THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH


FALL 2006 NEWSLETTER

# FOUNDATION LAUNCHES $5-MILLION *THERAPEUTICS DEVELOPMENT INITIATIVE* TO ATTRACT INDUSTRY PARTNERS AT PRECLINICAL STAGE

In spring The Michael J. Fox Foundation for Parkinson's Research launched a *Therapeutics Development Initiative* to promote increased industry involvement in preclinical research for Parkinson's disease. The program will provide up to $5 million in total funding, available only to principal investigators working within biotech and pharmaceutical firms, to drive translational research with potential to forward the development of improved PD therapeutics.

"With this initiative the Foundation aims to catalyze an overall expansion of industry interest in Parkinson's disease," said Deborah W. Brooks, the Foundation's president and CEO. "This initiative is a key element of the Foundation's overarching strategy to drive translational and clinical research that will yield new therapies for patients."

Recent scientific advances in the understanding of biochemical pathways involved in Parkinson's onset and progression have resulted in growing numbers of promising targets for Parkinson's therapeutics. Yet with rising costs of drug discovery and development, biotech and pharmaceutical companies increasingly can allocate resources to investigate only a subset of the compounds and targets they view as promising. The *Therapeutics Development Initiative* is intended to help bridge this translational gap.

"It is very difficult for a therapeutic target to become a drug without industry involvement," said Todd Sherer, PhD, the Foundation's vice president of research programs. "The pharmaceutical industry places its research focus on late-stage translational research to further commercially attractive, potential new drugs. This is a necessary complement to the work of basic researchers, whose focus is typically on early-stage research that can unearth promising new therapeutic targets." The Foundation's driving goal, Dr. Sherer explained, is to strategically bridge this gap — to speed the translation of new knowledge about Parkinson's disease into drugs that can be tested in patients.

The decision to launch the *Therapeutics Development Initiative* was informed by a survey the Foundation commissioned to assess industry views of Parkinson's disease from a commercial, clinical and scientific perspective. The survey was conducted in 2005 and 2006 by Health Advances, LLC, a strategic consultancy to the health care industry. It comprised in-depth interviews with researchers from academia and industry, as well as leaders of other nonprofits and foundations that have launched drug development partnerships with industry.

The survey revealed that the PD patient population represents a sufficient market to attract industry attention. However, a few key challenges dampen industry interest in developing disease-modifying therapies for PD. It is difficult to assess a drug candidate's potential to offer neuroprotection preclinically, and clinical trials for central nervous system disorders are long and costly. It is also hard to conclusively demonstrate an effect on underlying PD pathology.

"While the Foundation is working aggressively to address these obstacles, it is critical that we also make direct investments that can get industry more involved in preclinical research for PD," noted Ms. Brooks.

Funding under the *Therapeutics Development Initiative* is anticipated by December 2006.

## NEWS FROM THE PRESIDENT AND CEO


Mark Seliger

I'm often asked: Of all the potentially high-impact Parkinson's research the Foundation is funding, which project am I most excited about? The answer is that the Foundation's unique value-add lies not in any single investment, but in pursuing multiple promising initiatives at once.

As a private funder, with a bird's eye view of the field and proactive management of the grants in our portfolio, the Foundation is ideally positioned to identify opportunities and create synergies all along the continuum from basic to clinical research. We do this in service of one principal goal: systematically shepherding basic discoveries and translational advances toward meaningful clinical outcomes.

This newsletter, for example, reports on our new $5 million *Therapeutics Development Initiative* to catalyze industry development of potential neuroprotective therapies. Another story details the $2.6 million we've just invested under Progressive, *Predictive Animal Models* to drive creation of the models required to test those therapies. Each of these programs holds great promise in itself. More compellingly, each can potentially come to fuller fruition, and better serve patients' needs, because of the other.

It's only one example among many. But it illustrates why we believe our portfolio approach — in combination with strategic planning, sizeable funding and a tireless focus on patient-relevant outcomes — is the best way to speed new treatments and a cure for Parkinson's. Thank you for helping us get closer every day.

Warm regards,

Debi Brooks

Deborah W. Brooks
President and CEO

## IN THIS ISSUE

## FOUNDATION AWARDS $2.6 MILLION FOR DEVELOPMENT OF PROGRESSIVE ANIMAL MODELS OF PARKINSON'S DISEASE

This summer The Michael J. Fox Foundation for Parkinson's Research awarded $2.6 million in total funding to seven research groups working to develop improved animal models of Parkinson's disease. The absence of validated models of this kind is a primary roadblock to the development of neuroprotective and neurorestorative treatments to prevent, slow or stop the progression of Parkinson's disease — something no current treatment has been proven to do. The grants were made under the Foundation's *Progressive, Predictive Animal Models* initiative.

