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'Alzheimer's protein' plays role in maintaining eye health and muscle strength

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Amyloid precursor protein (APP), a key protein implicated in the development Alzheimer's disease, may play an important role in eye and muscle health. In a new report published in the June 2015 issue of *The FASEB Journal*, scientists have discovered that when proteins that bind to the APP, called FE65 and FE65L1, are deleted, they cause cataracts and muscle weakness in mice. Additionally, this study demonstrates that the expression of laminin, a protein pivotal for the interaction between lens epithelial cells and the lens capsule, is severely altered in mice lenses missing both FE65 and FE65L1 genes. If confirmed in human studies, the FE65 and FE65L1 proteins may become a therapeutic target for cataracts, muscular dystrophy and Alzheimer's disease.

"We hope the discoveries in this study would help to expand our understanding of the normal function of FE65 and APP," said Jaehong Suh, Ph.D., a researcher involved in the work from the Genetics and Aging Research Unit, MassGeneral Institute for Neurodegenerative Disease at Massachusetts General Hospital in Boston, MA. "From this kind of very basic research, we may be able to find more clues for the causes of, and ultimately to discover effective treatments for related human diseases such as cataract, congenital muscular dystrophies and Alzheimer's disease."

To make their discovery, Suh and colleagues examined and compared the eyes and muscles of four different mouse groups: one without the FE65 protein, one without FE65L1, one without both FE65 and FE65L1, and one that was normal control mice. They found that mice

lacking both FE65 and FE65L1 develop severe lens degeneration that may be an extreme manifestation of cataract and muscle weakness. Milder deficits in muscle were found in the mice with only one gene deleted, while no changes were seen in the normal mice. Interestingly, cortical cataracts were observed in old mice lacking the FE65L1 protein.

"It's rare that in any living system, one gene or one protein performs only one function," said Gerald Weissmann, M.D., Editor-in-Chief of *The FASEB Journal*. "Although this is a new find, the fact that a protein implicated in Alzheimer's disease has a function in tissues other than the brain should come as no surprise—but APP's function in the eye is unexpected!"

More information: Jaehong Suh, Juliet A. Moncaster, Lirong Wang, Imran Hafeez, Joachim Herz, Rudolph E. Tanzi, Lee E. Goldstein, and Suzanne Y. Guénette. FE65 and FE65L1 amyloid precursor protein-binding protein compound null mice display adult-onset cataract and muscle weakness. *FASEB J.* June 2015 29:2628-2639; DOI: 10.1096/fj.14-261453

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