

Researchers identify a new candidate therapeutic target for Parkinson's disease

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Immunohistochemistry for alpha-synuclein showing positive staining (brown) of an intraneuronal Lewy-body in the Substantia nigra in Parkinson's disease. Credit: Wikipedia

The human brain is lipid rich. Lipids and fatty acids contribute to many important cellular processes. Alpha-synuclein—a protein that plays a critical role in Parkinson's disease (PD)—is known to interact with and alter the balance of lipids and fatty acids.

Investigators from the Brigham and Harvard Medical School are exploring how to rebalance [fatty acid metabolism](#) in the brain to find new therapeutic approaches for PD and related conditions. Their previous work has led to the identification of an inhibitor of an enzyme called stearyl-CoA-desaturase, which is now being tested in human clinical trials.

In a new study published in *npj-Parkinson Disease*, they identify LIPE, a lipase that degrades triglycerides to produce [fatty acids](#), as a candidate therapeutic target. Inhibiting LIPE reduced the

formation of clusters of α -synuclein inclusions and other characteristics associated with PD in patient-derived neurons. LIPE reduction also alleviated neurodegeneration in a *C. elegans* model of α -synuclein toxicity.

"Our research led us to become increasingly aware of the role lipid and fatty acid balance may play in Parkinson's disease," said co-corresponding author Saranna Fanning, Ph.D., of the Ann Romney Center for Neurologic Diseases at the Brigham. "Ultimately, we hope this lipid-related target will have promise as a small-molecule therapy for Parkinson's disease."

Co-corresponding author Dennis Selkoe, MD, also of the Ann Romney Center for Neurologic Diseases at the Brigham, added that "the identification of LIPE inhibition and a unique co-regulation of fatty acid synthesis and degradation pathways are further evidence that targeting fatty acid metabolism holds promise for Parkinson's disease."

More information: Saranna Fanning et al, Lipase regulation of cellular fatty acid homeostasis as a Parkinson's disease therapeutic strategy, *npj Parkinson's Disease* (2022). [DOI: 10.1038/s41531-022-00335-6](https://doi.org/10.1038/s41531-022-00335-6)

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