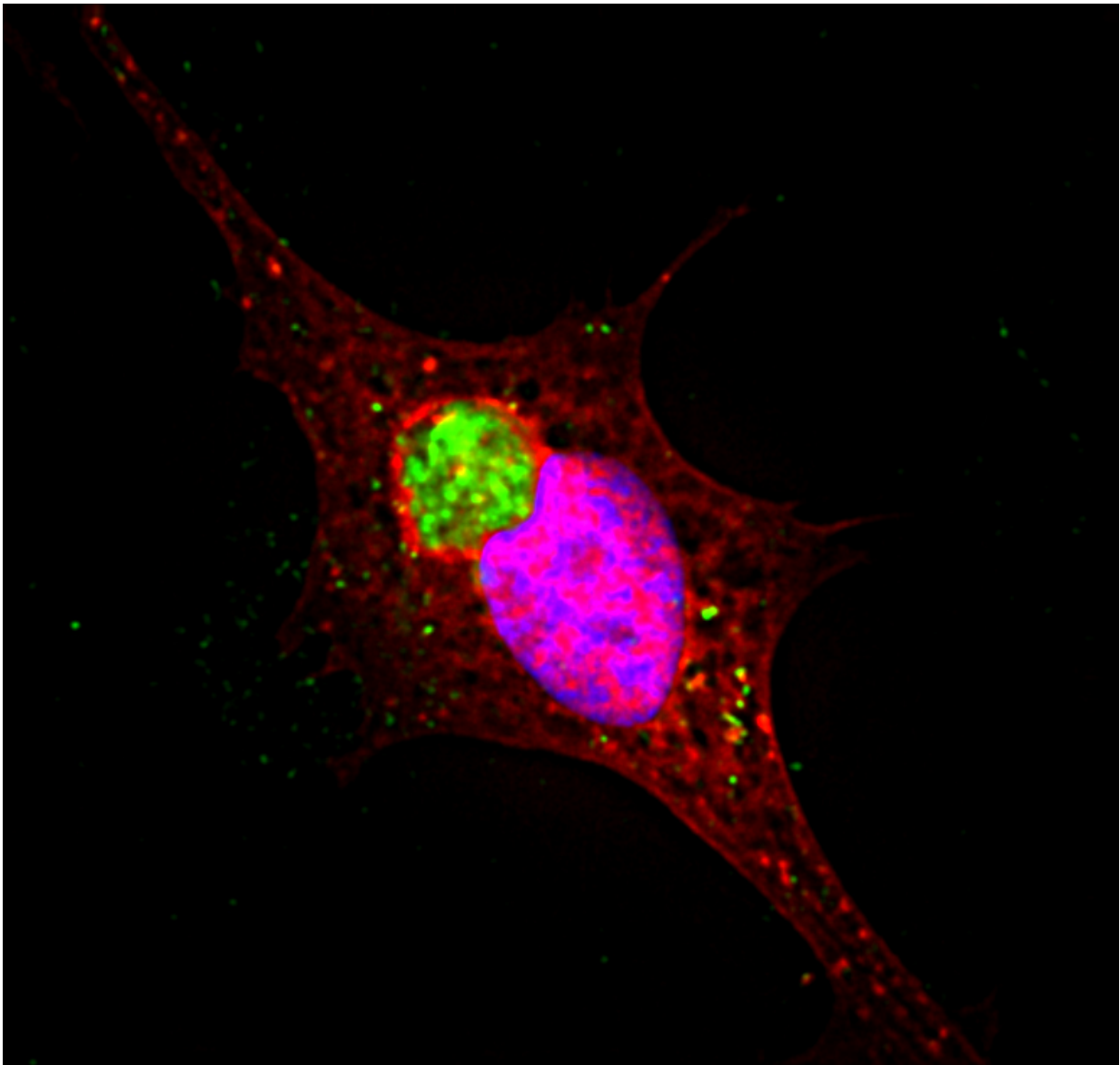


Alzheimer's, Parkinson's, and Huntington's diseases share common crucial feature

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The fusion of ruptured vesicles containing alpha-synuclein protein (green) leads

to the formation of large protein clumps resembling the proteins that form in the brains of Parkinson's disease patients. Credit: Loyola University Chicago

A Loyola University Chicago study has found that abnormal proteins found in Alzheimer's disease, Parkinson's disease, and Huntington's disease all share a similar ability to cause damage when they invade brain cells.