"Drug development for PD has historically centered on symptomatic therapies, due in part to the existence of animal models that show the effects of dopamine replacement on motor symptoms," said Deborah W. Brooks, the Foundation's president and CEO. "While relieving symptoms remains a priority, our greater hope is to facilitate development of disease-modifying therapies that can truly transform patients' lives. With *Progressive, Predictive Animal Models* we aim to accelerate such treatments by driving the creation of validated, reproducible models that can help make neuroprotective therapies possible."

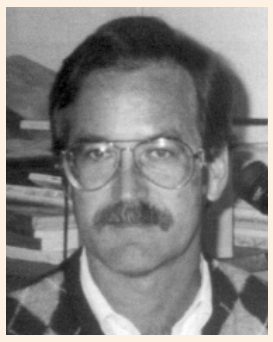
Reflecting the urgency of the need for models to advance disease-modifying therapies, the *Animal Models* initiative includes the Foundation's first-ever contractual work-sharing stipulation: Awardees must make any new model resulting from their work under this initiative available to the Parkinson's research community at large within six months of project completion.

Projects funded include the development or modification of models of several known genetic and environmental factors in PD onset and etiology. Chenjian Li, PhD, of Weill Medical College of Cornell University aims to create the first mammalian models of PD that reproduce the cardinal PD pathology of dopaminergic neuronal death in the substantia nigra. Dr. Li will use bacterial artificial chromosome (BAC) technology to create a transgenic rat overexpressing the human genes LRRK2 and alpha-synuclein, both of which play a role in Parkinson's disease. BAC technology, of which Dr. Li was an original co-inventor, enables large amounts of human DNA to be introduced into an animal model via a vector and then overexpressed, allowing researchers to observe the effects of the human DNA in the animal system. Once the rats have been generated, Dr. Li's group will put the animals through a standard battery of motor behavior and neurochemical tests to determine whether they exhibit the progressive nigral neuronal death seen in Parkinson's patients.

The animal model proposed by Robert Nussbaum, MD, of the University of California, San Francisco, School of Medicine could potentially offer researchers a way to study early disease development. Dr. Nussbaum will breed different lines of mice expressing the normal or mutated forms of human alpha-synuclein in the absence of the mouse's own alpha-synuclein gene. The resulting mice will be followed for two years to see if those with a double-dose of mutated alpha-synuclein develop any of the abnormalities seen in PD. Studies will include testing the mice for how well they walk and move, examining their brains for loss of relevant nerve cells and for the abnormal alpha-synuclein clumping seen in PD patients, and measuring levels of dopamine and related chemicals in their brains. If the mice develop PD, researchers will be able to use the model to study early changes associated with the disease and to test novel interventions to reverse, slow down or halt progression.

For a full list of grants awarded under *Progressive, Predictive Animal Models* and to read grant abstracts and researcher bios, please visit the Foundation's Web site at www.michaeljfox.org.

## SAB MEMBER BOB BURKE RECEIVES 2005–2006 LANGSTON AWARD



The Foundation announced that its 2005-2006 Langston Award would honor Robert Burke, MD, Professor and Director of the Laboratory for Research in Parkinson's Disease and Related Disorders at Columbia-Presbyterian Medical Center in New York City. The Langston Award is an annual $25,000 unrestricted research grant recognizing the outstanding contributions of one member of the Foundation's Scientific Advisory Board (SAB).

"I was honored and delighted to learn I had been selected to receive the award named for Bill, who has been such an important leader for the Foundation," said Dr. Burke. "Most importantly, I look forward to continued work with the Foundation's staff and scientific advisors toward the goal we all share — ending Parkinson's disease within our lifetime."

Dr. Burke has served on the Foundation's SAB since 2001 and has made outstanding contributions across the board including chairing the *Community Fast Track* program for the past three years with Michael Zigmond. Dr. Burke served as a reviewer in the *Clinical Discovery Program* in its inaugural year, helping to ensure that the Foundation fulfilled its objectives for the new program. His experience and expertise also came to the forefront at the Animal Models workshop convened by the Foundation and in assessments for the *Developmental Biology* and *Community Fast Track* programs.

"Whenever called upon, Bob has made himself available to the Foundation," said Debi Brooks, the Foundation's president and CEO. "He has given his time and energy unselfishly and with a great enthusiasm for our efforts. We are pleased to award him the 2005-2006 Langston Award in recognition of his extraordinary dedication."

