

# FOUNDATION PROGRESS REPORT 2000 – 2005



*2005 was an important year at The Michael J. Fox Foundation. With growing resources, we continued to sharpen our focus on*

*the pre-clinical, clinical and translational research that we believe will make strides toward a cure.*

*Because 2005 marked the Foundation's fifth year, it is fitting to assess our progress to date.*

When the Foundation began in 2000, not only was there insufficient funding of Parkinson's research, but the funding took too long to reach scientists mired in grant-application processes. Our initial goal was to cut red tape and compress the timeline from application to funding. With a quick review time, speedy funding and sizable awards, our *Fast Track* initiative cut the typical funding cycle in half, while preserving the high quality of a peer-review process modeled on NIH.

Armed with this fast track process, and together with our scientific advisory board, the Foundation soon lit on a strategy of providing seed funding for "gaps": high-risk areas or cutting-edge science overlooked, ignored or simply not funded by NIH or other funders. We forged relationships with and among academia, industry and other private funders. We convened workshops to identify research areas with significant leverage and high payoff. Our birds-eye view of the field led to an increasingly directed approach, where we determined the potentially highest-impact — yet underfunded — areas, then created funding channels to address them.

We were gratified that our disciplined approach was positively received by

both the scientific community and by national organizations such as the Parkinson's Disease Foundation, the National Parkinson Foundation, The Parkinson Alliance and Parkinson's Unity Walk who, with regional funders, contributed some \$3.1 million to our efforts. At the same time, our media and advocacy efforts triggered an increase in awareness of Parkinson's, leading to an unprecedented \$11.4 million joint initiative in collaboration with NIH and other private funders.

## Translational Efforts

With a strong scientific grounding in place, the Foundation and its advisors realized that multidisciplinary, multi-institutional collaborations were increasingly achieving the greatest success in translational efforts. Such projects require not only significant funding, but strong, on-staff scientific experience and expertise in managing collaborative efforts to emphasize outcomes and accountability. The Foundation in 2003 created *LEAPS (Linked Efforts to Accelerate Parkinson's Solutions)*, an entirely new research paradigm designed to hasten progress by funding collaborative, milestone-driven approaches to important research questions. With a commitment of up to \$20 million, *LEAPS* soon emerged as one of the Foundation's signature initiatives.

But most important, the translational efforts in our portfolio required the development of an overarching strategic framework. So in 2005 we created

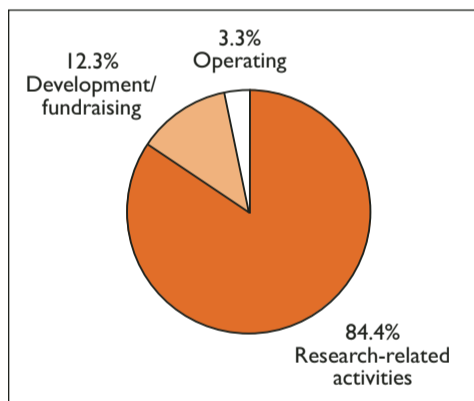
*Pathways*, a strategic tool for Parkinson's, to provide just such a context for funding decisions, and management of the scientific process. *Pathways* consists of five strategies for curing Parkinson's. Each is a step-by-step outline of the road from basic to clinical research based on a leading area of PD research. *Pathways* provides a tool to systematically shepherd translational research toward meaningful clinical outcomes and to allow those outcomes, including setbacks, to inform and redirect research to understand the disease.

## Focus on Transformative Research

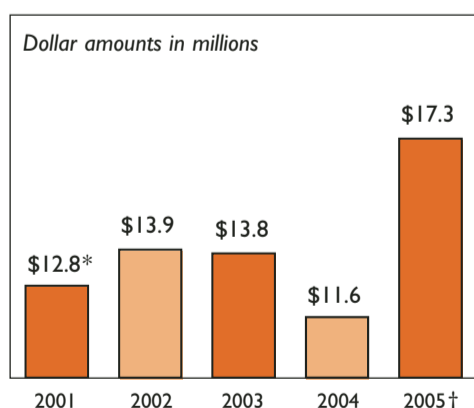
Science shifts rapidly and there is no one perfect way to seek a cure for a disease. As we enter 2006, we remain committed to seeking out new and novel ideas to understand the disease, develop new therapies and create technology and tools that can propel research forward at top speed. As always, we believe in maximizing efficiency, and are proud of investing 84 cents of every dollar raised on research since we began.

