

Michael J. Fox Foundation Awards \$2.4 Million For Validation Of Nine Promising Therapeutic Targets For Parkinson's Disease

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The Michael J. Fox Foundation for Parkinson's Research has announced approximately \$2.4 million in total funding to nine research teams under its *Target Validation* initiative. This annual MJFF program provides intellectual and financial resources to help push potential PD drug targets forward toward clinical trials and ultimately the nearly five million Parkinson's patients worldwide.

"The discovery of a new potential therapeutic target generates great excitement among patients and researchers," said Katie Hood, CEO of The Michael J. Fox Foundation. "But to attract an industry sponsor with the resources and expertise to chaperone it through optimization, preclinical work and ultimately clinical testing, that target needs a critical mass of evidence behind it, demonstrating that it is involved in the disease and that manipulating it impacts symptoms or progression. MJFF's Target Validation program helps accumulate this evidence, reducing the risk of investment for industry and building the case for prioritization of the most promising targets in the pipeline."

Target validation is an essential and historically underresourced phase of drug development in which researchers work to determine whether a molecule or mechanism of interest is a true drug target. While researchers have continued to identify novel targets in recent years through genetic, biochemical and epidemiological studies, a lack of funding for validation studies has long been a major roadblock to the efficient translation of these discoveries into practical therapies that benefit people living with PD.

Projects funded in this cohort of Target Validation awardees fall into three categories: targets for therapies to alleviate symptoms of PD; approaches focused on dyskinesias, the excessive, uncontrollable movements brought on by long-term dopamine replacement therapy; and targets with potential to slow or stop progression of Parkinson's, something no currently approved treatment has been proven to do.

Two investigators will be continuing projects initiated under previous MJFF programs, reflecting the Foundation's desire to keep promising work moving forward quickly. Stephen F. Traynelis, PhD, of Emory University was funded under MJFF's *Community Fast Track* 2005 initiative to screen small-molecule compound libraries for molecules that inhibit a certain type of brain receptor - called the NR2D-containing NMDA receptor - in the basal ganglia, a part of the brain involved in Parkinson's disease. His new award will allow him to take this work to the next level, testing these molecules to see if they can reduce PD-like symptoms in rodent models. Kalipada Pahan, PhD, of Rush University is investigating a protein called NF-kB, which is involved in the inflammation process that some believe might trigger or promote continued loss of cells in the Parkinson's brain. Dr. Pahan has already shown that delivering specific inhibitors against NF-kB is neuroprotective in a rodent model of Parkinson's. He will now work to confirm his results in a non-human primate model of PD as the next step toward possible clinical trials.

Other investigators will be looking at various targets for possible relevance to therapeutic strategies for PD. Danny G. Winder, PhD, and Roger J. Colbran, PhD, both at Vanderbilt University and Ann M. Graybiel, PhD, at the Massachusetts Institute of Technology are each investigating new targets for possible roles in the development of dyskinesias. To identify strategies that could protect from loss of brain cells in PD, investigators Pamela J. McLean, PhD, of Massachusetts General Hospital (Harvard University), Malu G. Tansey, PhD, of University of Texas Southwestern Medical Center and Benjamin Wolozin, MD PhD, of Boston University School of Medicine will manipulate various proteins in PD animal models. Finally, Yvette F. Tache, PhD, of the University of California, Los Angeles, has developed a possible rodent model of PD-associated gastrointestinal (GI) dysfunction. She will use the model to test drugs that can alleviate this 'non-motor' symptom, which might also allow for better delivery of existing drugs such as levodopa that must pass through the GI tract to enter the bloodstream.

The following is a complete list of researchers who were awarded grants under Target Validation 2007. For grant abstracts and researcher bios, visit <http://www.michaeljfox.org>.

Roger J. Colbran, PhD, and Ariel Deutch, PhD, Vanderbilt University School of Medicine
"CaMKII as a Therapeutic Target in Parkinson's Disease"

Ann M. Graybiel, PhD, Massachusetts Institute of Technology
"Evaluation of the Striatum-enriched Genes CalDAG-GEF1 and CalDAG-GEF2 as Targets for the Treatment and Prevention of L-DOPA Induced Dyskinesia"

Pamela J. McLean, PhD, Massachusetts General Hospital (Harvard University)
"Hsp90 as a Target for Neuroprotective Agents in Parkinson's Disease"

Kalipada Pahan, PhD, Rush University Medical Center
"NBD Peptides in a Non-Human Primate Model of Parkinson's Disease"

Yvette F. Tache, PhD, University of California, Los Angeles
"Mu Opioid Receptors as a Drug Target for Treating Motor Fluctuations in PD"

Malu G. Tansey, PhD, University of Texas Southwestern Medical Center
"Dopaminergic Neuroprotection by Regulator of G-protein Signaling 10 (RGS10)"

Stephen F. Traynelis, PhD, and Stella Papa, MD, Emory University School of Medicine
"Validation of the NR2D Subunit of the NMDA Receptor as a Therapeutic Target for Parkinson's Disease"

Danny G. Winder, PhD, Roger Colbran, PhD, and Eric Delpire, PhD, Vanderbilt University School of Medicine
"NR2B as a Therapeutic Target in Parkinson's Disease"

Benjamin Wolozin, MD, PhD, Boston University School of Medicine
"SIRT1 Activators as Therapy for Parkinson's Disease"

About The Michael J. Fox Foundation

Founded in 2000, The Michael J. Fox Foundation for Parkinson's Research is dedicated to ensuring the development of a cure for Parkinson's disease within the decade through an aggressively funded research agenda. The Foundation has funded \$123 million in research to date.

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