

March 22, 2021

A World First: Mechanism of Milk-derived β -lactopeptide Demonstrated

- Yes, an ingredient in cheeses can help your brain -

TOKYO, Monday March 22, 2021 – The Kirin Central Research Institute of Kirin Holdings Company, Limited (Kirin Holdings), in a world first^{*1} has demonstrated a part of the mechanism by which a type of milk-derived β -lactopeptide^{*2} (GTWY peptide^{*3}) boosts concentration as part of joint research with Keio University. The company will announce the research results at the annual meeting of the [Japan Society for Bioscience, Biotechnology, and Agrochemistry](#), held from March 18 to 21, 2021.

*1 The world's first discovery of a whey protein-derived peptide supporting according to Kirin Holdings' research (based on publicly available information as of March 15, 2021)

*2 A general term for peptides that have the effect of improving cognitive function. These peptides contain the amino acid sequence tryptophan-tyrosine (WY) and are derived from whey protein.

*3 GTWY is a key component of β -lactopeptides and a tetrapeptide with a sequence of four amino acids called glycine-threonine-tryptophan-tyrosine.

● Background to the research

In the ultra-aging society of Japan, dementia and the cognitive decline due to aging are huge social issues. Since there is no effective medical treatment for dementia, attention is being focused on prevention through actions taken in daily life, such as by improving dietary habits. In recent years, epidemiological research on the Japanese population have found that the consumption of milk and dairy products reduces the risk of dementia and impaired cognitive function.^{*4}

In 2018, as the result of long years of collaboration in neuroscientific research with the University of Tokyo and Kyowa Kirin Co., Ltd., Kirin Holdings announced the discovery of β -lactopeptide as a milk-derived peptide contained in large amounts in fermented dairy products. These include camembert cheese, that improves cognitive function.^{*5} In 2019, Kirin Holdings also announced that a collaboration with Keio University in human trials showed that the GTWY peptide improves memory and attention.^{*6}

● Outline of the research

As part of the joint research efforts between Kirin Holdings and Keio University, a randomized, double-blind controlled trial was carried out on middle-aged to elderly healthy participants,^{*7} which verified the effect of the supplementations with GTWY peptide on human brain activity. The measurement of the brain waves of participants who consumed the GTWY peptide as they tackled an assigned cognitive task that required concentration, the amplitude in the P300 measurement points from the frontal lobes to the parietal lobes increased significantly in statistical terms compared with the placebo group. P300 is considered to be an indicator of neural activity related to concentration, and these results will lead to the elucidation of the intracerebral mechanism by which the GTWY peptide boosts concentration.

<Trial methodology>

The joint research carried out a double-blind trial of six weeks of intake by 30 healthy, middle-aged to elderly (between 45 and 65) men and women, who were randomly assigned to either a GTWY peptide group or a placebo group. The state of intracerebral neural activity was measured at week zero and week six, using a 64-channel electroencephalograph, while participants carried out cognitive function tasks.

<Trial results>

It was found that the amplitude of P300 brain waves at the measurement points in the frontal lobes, and from the frontal lobes to the parietal lobes, increased significantly in statistical terms in the GTWY peptide intake group in the sixth week of intake during a cognitive function task that required concentration, compared with the placebo group (see Figure 1).

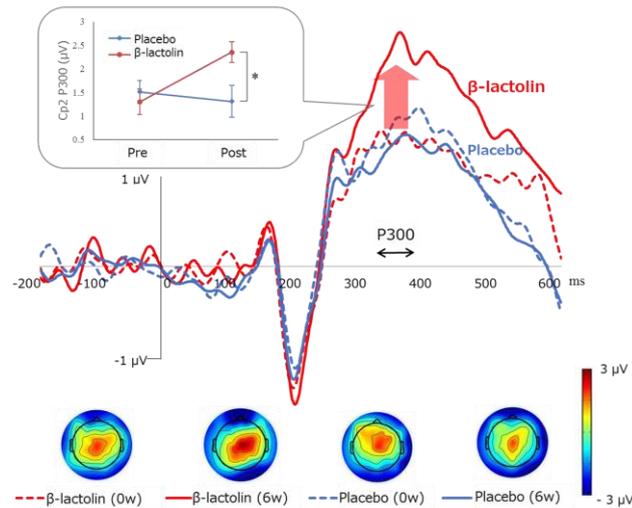


Figure 1. Result of brain wave measurement during a hearing task, before and after intervention. The change in P300 brain waves in the GTWY intake group increased significantly compared with the placebo group. Bars are mean \pm S.E. (each group N=15), $p^* < 0.05$

● **Future developments**

With the establishment of its long-term management vision, Kirin Group Vision 2027, the Kirin Group aims to become a global leader in CSV,^{*8} creating value across our world of Food & Beverages to Pharmaceuticals. To achieve that, as well as the existing businesses in the Food & Beverages domain and the Pharmaceuticals domain, based on the advanced Fermentation and Biotechnology techniques that the Kirin Group has cultivated over many years, we have established and are growing our Health Science domain business in order to improve people’s health. In the Health Science domain, we are carrying out various R&D projects with emphasis on the areas of immunity, brain function, and the intestinal environment.

Going forward, through collaboration with universities and municipalities, we will advance initiatives to create a society that supports brain health.

● **KIRIN Brain Research**

Japan’s average life expectancy has been increasing and the country has entered a super-aged society in which one in four people is elderly.^{*9} Given that an estimated one in five elderly people will suffer from dementia in 2025,^{*10} the extend of healthy life expectancy is a social issue.



Kirin Brain Research Logo

The Kirin Group understands that the joys and concerns in a daily life are intimately associated with brain activity, and thus launched KIRIN Brain Research to develop the new solutions mainly in health science to promote brain health and create joy.

KIRIN Brain Research based on Kirin’s distinct technology and ways of thinking contributes to promote brain health in an effort to help resolve social issues and will create a society conducive to psychologically prosperous living, where everyone has confidence and ambition and feels free to experience their emotions.

*4 Ozawa M, et al., Journal of the American Geriatrics Society, 2014, 62(7): 1224-1230

*5 Ano Y, Nakayama H, et al., Neurobiology of Aging, 2018, 72: 23-31

*6 Kita M, Ano Y, et al., *Frontiers in Neuroscience*, 2019, 13: 399

*7 A testing methodology used in clinical trials in which participants are randomly divided into groups to receive the placebo or the actual drug, and which group is which is unknown until the trial is completed.

*8 This stands for “Creating Shared Value,” meaning to create values that can be shared with customers and society as a whole.

*9 Cabinet Office, *White Paper on the Aging Society FY 2020*

*10 Grants-in-Aid for Scientific Research, MHLW Special Research Project, *Research on Future Trends in the Prevalence of Dementia among Elderly People in Japan, 2014, Report on General & Specialized Research, 2015*

Overview:

1. Name of presentation: Improved focusing attention due to stimulation of parietal lobe region’s neural activity by milk-derived β -lactolin
2. Name of academic: Japan Society for Bioscience, Biotechnology, and Agrochemistry, 2021 Annual Meeting
3. Date of presentation: Thursday, March 18 to Sunday, March 21, 2021
4. Presented by: Ayana Kanatome and Yasuhisa Ano from Kirin Central Research Institute, Research and Development Division, Kirin Holdings Company, Limited
Kazushi Shinagawa, Midori Shibata, and Satoshi Umeda from Psychology Laboratory, Faculty of Letters, Keio University

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