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

# FOUNDATION AWARDS $1.8 MILLION FOR TRANSLATIONAL RESEARCH UNDER *TARGET VALIDATION* 2006

In June the Foundation awarded $1.8 million in total funding to 10 research teams working to validate the therapeutic potential of various basic science discoveries, with the goal of advancing these "possible" therapeutic targets from to "probable" therapeutics targets worthy of significantly more research attention. The projects are being funded under the Foundation's annual *Target Validation* initiative.

"It's exciting when early discovery work yields potential new drug targets for PD, but these discoveries must then be chaperoned through a series of steps to make them ripe for investment by biotech and pharmaceutical firms," said Debi Brooks, the Foundation's president and CEO.

Translation of research labs' basic cellular results into actual therapeutic interventions requires narrowly focused validation studies to confirm that altering a biological target yields a beneficial effect in a relevant PD model. This crucial step of the therapeutics development process is the focal point of *Target Validation*. The majority of awardees will work to generate new neuroprotective strategies with potential to slow or stop disease progression, something no treatment on today's market can do:

Mathias Baehr, MD, of University Hospital Göttingen (Germany) and colleagues will work to validate recent studies showing that G-CSF (granulocyte-colony stimulating factor) — a drug already approved for use in cancer patients — can protect dopamine neurons in mice exposed to the PD toxin MPTP.

Benjamin Wolozin, MD, PhD, of Boston University School of Medicine will screen for compounds that protect against oxidative stress.

Two separate awardees — Valina Dawson, PhD, of Johns Hopkins School of Medicine and Richard Eglen, PhD, of DiscoverRx Corporation — will independently identify small molecules that can bind to and inhibit LRRK2 enzymatic activity. Overactivity of LRRK2 is associated with both familial and sporadic forms of Parkinson's.

Michael Schlossmacher, PhD, of Harvard Medical School will screen small molecule libraries for compounds that can either reduce expression of the protein alpha-synuclein or increase expression of the protein parkin. Reducing alpha-synuclein may block formation of toxic aggregates, while increasing parkin has been shown to be protective in PD models.

Mona Thiruchelvam, PhD, of Robert Wood Johnson Medical School will screen non-feminizing estrogen analogs (synthetic or natural chemical compounds that resemble naturally occurring estrogens, but eliminate some potentially adverse side effects) for their ability to protect dopamine neurons in culture. The evidence for estrogen's neuroprotective potential is considerable: Epidemiological data demonstrate a lower risk of PD in women than in men; estrogen replacement therapy further reduces risk; and protective effects of estrogen have been seen in animal models of PD.

Other teams will investigate potential approaches to alleviate the symptoms of Parkinson's and/or reduce levodopa-induced dyskinesias:

Alan Kopin, MD, of Tufts-New England Medical Center, will screen small molecule compounds to detect chemical activators of GRP88, a novel receptor whose location and similarity to certain other receptors suggest that it may play a role in modulating motor function. GRP88 is expressed almost exclusively in the striatum, a region of the brain that becomes impaired with the dopamine loss characterizing PD.

Cecilia Lundberg, PhD, of Lund University (Sweden), will use a gene therapy approach to target the enzyme GAD67, which may be responsible for basal ganglia overactivity that potentially underlies the disease's motor symptoms.

Erwin Bezard, PhD, of the University of Bordeaux (France) and colleagues will use gene therapy to deliver proteins called GRKs to the brains of dyskinetic animal models. GRKs limit the duration of dopamine signaling, and their levels are reduced in animal models of dyskinesia as well as in postmortem brain tissue from dyskinetic Parkinson's patients.

Gretchen Snyder, PhD, of Intra-Cellular Therapies, Inc., a New York biotech firm, will investigate strategies to boost the strength of any remaining dopamine in the PD brain by targeting phosphodiesterases, enzymes that are normally involved in regulating dopamine signaling in the brain.

To read researchers' bios and lay-oriented abstracts of the grants funded, visit the Foundation's Web site at www.michaeljfox.org.

## SUMMER MEETINGS

The Foundation convened several workshops and assessments over the summer:

The Foundation held a midpoint progress assessment meeting for its ***Target Validation 2005*** initiative. The Foundation awarded seven projects approximately $1.5 million under this program. The assessment committee was excited about the progress of the awardees and looks forward to the projects' final outcomes. *Target Validation* awardees conduct applied studies designed to validate or disconfirm the potential of identified drug targets.

A midpoint assessment was also conducted for ***Biomarkers II***. Six grants were funded in 2005, receiving awards totaling $1.7 million to identify, develop and/or validate biomarkers for Parkinson's disease. In general, projects demonstrated good progress, with patient recruitment and setup of experimental assays ongoing. Feedback from the meeting will help focus efforts for the second year of funding.

