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RIKEN Brain Science Institute
The Laboratory for Proteolytic Neuroscience
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Discovery of a Substance to Decompose a Causative Substance of Alzheimer Disease

The Laboratory for Proteolytic Neuroscience (Laboratory Head: Dr. Takaomi C. Saido, BSI), RIKEN Brain Science Institute, have discovered a physiologically active substance that controls the decomposition of a causative substance of Alzheimer disease. Alzheimer disease is expressed due to the accumulation of a protein called amyloid β peptide ($A\beta$) in the brain.

A research team had previously discovered the enzyme neprilysin that degrades $A\beta$, and showed that when its activity decreased the $A\beta$ level in the brain increased. The researchers also demonstrated that $A\beta$ accumulation could be suppressed through an experimental genetic treatment.

The researchers this time sought a pharmacological method for regulating the neprilysin activity in the brain without using a surgical method such as genetic treatment. As a result, they discovered that "somatostatin," a kind of neuropeptide (physiologically active substance), increased the activity of neprilysin and decreased the level of $A\beta$. It was also found that somatostatin selectively controls the level of a highly pathogenic $A\beta$ strain ($A\beta_{42}$).

Furthermore, since somatostatin expresses physiological activity after combining with a somatostatin receptor on the surface of cells, the production of a new medicine targeting this receptor is possible. This research is expected to open the way for the elucidation of the cause of sporadic Alzheimer disease that generates a large number of patients.

The research results were published in the online version of the U.S. science journal "*Nature Medicine*" dated March 20.



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