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Scientists begin to untangle root cause of Alzheimer's disease

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In a research report published online in the FASEB Journal, an international team of scientists describe how the N60 fragment of the RanBP9 protein increases the production of the amyloid beta protein, which is present in excessive amounts in the brains of people with Alzheimer's disease.

"N60" might not be the first thing that comes to mind when people think of Alzheimer's disease, but thanks to researchers from the United States, South Korea and France, this might change. That's because these researchers have found that the N60 section of a protein called "RanBP9" might be the key that unlocks an entirely new class of Alzheimer's drugs, and with them, hope. In a research report published online in The *FASEB Journal*, these scientists describe how the N60 fragment of the RanBP9 protein increases the production of the amyloid beta protein, which is present in excessive amounts in the brains of people with Alzheimer's disease.

Most experts believe that if the creation of amyloid beta protein can be halted or slowed, the devastating effects of Alzheimer's disease may also be stopped or slowed too. Knowing which portion of the RanBP9 protein to target is particularly important because it gives researchers a more specific focus for developing new Alzheimer's drugs.

According to David Kang, assistant professor of neurosciences at the University of California, San Diego, and one of the researchers involved in the work, "Our study suggests that targeting RanBP9 expression

and/or N60 fragment generation may lead to novel strategies to combat this devastating disease."

To make this discovery, Kang and colleagues examined extracts from brains with Alzheimer's disease and age-matched healthy controls and found that the N60 section of RanBP9 was increased in Alzheimer's brain. When control DNA, full-length RanBP9 DNA, and RanBP9-N60 DNA were individually expressed in cultured cells, they found that cells expressing the full length RanBP9 protein had an increased amount of the amyloid beta protein that was 3-fold over control, and cells expressing the RanBP9 protein and N60 section had an increased amount of the amyloid beta protein that was 5-fold over control.

"Alzheimer's might seem hopeless to some, but this research shows that we're closer than ever to unraveling both the protein tangles and mysteries surrounding this devastating disease," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal.

According to the U.S. Centers for Disease Control and Prevention, Alzheimer's disease is the most common form of dementia among older adults, affecting as many as 5 million Americans. Alzheimer's disease involves parts of the brain that control thought, memory, and language and can seriously affect a person's ability to carry out daily activities. The disease usually begins after age 60, and risk goes up with age. About 5 percent of men and women ages 65 to 74 have Alzheimer's disease, and nearly half of those aged 85 and older may have the disease.

More information: Madepalli K. Lakshmana, John Y. Chung, Supul Wickramarachchi, Eileen Tak, Elisabetta Bianchi, Edward H. Koo, and David E. Kang. A fragment of the scaffolding protein RanBP9 is increased in Alzheimer's disease brains and strongly potentiates amyloid-peptide generation, *FASEB J.* doi:10.1096/fj.09-136457

Source: Federation of American Societies for Experimental Biology (news : web)