The finding potentially could explain the mechanism by which Alzheimer's, Parkinson's, Huntington's, and other [neurodegenerative diseases](#) spread within the [brain](#) and disrupt normal brain functions.

The finding also suggests that an effective treatment for one neurodegenerative [disease](#) might work for other neurodegenerative diseases as well.

The study by senior author Edward Campbell, PhD, first author William Flavin, PhD, and colleagues is published in the journal *Acta Neuropathologica*.

"A possible therapy would involve boosting a brain cell's ability to degrade a clump of proteins and damaged vesicles," Campbell said. "If we could do this in one disease, it's a good bet the therapy would be effective in the other two diseases."

Neurodegenerative diseases are caused by the death of neurons and other [cells](#) in the brain, with different diseases affecting different regions of the brain. Alzheimer's destroys memory, while Parkinson's and Huntington's affect movement. All three diseases are progressive, debilitating and incurable.

Previous research has suggested that in all three diseases, proteins that are folded abnormally form clumps inside brain cells. These clumps spread from cell to cell, eventually leading to cell deaths. Different proteins are implicated in each disease: tau in Alzheimer's, alpha-synuclein in Parkinson's and huntingtin in Huntington's disease.

The Loyola study focused on how these misfolded protein clumps invade a healthy brain cell. The authors observed that once proteins get inside the cell, they enter vesicles (small compartments that are encased in membranes). The proteins damage or rupture the vesicle membranes, allowing the proteins to then invade the cytoplasm and cause additional dysfunction. (The cytoplasm is the part of the cell that's outside the nucleus).

The Loyola study also showed how a cell responds when protein clumps invade vesicles: The cell gathers the ruptured vesicles and protein clumps together so the vesicles and proteins can be destroyed. However, the proteins are resistant to degradation. "The cell's attempt to degrade the proteins is somewhat like a stomach trying to digest a clump of nails," Campbell said.

Flavin said the finding that protein clumps associated with the three diseases cause the same type of vesicle damage was unexpected. Loyola researchers initially focused on alpha-synuclein proteins associated with Parkinson's disease. So they asked collaborator Ronald Melki, PhD, to send them samples of different types of alpha-synuclein. (To do the experiment in a blinded, unbiased manner, the Loyola researchers did not know which types of alpha-synuclein were which.) Melki, a [protein](#) researcher at the Paris-Saclay Institute of Neuroscience, is known for his ability to generate distinct types of alpha-synuclein. Without telling the Loyola researchers, Melki sent other types of proteins as well. This led to the surprise finding that tau and huntingtin proteins also can damage vesicles.

Campbell stressed the study's findings need to be followed up and confirmed in future studies.

The Loyola study is titled, "Endocytic vesicle rupture is a conserved mechanism of cellular invasion by amyloid proteins." It was supported by grants from the Michael J. Fox Foundation, Parkinson's Disease Foundation, Illinois chapter of the ARCS Foundation, Arthur J. Schmitt Foundation and other sources.

Campbell is an associate professor in the Department of Microbiology and Immunology at Loyola University Chicago Stritch School of Medicine. Flavin is a Loyola University Chicago MD/PhD student. Other co-authors are Zachary Green, Stratos Skarpathiotis, and Michael Chaney of Loyola University Chicago; Luc Bousset and Ronald Melki of the Paris-Saclay Institute of Neuroscience; and Yaping Chu and Jeffrey Kordower of Rush University Medical Center.

More information: William P. Flavin et al, Endocytic vesicle rupture is a conserved mechanism of cellular invasion by amyloid proteins, *Acta Neuropathologica* (2017). [DOI: 10.1007/s00401-017-1722-x](https://doi.org/10.1007/s00401-017-1722-x)

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