How the APOE gene can modify your risk for Alzheimer's disease

November 13 2008

One of the hallmarks of the brain of an individual with Alzheimer disease is the accumulation of amyloid-beta peptide (A-beta), something that is believed to be toxic to many brain cells (specifically neurons) and to therefore contribute to the underlying cause of disease. Berislav Zlokovic and colleagues, at the University of Rochester Medical School, have now generated data in mice that mechanistically links a genetic risk factor for Alzheimer disease with accumulation of A-beta in the brain.

Individuals carrying one form of the APOE gene, APOE4, have a greater risk of developing Alzheimer disease than individuals with other forms of the APOE gene (APOE2 and APOE3). In the study, the proteins generated by the different forms of the APOE gene were found to differentially affect the clearance of A-beta from the brain of mice.

Specifically, A-beta binding to apoE4 led to substantially slower clearing of A-beta from the brain than A-beta binding to either apoE2 or apoE3.

The authors therefore suggest that a decreased rate of A-beta clearance from the brain might contribute to the increased risk of developing Alzheimer disease observed for individuals carrying the APOE4 form of the APOE gene.

The study is published in the current issue of the *Journal of Clinical Investigation*.

Source: Journal of Clinical Investigation