



Science Advancement & Outreach  
A DIVISION OF PETA

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## **National Plan to End Parkinson's Request for Information(RFI) Strategy**

Submitted to [nationalPDplan@nih.gov](mailto:nationalPDplan@nih.gov) on August 20, 2026

*Please provide your perspective on any topics related to **research** on Parkinson's disease and related neurodegenerative parkinsonisms, including multiple system atrophy, corticobasal degeneration, progressive supranuclear palsy, Parkinson's disease dementia, Lewy body dementia and dementia with Lewy bodies. **We encourage you to indicate the level of priority if you provide feedback on multiple topics.** Consider including information on the below topics or please highlight any additional research priorities for Parkinson's disease and related disorders.*

- *Highest priority areas of research to understand the underlying factors contributing to Parkinson's disease and related disorders*
- *Ways to accelerate the development of safe and effective treatments to prevent, slow, or stop Parkinson's disease and related disorders, or ameliorate symptoms and improve quality of life.*
- *Research on the association between environmental triggers and Parkinson's disease and related disorders to help reduce exposure to potential triggers*
- *Ways to improve early diagnosis of Parkinson's disease and related disorders*

We are writing on behalf of Science Advancement and Outreach, a division of People for the Ethical Treatment of Animals—PETA entities have more than 10 million members and supporters globally, and PETA U.S. is the largest animal rights organization in the world—to make recommendations that will accelerate the development of safe and effective treatments for Parkinson's and disease-related disorders and improve the quality life for individuals affected by these conditions.

Parkinson's disease is human-specific and does not occur in other animals. Yet the National Institute of Neurological Disorders and Stroke (NINDS) is currently funding several projects that use [mice](#) in attempts to study Parkinson's disease. No current animal model can recapitulate the full complexity of Parkinson's disease. For example, the 6-OHDA and MPTP animal models rely on toxin-induced neuronal damage, producing an acute and immediate phenotype that does not capture the progressive nature of Parkinson's disease.<sup>1</sup> Genetically modified mouse models of Parkinson's disease exhibit inconsistent pathological and behavioral phenotypes, in part because of differences in transgenes, transgene insertion sites, expression levels, and mouse genetic backgrounds.<sup>2</sup> Furthermore, researchers often use young animals to model Parkinson's disease, despite aging being a major risk factor for the condition, further negating their relevance.<sup>3</sup>

Fundamental biological differences between humans and other species also hinder the translation of findings from animal studies. These differences include species-specific variation in blood–brain barrier transporters and enzymes expressed by brain endothelial cells; gene regulation, including transcriptional regulation of tyrosine hydroxylase; post-transcriptional regulation, including alternative splicing; and sensitivity to neurotoxins such as MPTP.<sup>4</sup>

**Because of these limitations, we recommend that the National Plan to End Parkinson’s Disease explicitly state that the NIH will not conduct or fund Parkinson’s disease research that uses other animals and will focus exclusively on non-animal, human-based research approaches, including patient-derived human induced pluripotent stem cell (hiPSC) models, “omic” technologies (e.g., genomics and proteomics), *in silico* approaches, neuroimaging, and epidemiological studies to improve early diagnosis, advance understanding of disease mechanisms and contributing factors, and accelerate the development of safe and effective treatments.**

Advanced human cell-based models, including organoids and organ-on-chip systems, can be used to investigate the biological mechanisms underlying Parkinson’s disease using human cells and tissues. Patient-derived models also enable precision medicine by using an individual’s own cells to capture patient-specific disease biology and evaluate therapeutic responses. For example, researchers have developed iPSC-based human CNS cell models that rapidly generate disease-associated protein inclusions to study how different inclusion subtypes affect neuronal survival and identify potential therapeutic targets;<sup>5</sup> created ventral midbrain–striatum–cortex assembloids to study dopaminergic neuron maturation, innervation, and function;<sup>6</sup> used patient-derived organoids and assembloids to investigate early stages of Parkinson’s disease and factors influencing susceptibility;<sup>7,8</sup> and engineered a human brain-on-chip system that models regions affected by Parkinson’s disease, reproduces disease-relevant features, and enables identification and testing of therapeutic targets.<sup>9</sup>

Computational approaches, including artificial intelligence (AI) and machine learning (ML), should be further leveraged in Parkinson’s disease research to improve early diagnosis and disease monitoring. These approaches can identify subtle patterns within complex, multidimensional datasets that may be difficult to detect through conventional approaches, enabling earlier detection and improved characterization of disease progression. In combination with digital biomarkers from wearable sensors, smartphone applications, and imaging technologies, AI and ML approaches could further improve diagnosis and treatment management through continuous monitoring.<sup>10</sup> These methods are already being applied to enable earlier diagnosis of Parkinson’s disease,<sup>11, 12</sup> including a multimodal deep learning approach capable of detecting the disease at the prodromal stage<sup>13</sup> and an AI model that detects and tracks its progression using nocturnal breathing signals.<sup>14</sup>

Epidemiological studies should be conducted to better understand associations between environmental exposures and Parkinson’s disease and related disorders. Environmental factors,

including pesticides, trichloroethylene, and air pollution, have been associated with Parkinson's disease;<sup>15</sup> however, additional epidemiological research is needed to better define these relationships and inform strategies to reduce exposure to potential risk factors.

