sasha Mobley Healdsburg Half Marathon

Amanda Neal Tour of Anchorage



Mary Ann Neilson 2nd Annual Keystone State Corvette Club Poker Run

Mike O'Brien and Tom O'Brien Ironman St. George

Patti Olszewski Chicago Rock 'n' Roll Half Marathon

Miranda Owens

Phoenix Rock 'n' Roll Marathon

Gaetano Parrinello
NYC Half Marathon

Jeanette Pena Chicago Rock 'n' Roll Half Marathon

Chris Piper

Chris Piper's Grand Loop Mountain Biking Adventure

Allison Platt
Party for Parkinson's

Larissa Raze Team Fox Fundraiser

Michael Redfern Multiple events

Jeannette Reiff
Pedal for Parkinson's

Mary Rich

Team Fox Wristbands

Staci Roberts Team Fox Athlete

Beth Salyers

Napa to Sonoma Wine Country Half-Marathon

Lenni Sand Team Fox Fundraiser

Reggie Scarpa Hartford Half Marathon

Nikki Schiro NYC Half Marathon

Molly Scott

Molly's Mission for Grandpa

Kara Sessums

NYC Half Marathon

Enzo Simone The Army of Change

Brad Smith

NYC Half Marathon

April Socci

NYC Half Marathon
Lee Sommers

Team Fox Fundraiser
Rik Snier

Mini Marathon 5K Walk/Run

Arun Subramaniyan Walk for Research to Fight Parkinson's

Jacqueline Talarico
Jewelry Sales

Mark and Mary Sue Taylor Kroger cards distribution

Thomas Tedesco Team Fox Athlete

Emily Twiss Austin Half Marathon

Andrew Vale

Marine Corps Marathon

Garth Wakeford

NYC Half Marathon

Jason Warner

Gordon Ferguson Yackle's 10K Run

Against Parkinson's

Renee Wegrzyn NYC Half Marathon

Meg Weidner Cupcake Mission

Diana Wiesner

Capital City Half Marathon

Brianne Yantz

NYC Half Marathon

Jonah Yesowitz

Kid's Carnival of Caring

Damon Zaleski Chicago Marathon

2009 Community Fundrasiers

The Foundation is grateful to the following donors for their generous efforts to raise funds and awareness for MJFF and Parkinson's research through community fundraising events.

\$25,000 or more

23andMe Michael Cotoia

\$10,000 or more

ITSource Technology Sydney Goldstein

\$5,000 or more

ALL TRI, Inc.

CSRA PD Support Group Walkathon

Preston L. Lowe

Parkinson's Support Group of

Rochester NY, Inc.
Debbie Shough

Summit County Parkinson's Support Group

\$2,500 or more

Robert Benjamin/Light of Day Foundation

California Jurisdictional Convention

Illinois Shotokan Booster Club

JTB International Ltd.

Megan Layer

Rocking For Parkinson's Disease Research Foundation, Inc.

Brad Schenker Bar Mitzvah

Sandy Smith

\$1,000 or more

Aeroquip Credit Union

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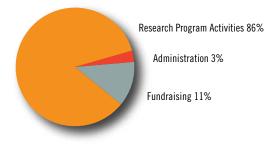
Westlake Golf and Country Club

We have made a concerted effort to accurately list all donors of significant contributions in 2009.

If your name is misspelled or missing from this report, please accept our apology and email the correct information to donations@ michaeljfox.org.

6 MJFF's place on Worth.com's 2009 Elite List of the 10 most fiscally responsible charities

MJFF Efficiency 2000-2009



2009 Financial Highlights

The Michael J. Fox Foundation believes donors have a right to look for measurable returns on their investment. We operate according to best practices and remain accountable to our donors and the Parkinson's community for ensuring maximum effectiveness. Our leadership was recruited from the worlds of finance, management and neuroscience, bringing strategic skills, scientific and operational expertise, and an investment professional's sensibility to the management of the Foundation.

- We constantly monitor costs to maximize the value of donations. Since inception, 86 cents of every dollar we've spent has gone straight to our research programs effort.
- We are outcomes-focused, tying grant payments to the achievement of specific milestones, troubleshooting challenges if



"Donors to The Michael J. Fox Foundation for Parkinson's Research have provided funds used to expedite grant processes, establish benchmarks for progress, apply continuous evaluation practices, and invest in a portfolio of promising research initiatives simultaneously... helping to reduce the overall risk of research investments, create new incentives for scientists and change the culture and expectations around medical research."

Issue Brief: Investing in Medical Research, Arabella Philanthropic Investment Advisors (2010)

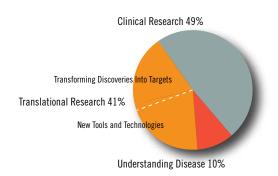
they arise, and halting funding if the science stalls. And we demand the same accountability and transparency of ourselves as we do of our awardees.

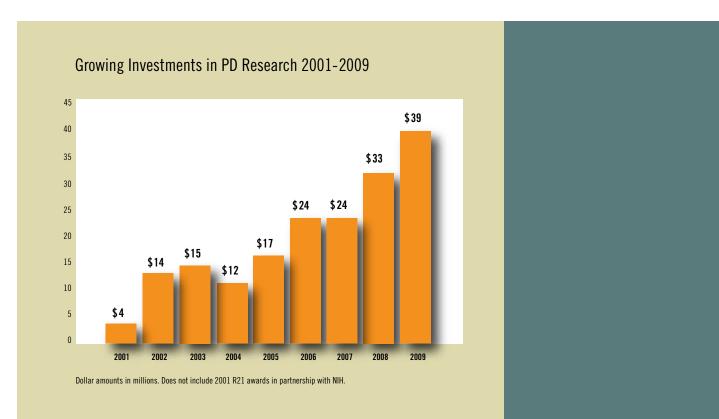
We deliberately have no endowment, because we believe that to speed a cure for Parkinson's disease, our capital needs to get into scientists' hands as quickly as possible — not sit in an endowment or reserve.