A workshop was convened to assess the field of **PD subtypes** — different clinical phenotypes of Parkinson's that may differ in etiology, pathology, and response to treatments. Validation and characterization of subtypes could significantly improve our ability to treat patients with existing therapies, and better design future Parkinson's clinical studies by improving patient selection and outcome measures.

The Foundation held the final assessment of its ***Developmental Biology*** initiative, under which the Foundation awarded $ 2.2 million to 10 teams in 2004 to improve understanding of dopamine neurons in the brain. Most excitement was generated for the work of Drs. Johan Ericson and Thomas Perlmann, who have identified a potentially effective method for generating 'authentic' dopamine neurons from embryonic stem cells. The Foundation is considering ways to further this work.

At the final assessment for the ***Edmond J. Safra Global Genetics Consortia***, several groups reported successful outcomes confirming (or invalidating) hypotheses about genetic contributors to PD. An even greater success is that groups will maintain their consortia after the end of the program. The *Safra Global Genetics Consortia* funded five projects a total of $1.2 million in 2004 to share and combine data from multiple laboratories to better characterize genetic bases for Parkinson's.

For more information, visit us on the Web at www.michaeljfox.org/research.

# NEW EVIDENCE THAT ALPHA-SYNUCLEIN GENE VARIABILITY IS A RISK FACTOR IN PARKINSON'S

## NATURAL "DOSE" OF ALPHA-SYNUCLEIN MAY AFFECT INDIVIDUAL PD RISK

A new Michael J. Fox Foundation-funded study suggests that variations on the alpha-synuclein gene could account for up to three percent of Parkinson's disease cases.

Demetrius Maraganore, MD, of The Mayo Clinic College of Medicine in Rochester, Minnesota, and colleagues studied variability within REP1, a DNA segment that regulates how much alpha-synuclein is produced in body cells. Their results indicate that this variability is indeed associated with PD risk across several different populations.

The researchers analyzed clinical and genetic data from 2,692 Parkinson's disease patients and 2,652 healthy subjects who were matched to the Parkinson's patients for age and gender. Results showed that people with longer lengths of REP1 had a 50-percent greater risk for Parkinson's disease, while those with a shorter-length version had a lower risk.

Explained Dr. Maraganore, "Our study provides compelling evidence that variability in the alpha-synuclein gene is a risk factor for Parkinson's disease worldwide. The common DNA variants that increase Parkinson's disease risk cause the gene to produce too much alpha-synuclein protein in a process known as overexpression. Our findings support the development of therapies that reduce alpha-synuclein gene expression. Such therapies have the potential to prevent or delay the onset of Parkinson's disease or to halt or slow its progression."

### SIGNIFICANCE OF THE RESEARCH

Previous small studies had showed that rare variations (mutations) in the alpha-synuclein gene caused Parkinson's disease in a few isolated families. Further small studies suggested that common variations in the gene, while not sufficient to cause Parkinson's, make people susceptible to the disease.

"Many of these studies, however, had conflicting results," said Brian Fiske, PhD, associate director of research programs at The Michael J. Fox Foundation. "A well-designed, large study was needed to see if common variations in the alpha-synuclein gene contribute to Parkinson's risk across populations. The current study provides support for the idea that an individual's natural 'dose' of alpha-synuclein can affect PD risk."

The study was funded under the Foundation's Edmond J. Safra Global Genetics Consortia.

***Continued on Page 8***

# SEVEN CLINICAL STUDIES RECEIVE $3.7 MILLION UNDER 2006 *CLINICAL DISCOVERY PROGRAM*

Last spring The Michael J. Fox Foundation announced approximately $3.7 million in total funding for seven clinical research studies under its 2006 *Clinical Discovery Program*. This annual initiative provides funding for potentially high-impact Parkinson's clinical research studies and trials that involve active patient participation.

"*Clinical Discovery* is an important element of the Foundation's continued focus on driving clinical and translational research," said Gene Johnson, PhD, the Foundation's chief scientific advisor. "We are enthusiastic and optimistic about the potential of the 2006 program not only to answer enduring questions about the disease, but also to help speed meaningful therapies and interventions to the millions living with Parkinson's."

Clinical Discovery Program provides critical funding for "proof of principle" clinical studies and for clinical trials involving the active participation of small sample populations. The program supports projects exploring new neuroprotective treatments, improvements on existing therapies, and development of treatments for unmet symptoms of PD.

