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Researchers first to map structure of protein aggregate that leads to Alzheimer's

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A research team including faculty at Binghamton University and University of Colorado Denver are the first to map the molecular structure of an aggressive protein aggregate that causes acceleration of Alzheimer's disease.

"Approximately 10 percent of Alzheimer's cases result from familial mutations," said Wei Qiang, assistant professor of biophysical chemistry

at Binghamton University. "The other 90 percent cases are caused by misfolded wild-type amyloid proteins. We need to understand the molecular basis of the disease pathology. In doing so, we might one day create drugs that prevent the degenerative effects of the disease."

Alzheimer's disease starts developing when toxic protein fragments called beta amyloids form into chains known as fibrils, which build upon and kill brain cells. Qiang, along with researchers at the University of Colorado Denver, used high-resolution solid-state nuclear magnetic resonance spectroscopy to study these fibrils. Their work revealed that these fibrils may possess major variations in the molecular structure of amyloid depositions in the human brain. More importantly, the fibrils could serve as "seeds" for further fibril deposition, which is a potential risk factor in Alzheimer's pathology.

"This work describes a molecular structural model for a pathologically relevant beta-amyloid fibril variant," said Qiang. "We showed that this variant could lead to rapid seeding of new amyloid fibrils, which potentially contributes to the spreading and amplification of amyloid deposition in human brains."

Qiang and his team are looking at several other types of fibril variants and specifically, the correlation between the structural variations, their seeding abilities and the resulted cellular toxicity levels.

"We have already obtained exciting results and a new manuscript describing these further finding is in preparation," said Qiang.

More information: Zhi-Wen Hu et al, Molecular structure of an N-terminal phosphorylated β-amyloid fibril, *Proceedings of the National Academy of Sciences* (2019). DOI: 10.1073/pnas.1818530116

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