MJFF ended 2009 closing in on the \$200-million mark in research funded since inception. Ultimately, though, we measure our impact not in terms of dollars spent, but in terms of scientific solutions that produce tangible improvements in patients' lives.

2009 financial highlights follow. Full audited financials and our most recent IRS Form 990s are available at michaeljfox.org.

Research Allocation 2009





The Michael J. Fox Foundation for Parkinson's Research

Consolidated Statements of Financial Position

As of December 31,	2009	2008	
Assets			
Cash, cash equivalents and investments	\$ 33,422,684	\$ 30,962,536	
Contributions receivable, net	35,401,415	26,762,424	
Prepaid expenses and other current assets	156,687	162,958	
Security deposits	33,061	33,061	
Inventory	28,036		
Property and equipment, net	278,893	388,610	
Total assets	\$ 69,320,776	\$ 58,309,589	
Liabilities and Net Assets			
Liabilities:			
Accounts payable and accrued expenses	\$ 1,713,780	\$ 1,066,594	
Grants payable, net	42,161,174	38,882,706	
Loan payable	1,000,196	1,000,196	
Interest payable	59,511	13,089	
Deferred rent	358,114	367,192	
Total liabilities	45,292,775	41,329,777	
Net Assets:			
Unrestricted	2,345,986	(5,516,236)	
Temporarily restricted	21,682,015	22,496,048	
Total net assets	24,028,001	16,979,812	
Total liabilities and net assets	\$ 69,320,776	\$ 53,309,589	

Note: Investments are highly liquid.

The Michael J. Fox Foundation for Parkinson's Research

Consolidated Statements of Activities

2009	2008	
\$ 45,433,897	\$ 35,335,877	
5,825,680	6,741,990	
119,440	662,655	
37,425	25,682	
51,416,442	42,766,204	
39,153,137	36,236,785	
1,263,737	1,093,996	
3,951,379	4,130,806	
44,368,253	41,461,587	
7,048,189	1,304,617	
16,979,812	15,675,195	
\$ 24,028,001	\$ 16,979,812	
	\$ 45,433,897 5,825,680 119,440 37,425 51,416,442 39,153,137 1,263,737 3,951,379 44,368,253 7,048,189 16,979,812	\$ 45,433,897

Todd Sherer (left), vice president, Research Programs, MJFF, and Andrew Singleton of the National Institute of Aging (NIH) and MJFF's Executive Scientific Advisory Board at the Investigators' Meeting for the Parkinson's Progression Markers Initiative (PPMI) study launching in 2010.



Progress:

The 2009 Annual Report of The Michael J. Fox Foundation for Parkinson's Research was published in June 2010. It is available in PDF format at www.michaeljfox.org.

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Michael J. Fox Founder

Deborah W. Brooks

Co-Founder

Editor:

Holly Barkhymer Associate Director, Communications

Writers:

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On the cover

Dopamine neurons and their death in Parkinson's disease. At left and center, cell death in the substantia nigra, the brain region affected in PD. At right, a dopamine neuron expressing LRRK2. LRRK2 mutations are now believed to be the most common genetic contribution to PD. Images courtesy of Robert Burke, PhD, Columbia University (left and center) and Mark Cookson, PhD, National Institute of Aging, National Institutes of Health (right).

Page 3

Photo of Katie Hood: Getty Images/Michael Buckner. Photos of Michael J. Fox and Debi Brooks: Wirelmage/Kevin Perry.

Page 4

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LRRK2 images courtesy of Mark Cookson.

Page 6

Dopamine neuron images courtesy of John Sinclair.

Pages 8-9

Dopamine schematic courtesy of Dr. Paul Greengard, The Rockefeller University, with the technical assistance of Elisabeth Griggs.

Photo courtesy of Vanderbilt Medical Center.

Crystal structure of G-CSF as published in the Protein Data Bank (PDB: 1RHG), public domain. Created from PDB 1RHG and rendered by Ramin Herati using Pymol, March 10, 2007.

Pages 10-11

Photo of Marina Emborg courtesy of the University of Wisconsin, Madison.

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Photo of nicotine patch: Getty Images.

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Photo of Angela Cenci-Nilsson courtesy of Lund University, Sweden.

Table depicts data produced in the laboratory of M.A. Cenci at Lund University, Sweden.

Structure of serotonin copyright 2005–2007 Karl Harrison.

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Zinc Finger Nuclease schematic courtesy of Sigma-Aldrich.

Photo courtesy of Weill Cornell Medical College.

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Elena Olivo.

Page 43

Elena Olivo.

Inside back cover

Yeast cells expressing human alpha-synuclein tagged with a green-fluorescent protein courtesy of Susan Lindquist, Whitehead Institute for Biomedical Research/Aaron Gitler, University of Pennsylvania.

The Michael J. Fox Foundation gratefully acknowledges Bulkley Dunton for donating the high-quality McCoy Silk Cover and Text paper on which this annual report was printed, and Yes Press for printing this report below cost.

Our gratitude to Hearst Corporation for facilitating both donations.

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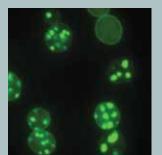
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