The 2006 projects fall into three categories: improving existing therapies, addressing unmet needs of Parkinson's patients and understanding Parkinson's etiology and pathogenesis through studies in patient populations.

Eliahu Heldman, PhD, chief scientific officer of NeuroDerm, Ltd., an Israeli biotech firm, will develop a transdermal skin patch for continuous delivery of levodopa and conduct initial testing in human subjects. Continuous dopamine delivery systems have generated a great deal of interest among Parkinson's researchers, because it is hypothesized that dyskinesias — disruptive, jerky movements associated with long-term levodopa therapy — result from the sharp fluctuations in dopamine blood levels that characterize oral administration of levodopa.

But to date, all attempts at achieving continuous delivery have proved impractical or infeasible, and attempts to deliver levodopa transdermally have failed because, among other reasons, the drug is unstable and has difficulty penetrating the skin. NeuroDerm has innovated a system involving stabilizers and skin penetration enhancers that has demonstrated early success in animal models, maintaining steady therapeutic levodopa blood levels with no significant side effects.

Emily Wang, PhD, of Rush University Medical Center in Chicago, will test a device that provides patients with altered auditory feedback to improve speech problems, common in people with Parkinson's. The device works as follows: Patients speak while wearing the device in one ear. The device plays back their speech in their own ear after a short time delay and with a shift in pitch. In preliminary testing, seven of eight patients who used the device made significant improvements in their speech, allowing them to express themselves more effectively with their families, caregivers and physicians.

Jonathan Haines, PhD, of Vanderbilt University has identified a population of Ohio Amish disproportionately affected by Parkinson's. He has completed initial work in this population to identify what he believes to be three novel genetic alterations associated with Parkinson's, and will next attempt to find a novel causal gene for the disease.

For a full list of grants awarded, and to read researchers' bios and lay-oriented abstracts, please visit the Foundation's Web site at www.michaeljfox.org/research.

# FOUNDATION AWARDEE FINDS A NEW WAY TO RESCUE DOPAMINE NEURONS IN ANIMAL MODELS

The Michael J. Fox Foundation has awarded a second grant supplement to a team of researchers investigating a potential new way to rescue dopamine neurons in the substantia nigra. In work highlighted in the September 13 *Journal of Neuroscience* and originally funded under the Foundation's *Inflammation* initiative, the researchers demonstrated that inhibiting the actions of a potent pro-inflammatory immune system protein called Tumor Necrosis Factor-alpha (TNF) in rat models of Parkinson's disease can rescue half the nigral dopamine neurons that would otherwise die.

## TNF AND INFLAMMATION

Malú Tansey, PhD, of the UT Southwestern Medical Center at Dallas and colleagues set out to learn how TNF and neuroinflammation affect the course of Parkinson's disease. "Inflammation promotes oxidative stress and had been implicated in contributing to development of Parkinson's disease, but its role had never really been demonstrated," said Dr. Tansey. "We set out to investigate if inhibiting TNF-dependent inflammation could rescue dopamine neurons."

TNF is an important cytokine (sight-oh-KINE) involved in systemic inflammation. Cytokines are a class of proteins that play a role in regulating immune response, and TNF is critical to normal immune function. There are two forms of TNF, one of which is membrane-bound and critical for the body's immune function, and the other of which is soluble, meaning that it circulates in the blood and cerebrospinal fluid; this is the form believed to mediate inflammation. When we cut our skin, the familiar swelling, redness and pain — the cardinal signs of inflammation — are caused in large part by a locally increased concentration of soluble TNF.

The problem comes with an excess of TNF. "Too much TNF may lead to enhanced pain and loss of appetite," Dr. Tansey explained. "TNF is primarily responsible for the inflammation that occurs in rheumatoid arthritis, for which the most effective drugs are anti-TNF agents. And dopaminergic neurons from the substantia nigra have been shown to be extremely sensitive to TNF."

Among the strong evidence pointing to a role for TNF in Parkinson's onset and progression: TNF is elevated in the cerebrospinal fluid and post-mortem brains of Parkinson's patients. A genetic variation in the TNF gene that results in higher than normal TNF production in humans has been linked to early-onset Parkinson's disease. And several studies have shown that knockout mice deficient in TNF or TNF receptors are resistant to dopamine depletion induced by MPTP (a toxin used to induce Parkinson's in animal models) in the substantia nigra.

There is also compelling evidence for the role of inflammation in the death of dopamine neurons and increased risk for Parkinson's. One example is a 2005 study published by MJFF scientific advisor Alberto Ascherio, MD, PhD, of Harvard Medical School. Dr. Ascherio and colleagues revealed that individuals on a regimen of NSAIDs, a type of anti-inflammatory drugs, had a significantly reduced risk of Parkinson's as compared to age-matched individuals who had not taken the drugs.