After five years, we remain passionate about our mission to accelerate a cure for Parkinson's. We are convinced that our portfolio approach — leveraging significant resources with strategic planning, rigorous accountability, and a zealous focus on research capable of producing clinically relevant outcomes — is the best way speed new treatments and find a cure.

### Our Efficiency 2000–2004



### Research Funded 2001–2005



\* Includes R21 grants through NIH with other funders (\$11.4 million).

† 2005 unaudited

## Accomplishments 2000 – 2005

- **First-ever dopamine-producing stem cell line.** MJFF-funded researchers grew the first human embryonic stem cells to produce dopaminergic neurons in vitro.
- **\$8.5 million in neurotrophic factor research to date.** MJFF is at the cutting edge of this highly promising approach to improving PD therapies.
- **Nearly \$4 million in biomarker funding to date.** We are leading the search for a Parkinson's biomarker, or diagnostic test, crucial to drug development efforts and accurate diagnosis.
- **Driving creation of the first whole-genome map of Parkinson's disease.** Result: 13 genetic changes that may increase PD risk for some people.
- **Pushing therapeutics to patients.** Funding clinical trials in neuroprotection, gene therapy and other treatments.

# 2005: DRIVING PROMISING THERAPIES INTO THE CLINIC



*The Michael J. Fox Foundation funded more than \$17 million in research in 2005. We enter 2006 as the largest nonprofit funder*

*of Parkinson's research, with more than \$70 million in research funded to date, either directly or through partnerships. 2005 was defined by a strong focus on clinical and translational research.*

condition in Parkinson's when the swallowing muscles weaken or do not work properly. The Foundation has earmarked up to \$3 million in 2006 for *Clinical Discovery*.

## New and Novel Research

Additionally, the Foundation in 2005 continued to feed the pipeline of new and novel research. The \$2-million *Community Fast Track 2005* departed from prior years in its shorter duration and greater emphasis on serving as a formalized pipeline for new ideas. We also announced a new \$2-million initiative to drive the creation of improved mammalian models of Parkinson's disease.

And in keeping with our emphasis on transformative research, we announced *Cell Line II* funding of nearly \$1 million to address obstacles in achieving the therapeutic potential of cell replacement.

## Raising Awareness

The Foundation remained committed in 2005 to raising consciousness about the crucial role of clinical research in the march toward a cure. In June we announced the results of a Harris survey on Parkinson's clinical trials. While almost all U.S. physicians who treat PD agreed that clinical trials are necessary to find better treatments, the majority had discussed them with just 10 percent or fewer of their Parkinson's patients and had never referred a patient to a trial. Ninety-five percent of patients agreed on clinical trials' importance, yet only 11 percent reported that their doctor had ever suggested they participate in a trial.

To help address challenges like these, the Foundation joined with the Parkinson's community to initiate a new campaign called PDtrials.org, led by the Parkinson's Disease Foundation, to help patients and their physicians determine whether enrollment in a clinical trial is an appropriate option. Its primary public face is a user-friendly Web site consolidating information on Parkinson's clinical trials.

In short, we continue to seek out new and bold ways to jump-start progress in bringing better treatments and, ultimately, a cure, to patients, because that is our only measure of success.

The search for a reliable biomarker of PD remains a major Foundation priority, with investments of nearly \$4 million to date. A biomarker would dramatically accelerate the development of new drugs and other neuroprotective strategies. Investigations under *Biomarkers II*, announced in August, are examining brain ultrasounds, olfactory (sense of smell) functioning, a PD-implicated protein called NURR1, an imaging agent for use with MRI that could allow clinicians to see alpha-synuclein clumping inside the body, and protein patterns in the cerebral spinal fluid of people with Parkinson's.

