Researchers find new piece in Alzheimer's puzzle

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Yale researchers have filled in a missing gap on the molecular road map of Alzheimer's disease. In the Feb. 26 issue of the journal Nature, the Yale team reports that cellular prion proteins trigger the process by which amyloid-beta peptides block brain function in Alzheimer's patients.

"It has been a black box," said Stephen M. Strittmatter, senior author of the study and the Vincent Coates Professor of Neurology and director of Cellular Neuroscience, Neurodegeneration and Repair at the Yale School of Medicine. "We have known that amyloid-beta is bad for the brain, but we have not known exactly how amyloid-beta does bad things to neurons."

After an extensive gene expression analysis, the first step in amyloid-beta damage appears to involve cellular prion proteins. These proteins are normally harmless and exist within all cells, but on rare occasions they change shape and cause notorious prion diseases such as Creutzfeldt- Jacob disease, or its well-known variant, mad cow disease.

When the Yale team searched hundreds of thousands of candidates for potential disease-mediating receptors for the specific amyloid-beta form known to play a role in the development of Alzheimer's disease, the most likely candidate was cellular prion proteins. It seems that amyloid-beta peptides latch onto these cellular prion proteins and precipitate the damage in brain cells.
"They start the cascade that make neurons sick" said Strittmatter, a member of the Kavli Institute for Neuroscience.

Since these cellular prion proteins act at an early stage of disease development, the receptors make a promising target for new Alzheimer's therapies, Strittmatter said.

The study does not suggest that the conversion of cellular prion proteins to an infectious agent occurs in Alzheimer's disease, Strittmatter noted. However, the *Nature* paper does suggest that the role of usually harmless cellular prion proteins in common neurodegenerative diseases should be studied more rigorously, he said.

Source: Yale University


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