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Researchers clear up Alzheimer's plaques in mice

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Blocking a common immune system response cleared up plaques associated with Alzheimer's Disease and enabled treated mice to recover some lost memory, Yale University researchers report Friday in the journal *Nature Medicine*.

Researchers hope the new approach may one day overcome one of the biggest obstacles to development of new dementia medications – the difficulty in finding drugs that can safely cross the blood-brain barrier.

The results of the research surprised the scientists working in the lab of Richard Flavell, senior author of the paper, chairman of the Department of Immunobiology at Yale and investigator with the Howard Hughes Medical Institute. Flavell's team originally thought that blocking the immune system molecule TGF-â(or transforming growth factor), might actually increase the buildup of amyloid plaques associated with Alzheimer's Disease

Earlier studies had shown that Alzheimer's patients tend to have elevated amounts of TGF-â, which plays a key role in activating immune system response to injury. Some had thought the presence of the molecule was simply an attempt to quiet the inflammatory response caused by a buildup of plaque.

Instead, the team found that as much as 90 percent of the plaques were eliminated from the brains of mice genetically engineered to block TGF-â in the peripheral immune cells.

It was like a vacuum cleaner had removed the plaques," Flavell said.

When the TGF-â pathway was interrupted in mice engineered to have Alzheimer's, the mice showed an improved ability to perform some tests, including navigating mazes when compared to mice without TGF-â blocked. Scientists also found lower levels of other biological markers associated with the dementia.

When TGF-â was blocked, the immune system seemed to unleash immune cells known as peripheral macrophages. The macrophages passed through the blood-brain barrier and surrounded the neurons and plaques in the brains of mice. "If results from our study in mice engineered to develop Alzheimer's-like dementia are supported by studies in humans, we may be able to develop a drug that could be introduced into the bloodstream to cause peripheral immune cells to target the amyloid plaques," said Terrence Town, lead author of the study.

Source: Yale University