Science Investor, Jeffrey Epstein, Backs Genetic Research Revealing a Vascular Cause for Alzheimer's

There is a well known link between Alzheimer's disease and a gene call ApoE4. In fact, people who carry two copies of the gene have approximately 8 to 10 times the risk of getting Alzheimer's than those who do not have the gene.

Up to now though, little was known about *how* ApoE4 contributed to Alzheimer's devastating deterioration of the brain. However, in a ground breaking study published in *Nature* and financed by the Alzheimer's Association and The Jeffrey Epstein VI Foundation amongst others, scientists from Rochester University and the University of Southern California have shown how ApoE4 can unleash an excess of the protein cyclophilin A into the cardiovascular system, causing inflammation in atherosclerosis and other conditions. Critically, the study also found that ApoE4 makes it more likely for cyclophilin A to accumulate in cells that help maintain the blood-brain barrier, reducing blood to the brain and allowing toxic substances to infiltrate the brain.

"We are beginning to understand much more about how ApoE4 may be contributing to Alzheimer's disease," said Dr. Robert Bell, from Rochester University and senior author of the study. "In the presence of ApoE4, increased cyclophilin A causes a breakdown of cells lining the blood vessels in the brain in the same way as found in cardiovascular disease or abdominal aneurysm. This establishes a new vascular target to fight Alzheimer's disease."

Specifically, the study found that a group of mice carrying the ApoE4 gene had five times as much cyclophilin A in their pericyte cells, cells that maintain the integrity of the blood-brain barrier. The Cyclophilin A caused an increase in the inflammatory molecule NF Kappa B which in turn increased levels of MMP molecules or matrix metalloproteinases that are known to damage blood vessels and reduce blood flow. The mice's blood vessels died, blood did not flow as completely through the brain as it did in other mice, and harmful substances like thrombin, fibrin, and hemosiderin, entered the brain tissue. When the team stopped the excess of cyclophilin A by removing the ApoE4 gene or by using cyclosporine A to inhibit it, the brain damage in the mice *was reversed*. Blood flow resumed to normal, and toxic substances from the blood vessels into the brain was reduced by 80%.

For years, amyloid beta, a protein that accumulates in the brains of Alzheimer patients was seen as the main culprit for damage. However, this recent study shows that there is also a serious vascular origin. "Our study has shown major neuronal injury resulting from vascular defects that are not related to amyloid beta," said Dr. Berislav Zlokovic, an adjunct professor at Rochester, deputy director of the Zilkha Neurogenetic Institute at USC, director of the Center for Neurodegeneration and Regeneration and professor and chair of the Department of Physiology and Biophysics. "This damage results from a

breakdown of the blood-brain barrier and a reduction in blood flow. Amyloid beta has an important role in Alzheimer's disease," added Zlokovic. "But it's very important to investigate other leads, perhaps where amyloid beta isn't as centrally involved."

“This cyclophilin A, genetic link is crucial,” Jeffrey Epstein asserts, whose organization, The Jeffrey Epstein VI Foundation, promotes cutting edge medical research around the world. “It will allow scientists to chemically inhibit vascular disease in conjunction with genetic therapy. But it will also help scientists concentrate on other protein inducing genes as possible offenders.”

The study was also funded by the National Institute of Neurological Disorders and Stroke and the National Institute on Aging.