

## The tangled web in Alzheimer's protein deposits is more complex than once thought

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Scientists from the National Institutes of Health in the United States have made an important discovery that should forever change the scope and direction of Alzheimer's research. Specifically, they have discovered that the protein tangles which are a hallmark of the disease involve at least three different proteins rather than just one. The discovery of these additional proteins, called neurofilaments and vimentin, should help scientists better understand the biology and progression of the disease as well as provide additional drug discovery targets. This discovery was published in the November 2011 issue of the *FASEB Journal*.

"Since neurofilaments are the predominant protein in nerve cells, our study suggests that we should refocus our research on the biology of these filamentous proteins in an effort to understand how they are normally regulated and deregulated in response to human aging," said Harish C. Pant, Ph.D., a senior researcher involved in the work from the Cytoskeletal Regulatory Protein Section of the Laboratory of Neurochemistry at the National Institute of Neurological Disorders and Stroke at the National Institutes of Health in Bethesda, Maryland.

To make their discovery, Pant and colleagues identified normal and abnormal proteins present in autopsy samples of the brains of Alzheimer's disease victims. Then they isolated and purified the tangles (which are knots of abnormally aggregated filaments that fill and compromise nerve cells) from the autopsy samples and compared their protein composition to age- and post mortem-matched samples of brains from patients who died of other causes, such as accidents. Through a



combination of improved instrumentation and informatics, it was possible to resolve the mixture of proteins successfully and identify the novel Alzheimer's disease proteins. Previous research suggested that only one protein, called "tau," is present in these tangles.

"This is a breakthrough of great importance: tau is not the only target," said Gerald Weissmann, M.D., Editor-in-Chief of the FASEB Journal. "Before this discovery, we approached these tangles as if they were woven of one piece of string. Now we know that there are at least three proteins involved, we're much closer to untangling the Alzheimer's web. Without question, discoveries like this bring us closer than ever to advanced Alzheimer's treatments, and it is a good example of why NIH funding is among the best investments our nation can make toward improving health and well being."

**More information:** Parvathi Rudrabhatla, Howard Jaffe, and Harish C. Pant. Direct evidence of phosphorylated neuronal intermediate filament proteins in neurofibrillary tangles (NFTs): phosphoproteomics of Alzheimer's NFTs. *FASEB J.* November 2011 25:3896-3905; doi:10.1096/fj.11-181297

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