

# Parkinson's Disease and Related Neurodegenerative Disorders

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## OFFICE OF RESEARCH AND DEVELOPMENT PROGRAM ANNOUNCEMENT

*Reply To: Department of Veterans Affairs (124), 810 Vermont Avenue, Washington, DC 20420*

### Parkinson's Disease and Related Neurodegenerative Disorders

Parkinson's disease and related neuronal degenerations such as Alzheimer's disease and motor neuron disease (amyotrophic lateral sclerosis) are progressive degenerative disorders that account for significant morbidity and mortality among veterans and the general population. The Department of Veterans Affairs (VA), in collaboration with the National Center for Human Genome Research, is launching a new initiative in Parkinson's disease research that will combine genetic, epidemiological, and clinical studies of the disease. VA's Office of Research and Development offers this program announcement to stimulate interest and solicit relevant research proposals. Proposals may be submitted to VA's Clinical Sciences Research and Development (CSR&D) Service, Biomedical Laboratory Research and Development (BLR&D) Service, Health Services Research and Development (HSR&D) Service, Rehabilitation Research and Development (RR&D) Service, or Cooperative Studies Program (CSP).

### Background:

Parkinson's disease typically appears in late middle aged and elderly persons and progresses over a period of several years. Its effects on patients, including motor function, cognitive function, and affect, are not usually life-threatening but are multiple and often devastating. They impose severe challenges to the affected individuals, their families, and the health care system.

The etiology of Parkinson's disease is unknown and both genetic and environmental factors are being explored. Recent studies suggest that a point mutation in the gene for alpha-synuclein can cause autosomal dominant, diffuse Lewy body Parkinson's disease (Polymeropoulos MH, et. al., Science 276: 2045-2047, 1997). Environmental

agents have also been implicated in the etiology of Parkinson's disease through such mechanisms as induction of oxidative injury.

The most common pharmacological treatment, L-dopa, initially provides adequate symptomatic relief but frequently loses its effect as dopaminergic neurons continue to die. Newer treatment approaches, with potential for more long-lasting benefit, include fetal neuronal transplantation, trophic factor injection, and transfusion of cells producing trophic factors.

There are similarities between Parkinson's disease and some other neurodegenerative disorders, especially Alzheimer's disease. For example, the production of Lewy bodies in Parkinson's disease is paralleled by the similar production of senile plaques in Alzheimer's disease (and to some extent in normal aging). The protein that is altered in familial Parkinson's disease has similarities to the non-beta amyloid component of Alzheimer's disease. These findings may suggest fruitful avenues of research.

### Research Interests

Research considered responsive to this announcement and of interest to the various components of VA's Office of R&D, is described below.

- Biomedical Laboratory and Clinical Sciences Research and Development Services (BLR&D and CSR&D). Proposals submitted to BLR&D or CSR&D should focus on the etiology, pathogenesis, genetics of Parkinson's disease or related neurodegenerative disease, or the efficacy of new treatments. Topics such as neuronal apoptosis, mitochondrial dysfunction, oxidative stress and free radical injury, trophic factor and cytokine effects, neuronal transplantation, gene transfer, genetic susceptibility to environmentally induced neuronal injury, and animal models of neuronal degeneration are responsive to this announcement. Proposals employing novel concepts or approaches are especially welcome.
- Health Services Research and Development Service (HSR&D). Proposals submitted to HSR&D should assess treatment effectiveness or quality, in terms of patient- or system-level outcomes. Important issues include patients' physical and cognitive function, quality of life, and cost of care. Relevant health systems issues could focus on approaches to comprehensive management, including organization of outpatient services, community based and institutional long-term care, management of comorbidities, environmental modifications, and advanced care planning.
- Rehabilitation Research and Development Service (Rehab R&D). Rehab R&D is interested in studies of approaches to improving dysphasia or other swallowing disorders, gait, falls, balance disorders, mobility, and other aspects of physical functioning that jeopardize patients' independence and well-being.

- Cooperative Studies. Phase II, III or IV treatment trials, including trials of medical or surgical approaches requiring large numbers of participants or multiple sites, are considered responsive to this announcement.

Eligibility to submit proposals will follow the same rules established by the individual services for submission of investigator-initiated proposals.

Application procedures: Preparation and submission of proposals should follow the guidelines of the individual Service to which application is made.

Due Date: This is an ongoing announcement with multiple receipt dates. Until further notice, Letters of Intent and research proposals may be submitted for any of the regular receipt dates established by the relevant Service.

Review: Proposals accepted for review by CSR&D, BLR&D, HSR&D and RR&D will be reviewed with all other investigator-initiated proposals in the normal cycle. Proposals will be evaluated on the basis of scientific quality, significance of the research question(s), rigor of the methodological approach, and feasibility.

Inquiries: For further information, contact:

Biomedical Laboratory/Clinical Science R&D:	William Goldberg, PhD	202 254-0294
Health Services R&D:	William Goldberg, PhD	202 254-0294
Rehabilitation R&D:	Danielle Kerkovich, PhD	202 254-0258
Cooperative Studies Program:	Grant Huang, PhD	202 254-0252

Stephan D. Fihn, M.D., M.P.H., F.A.C.P.

(Acting) Chief Research and Development Officer