

Researchers show how Alzheimer's plaques lead to loss of nitric oxide in brain

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A researcher at the University of Pittsburgh School of Medicine, in collaboration with scientists from the National Institutes of Health (NIH), has discovered that the deadly plaques of Alzheimer's disease interact with certain cellular proteins to inhibit normal signals that maintain blood flow to the brain. Their findings, which could lead to new approaches to treat the dementia, were recently published in *Public Library of Science One*.

Levels of nitric oxide (NO) – a signaling molecule that helps regulate [blood flow](#), immune and neurological processes – are known to be low in the brains of people who have [Alzheimer's disease](#), but the reason for that hasn't been clear, said study co-author Jeffrey S. Isenberg, M.D., M.P.H., associate professor, Division of Pulmonary, Allergy, and Critical Care Medicine, Pitt School of Medicine.

"Our research sheds light on how that loss of NO might happen, and reveals biochemical pathways that drug discoverers might be able to exploit to find new medicines for Alzheimer's," he said. "There is evidence that suggests enhancing NO levels can protect neurons from degenerating and dying."

The researchers, led by first author Thomas Miller, Ph.D., and senior author David D. Roberts, Ph.D., both of the Laboratory of Pathology in NIH's National Cancer Institute (NCI), found in mouse and human cell experiments that amyloid-beta, the main component of the plaques that accumulate on brain cells in Alzheimer's, binds to a cell surface receptor

called CD36, which causes decreased activity of the enzyme soluble guanylate cyclase to reduce NO signaling. But that inhibitory effect required the presence of and interaction with CD47, another cell surface protein, indicating that additional steps in the pathway remain to be identified.

"It's possible that an agent that could block either CD36 or CD47 could slow the progress of neuronal degeneration in Alzheimer's by protecting the production of NO in the [brain](#)," Dr. Isenberg said. "Importantly, we have already indentified therapeutic agents that can interrupt the inhibitory signal induced by these interactions to maximize NO production, signaling and sensitivity."

He and his colleagues currently are studying such blockers in a variety of disease models.

Co-authors of the paper include Hubert B. Shih and Yichen Wang, both of NCI. The research was funded by NCI and the Howard Hughes Medical Institute.

Provided by University of Pittsburgh

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