Based on these and other findings, Dr. Tansey and colleagues hypothesized that TNF causes inflammation that plays a major role in the dopamine neuron degeneration, and that blocking or modifying TNF signaling would provide neuroprotection and reduce neurodegeneration.

## METHODOLOGY AND RESULTS

The researchers worked with an inhibitor of TNF called "dominant-negative TNF" (DN-TNF), engineered by a team of researchers at Xencor Inc. in Monrovia, California, that included Dr. Tansey (in work that was published in the journal *Science* in 2003). DN-TNF is a "selective inhibitor" of soluble TNF — that is, it does not affect membrane-bound TNF function, but exchanges and inactivates the activity of only the soluble form of TNF, which plays a role in inflammation.

Working with a standard neuroinflammatory rat model of Parkinson's (a model in which the disease is induced by inflammation), the researchers continuously administered DN-TNF into the substantia nigra using an osmotic pump during a two-week inflammatory stimulus. Loss of dopamine was delayed by four to eight weeks.

The Foundation moved quickly to provide a supplement to the original grant with the goal of determining whether the results could be reproduced in a different kind of model where Parkinsonism was induced by the administration of an oxidative toxin. In this model, the researchers blocked TNF signaling with DN-TNF for two weeks following toxin administration. The second experiment confirmed the results of the first: Infusion of DN-TNF into the substantia nigra of either model reduced dopamine neuron loss by an astounding 50 percent.

"By testing the importance of TNF signaling in both models, we could assess whether increased TNF signaling acts as a universal mechanism in eliciting dopamine neuron death," said Dr. Tansey. "In addition, future in vitro experiments will allow us to determine mechanisms common to both models that may initiate or contribute to dopamine neuron loss.

"These results suggest that there is a therapeutic window of time during which anti-TNF treatment may provide neuroprotection," said Dr. Tansey. "The Foundation has been an ideal funding partner for this project. Its continued interest in our work, and the speed with which it has approved supplemental funding, have allowed us to advance our hypothesis on TNF and Parkinson's much closer to an outcome that could potentially be very beneficial to people living with the disease."

## FUTURE STEPS

The researchers are now investigating the cellular signaling pathways that play a role in TNF-induced neurotoxicity, and the ability of DN-TNF to provide neuroprotection in other chronic models of Parkinson's disease.

Because TNF inhibitors are not believed to cross the blood-brain barrier, an orally administered TNF-based therapy is not currently possible. The Foundation has therefore quickly approved supplemental funding to drive investigation of a potential gene therapy TNF approach. The funding will allow Dr. Tansey to partner with a new collaborator who is an expert in viral vectors for gene therapy.

"If you could successfully introduce a gene encoding a TNF inhibitor into a patient's brain to block TNF action, theoretically you could prevent the excessive TNF signaling that leads to inflammation and dopamine neuron loss," said Todd Sherer, PhD, the Foundation's vice president of research programs. "If the upcoming gene therapy experiments in animal models yield results as encouraging as those we saw with infusion, the Foundation will strongly consider additional ways to further pursue this promising avenue."

TEAMFOX
FOR PARKINSON'S RESEARCH

## FILM HITS A HOME RUN FOR PARKINSON'S AWARENESS AND FUNDS

Robert and Dan Cochrane

In the 150 years or so since the United States' first professional baseball league was founded, the sport has created a bond for countless fathers and sons. Among the latest: Robert Cochrane and his father, Dan, of Walnut Creek, California, who was diagnosed with Parkinson's in 2001. Inspired by the well-loved 1989 film Field of Dreams starring Kevin Costner, father and son set out in 2004 on a two-month, 20,000-mile road trip to see a game at every Major League Baseball park.

Robert, a filmmaker, decided to make the journey the subject of a documentary called *Boys of Summer*. He began interviewing the fathers and sons, mothers and daughters touched by PD whom he and Dan met along the way.

The interviews gave the filmmaker and his father a broader understanding of the impact of Parkinson's on families all over the United States. "Meeting fascinating people who were so hopeful and optimistic was one of the most inspiring and motivating parts of the trip," Robert says. Another worthy outcome: Robert and Dan came to know each other on a deeper level. Though a Parkinson's diagnosis was instrumental in making it happen, "neither of us would change anything about the trip," Robert adds.

*Boys of Summer* has been screened at film festivals around the country. At the Riverside International Film Festival in California, it took home the Audience Award for Best Documentary. It was also a success at the Phoenix Film Festival in March, playing closing night on the largest screen in Arizona to over 500 people.