## Increasing Industry Investment in Parkinson's

It has become evident that to meet our ambitious goals for driving clinical research, we must engage industry partners more deeply and innovate ways to "de-risk" the investment of R&D dollars in new Parkinson's therapies. Our short-term goal on this front is to increase biotech and pharma industry decision-makers' awareness of the Foundation as a resource partner that can help hasten promising compounds on their path to the clinic and the market.

The Foundation funded about \$1.5 million in research under the annual *Target Validation* initiative and launched a second program, *PD Drug Discovery and Development*. These programs strive to speed new Parkinson's therapies to market by validating the therapeutic potential of scientific discoveries, pushing them one step closer to the clinic. They are integral to supporting applied science that can legitimize identified drug targets, and to opening the door for clinical research to bring these therapies to patients.

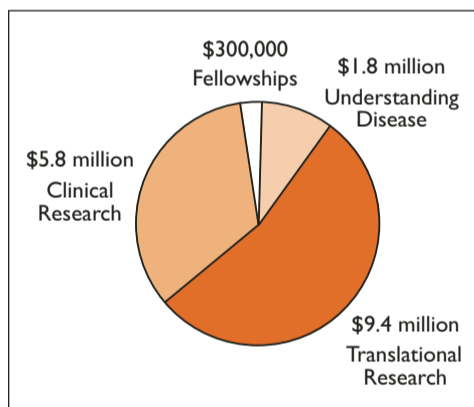
The *LEAPS* team investigating ECT (encapsulated cell technology) delivery of growth factor GDNF progressed steadily toward the clinic. In 2005, the Foundation furnished a \$1-million supplement for additional pre-clinical studies to speed the efficient design of a Phase I clinical trial slated to begin in 2007.

The Foundation also maintained its focus on clinical research with two projects funded under the second round of *LEAPS* awards in December: A joint industry-academic team led by RheoGene Inc. will develop a regulatable gene therapy system for the delivery of GDNF (and a second protein) with potential to slow or stop disease progression. After four years the researchers hope to file an application with the FDA for a Phase I clinical trial. A second team led by ProteoTech Inc. will develop a treatment to inhibit alpha-synuclein clumping, a hallmark of PD pathology. This team aims to apply for a Phase I trial within three years.

Additionally, the Foundation is providing supplemental funds for a Phase I trial being conducted by Ceregene Inc. to test a novel gene therapy product that may slow or stop disease progression by delivering the growth factor neurturin. Foundation funds are allowing for collection of more robust data on efficacy than would otherwise be possible, hastening progress toward a Phase II trial.

This project is funded under our annual *Clinical Discovery* initiative designed to address the lack of resources for small-to-medium clinical research projects. Other *Clinical Discovery* projects include a study of green tea's effects on Parkinson's under way in China and trials of a novel strength training technique to address dysphagia, a common

### Research Grant Allocation 2005\*



\* 2005 unaudited

### Recent Investments Close to the Clinic

Programs that feed this pipeline include *LEAPS*, *Clinical Discovery*, *PD Drug Development and Discovery* and *Biomarkers*.

In Trials
<p><b>Trophic Factors/ Gene Therapy:</b></p> <ul style="list-style-type: none"> <li>Delivering neurturin to slow/stop disease progression</li> </ul> <p><b>Antioxidants:</b></p> <ul style="list-style-type: none"> <li>Neuroprotective effects of green tea</li> </ul> <p><b>Symptomatic Treatment:</b></p> <ul style="list-style-type: none"> <li>Strength training for dysphagia (swallowing)</li> </ul>
Near-term
<p><b>Trophic Factors:</b></p> <ul style="list-style-type: none"> <li>Alternate delivery of GDNF through encapsulated cell technology (ECT)</li> </ul> <p><b>Gene Therapy:</b></p> <ul style="list-style-type: none"> <li>Regulatable vector to deliver symptomatic or neuroprotective treatment</li> </ul> <p><b>Biomarkers of PD:</b></p> <ul style="list-style-type: none"> <li>To improve diagnosis and better track disease progression</li> </ul>