By shifting investment toward non-animal, human-based approaches and away from experiments on animals, NINDS can advance research strategies that accurately reflect human disease biology and can improve diagnosis, treatment, and quality of life for individuals affected by Parkinson's disease.

Additional information on the recommendations outlined in this response can be found in our policy roadmap, [Research Modernization NOW](#), which provides a comprehensive action plan for advancing biomedical research in the U.S. across multiple research areas, including [Parkinson's disease and other neurodegenerative disorders](#). You may also reach us at [info@scienceadvancement.org](mailto:info@scienceadvancement.org).

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<sup>1</sup> Potashkin JA, Blume SR, Runkle NK. Limitations of animal models of Parkinson's disease. *Park Dis*. 2011;2011:1-7. doi:10.4061/2011/658083

<sup>2</sup> Meredith GE, Sonsalla PK, Chesselet MF. Animal models of Parkinson's disease progression. *Acta Neuropathol (Berl)*. 2008;115(4):385-398. doi:10.1007/s00401-008-0350-x

<sup>3</sup> Lane E, Dunnett S. Animal models of Parkinson's disease and L-dopa induced dyskinesia: how close are we to the clinic? *Psychopharmacology (Berl)*. 2008;199(3):303-312. doi:10.1007/s00213-007-0931-8

<sup>4</sup> Potashkin et al.

<sup>5</sup> Lam I, Ndayisaba A, Lewis AJ, et al. Rapid iPSC inclusionopathy models shed light on formation, consequence, and molecular subtype of  $\alpha$ -synuclein inclusions. *Neuron*. 2024;112(17):2886-2909.e16. doi:10.1016/j.neuron.2024.06.002

<sup>6</sup> Reumann D, Krauditsch C, Novatchkova M, et al. In vitro modeling of the human dopaminergic system using spatially arranged ventral midbrain–striatum–cortex assembloids. *Nat Methods*. 2023;20(12):2034-2047. doi:10.1038/s41592-023-02080-x

<sup>7</sup> Barnmpa K, Saraiva C, Lopez-Pigozzi D, et al. Modeling early phenotypes of Parkinson's disease by age-induced midbrain-striatum assembloids. *Commun Biol*. 2024;7(1):1561. doi:10.1038/s42003-024-07273-4

<sup>8</sup> Rosety I, Zagare A, Saraiva C, et al. Impaired neuron differentiation in GBA-associated Parkinson's disease is linked to cell cycle defects in organoids. *Npj Park Dis*. 2023;9(1):166. doi:10.1038/s41531-023-00616-8

<sup>9</sup> Pediaditakis I, Kodella KR, Manatakis DV, et al. Modeling alpha-synuclein pathology in a human brain-chip to assess blood-brain barrier disruption. *Nat Commun*. 2021;12(1):5907. doi:10.1038/s41467-021-26066-5

<sup>10</sup> Twala B. AI-driven precision diagnosis and treatment in Parkinson's disease: a comprehensive review and experimental analysis. *Front Aging Neurosci*. 2025;17:1638340. doi:10.3389/fnagi.2025.1638340

<sup>11</sup> Twala et al.

<sup>12</sup> Shokrpour S, MoghadamFarid A, Bazzaz Abkenar S, Haghi Kashani M, Akbari M, Sarvizadeh M. Machine learning for Parkinson's disease: a comprehensive review of datasets, algorithms, and challenges. *Npj Park Dis*. 2025;11(1):187. doi:10.1038/s41531-025-01025-9

<sup>13</sup> Dentamaro V, Impedovo D, Musti L, Pirlo G, Taurisano P. Enhancing early Parkinson's disease detection through multimodal deep learning and explainable AI: insights from the PPMI database. *Sci Rep*. 2024;14(1):20941. doi:10.1038/s41598-024-70165-4

<sup>14</sup> Yang Y, Yuan Y, Zhang G, et al. Artificial intelligence-enabled detection and assessment of Parkinson's disease using nocturnal breathing signals. *Nat Med*. 2022;28(10):2207-2215. doi:10.1038/s41591-022-01932-x

<sup>15</sup> Dorsey ER, Bloem BR. Parkinson's disease is predominantly an environmental disease. *J Park Dis*. 2024;14(3):451-465. doi:10.3233/JPD-230357