The documentary has received excellent reviews, and Robert plans to sell the film on DVD, with part of the proceeds benefiting The Michael J. Fox Foundation. To see trailers, pictures and media interviews, or to inquire about screening the film as a fundraiser in your community, visit www.baseballdoc.com.

2005 Team Fox Marathoner
Dorrie Harris

## RUNNING LIKE A FOX FOR PARKINSON'S

**On Sunday, November 5, over 75 Team Fox athletes participate in the ING NYC Marathon. Each runner has pledged to raise a minimum of $2,500 for The Michael J. Fox Foundation. Cheer them on as they run through New York's five boroughs to raise funds and awareness for Parkinson's research. For more information visit www.ingnycmarathon.com.**

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

## HAVE FUN AND MAKE A DIFFERENCE WITH TEAM FOX

Organizing a fundraising event is a great way to have fun and support The Michael J. Fox Foundation while raising awareness and funding for Parkinson's research. Fall and winter offer a host of opportunities to get friends, family and community members involved. Consider these ideas:

**Costume Party** — Halloween is the perfect occasion for a costume party that everyone will love. Invite friends, family and co-workers to the best costume party of the year! Provide music, refreshments and a place to dance. Charge an admission fee, and give half of what you earn to the person with the best costume and the other half to Parkinson's research. Ask local businesses to support you by donating the refreshments, location, entertainment or anything else that would help make the party one to remember.

**Pumpkins for Parkinson's** — Organize a pumpkin-carving contest at your school or place of business. Ask each participant to pay an entrance fee to compete. Give half of the proceeds to the winner and donate half to Parkinson's research. You can give your fundraising an added kick by selling homemade pumpkin pies at your event or raffling off the carved pumpkins to the highest bidders.

**Raffle a Turkey Dinner** — Approach your local grocery store or farmer's market to donate a turkey dinner for Thanksgiving. Sell raffle tickets to raise money and choose one lucky winner out of a hat to walk away with a free Thanksgiving dinner!

**Holiday Party or New Year's Celebration** — Ward off winter chill with a warm and festive celebration in December, January or February. Encourage your friends and family to make a commitment to helping in the fight against Parkinson's disease while showing them a good time! Throw a party, hold an auction or run a contest with a holiday theme.

For more creative fundraising ideas or to learn more about Team Fox, The Michael J. Fox Foundation's grassroots community fundraising program, please visit www.teamfox.org.

## KNOW WHEN TO HOLD 'EM, KNOW WHEN TO FOLD 'EM

MJFF Board Member David Einhorn

During the dog days of August, David Einhorn, a member of the Foundation's Board of Directors, played his cards right and lifted the spirits of people touched by Parkinson's disease.

After traveling to Las Vegas to enter the World Series of Poker (WSOP) — the game's most prominent tournament — David unexpectedly came in 18th out of over 8,000 contestants. He won about $660,000, which he donated to the Foundation.

David, a hedge fund manager whose grandfather had Parkinson's disease, joined the Foundation's Board in 2005. He is currently the co-chair of the Foundation's largest fundraising event, "A Funny Thing Happened on the Way to Cure Parkinson's Disease," to be held November 11 in New York City.

"We don't have a poker face when it comes to thanking David Einhorn," Board Chairman David B. Golub told CNBC's "On the Money," which reported the story, as did the *New York Times*. "It means a great deal to the Foundation and to the millions of people around the world who suffer from Parkinson's disease."

"Seven hundred thousand dollars out of the clear blue sky, that's pretty great for Parkinson's research," Michael J. Fox told the *New York Times*. Mr. Fox added that he had planned to go to Las Vegas to cheer Einhorn on, had he made it to the final round.

According to David, his experience was "a real easy, fun way to raise money" for the Foundation. His successful run at the WSOP is a testament not only to his skill at poker, but also to his generosity.

## FAMILY TOUCHED BY YOUNG-ONSET PARKINSON'S WALKS FOR A CURE

Two years ago, Ann Glowienke of Oswego, Illinois, and her husband, Ken, learned that Ken had Parkinson's disease. At age 38, with his whole life ahead of him, Ken found himself putting his dreams and goals on hold to learn about the disease and try to determine what his future might hold.

Unfamiliar with Parkinson's, Ann decided to take the lead in researching the disease; she soon discovered Team Fox. Reading the stories of so many people working to raise funds and awareness, Ann realized she could inspire her family, too, to approach her husband's diagnosis with optimism and hope. From that moment, she knew, they would focus on a cure.

"I decided that rather than sitting and watching PD take control of our lives," Ann said, "we were going to take some ownership in finding a cure." The family was inspired to host a large fundraising event that would help them and their community take action to speed a cure. Together they lit on the idea of a walkathon, called "Focus on a Cure."

The first Focus on a Cure took place on May 20, the weekend of Ken's birthday. It was a great success and a great way to celebrate. Over 50 people attended, walked, enjoyed donated food and raffle prizes, and raised more than $3,500 for Parkinson's research.

"I have always said things happen for a reason," Ann concluded, "and Ken now believes this too — we think in some way, being a part of the big picture and focusing on a cure, is our reason."

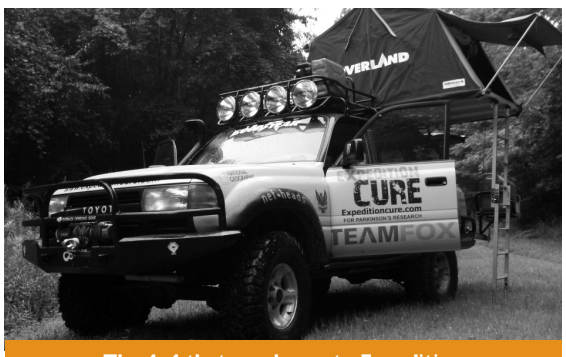
## UPCOMING REGIONAL FUNDRAISERS

**Looking for fundraisers in your neck of the woods? Here are some upcoming regional events where you can have a great time while raising funds and awareness for Parkinson's research.**

**NOSTALGIA STREET RODS**
**FIFTH ANNUAL CAR SHOW**
**Saturday, November 4, 2006**
**Las Vegas, NV**
***Contact: www.nostalgiastreetrods.com***

**HOLIDAY CONCERT FOR PARKINSON'S**
**Saturday, December 16, 2006**
**St. Augustine, FL**
***Contact: Roger Geronimo at tenore2@hotmail.com***

## FUNDRAISERS GO OFF THE BEATEN PATH FOR PARKINSON'S RESEARCH




The 4x4 that was home to Expedition Cure for three weeks

One of the best ways to support a cause close to your heart is to turn your passions or interests into an effective fundraiser. A couple of enthusiastic Team Fox members, for example, recently set out for the ride of their lives in an effort to raise money for Parkinson's research.

The daring idea was to combine an extreme off-road challenge with an extreme medical challenge. So driver Hanley Noel and navigator Brent Hatherill of Indianapolis, Indiana, embraced the unique challenge of off-roading the North American Continental Divide. The two planned to drive from border to border in just 21 days, motivated by the impact they could have on the Parkinson's community.

There was no room in their Toyota Land Cruiser for all of their supporters, but everyone tracked their progress via the Web site, www.expeditioncure.com. The site linked to Team Fox and offered forums, games and e-mails as a way to stay in touch with the off-roaders throughout their adventure.

Visit www.teamfox.org to get an update on how much Expedition Cure has raised for Parkinson's research and for more unique ideas on how to fundraise for PD.

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

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FALL 2006 NEWSLETTER

# "ALPHA-SYNUCLEIN GENE VARIABILITY" CONTINUED

## ALPHA-SYNUCLEIN: WHERE DO WE GO FROM HERE?

The role of alpha-synuclein in PD has for several years been a major force driving understanding of PD and development of potential neuroprotective therapies. Despite this effort, numerous questions and controversies exist as to whether alpha-synuclein plays a direct causative or pathogenic role in PD and, if so, how.

The Foundation has invested approximately $11 million dollars in alpha-synuclein research to date, primarily to further its potential as a therapeutic target and as a biomarker. Last July, to help prioritize avenues of research focused on tackling critical hurdles in this field, the Foundation convened the workshop "Alpha-synuclein: Where Do We Go from Here?" Participants focused primarily on the function and dysfunction of alpha-synuclein in and beyond the brain, the protein's potential for use as a therapeutic target or biomarker, and animal models.

"The general consensus from this meeting was that developing strategies to simply lower levels of alpha-synuclein in the brain could hold the most promise," said Dr. Fiske, "although attempts to break up alpha-synuclein protein clumping also hold theoretical promise." Dr. Fiske noted that the Foundation is already funding several approaches to target these two mechanisms. For example, a current *LEAPS* award is funding a team led by ProteoTech Inc. (Kirkland, WA) to develop a treatment that can disrupt or inhibit clumping of alpha-synuclein. The researchers theorize that blocking this protein clumping could prevent further cell loss and stop Parkinson's disease progression.



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

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