

August 2, 2019 SBI Pharmaceuticals Co., Ltd. Saitama Medical University Chiba Children's Hospital Juntendo University

A Collaboration Research Related to Development of Mitochondrial Disease Treatment by 5-Aminolevulinic Acid and Sodium Ferrous Citrate was Published

SBI Pharmaceuticals Co., Ltd., (Head office: Minato-ku, Tokyo; Representative Director, President: Yoshitaka Kitao), a subsidiary of SBI Holdings, Inc., Saitama Medical University, <u>Chiba Children's Hospital</u> and Juntendo University published a result from a collaboration study on <u>Scientific Reports</u>, of Nature Publishing Group.

Mitochondrial disease is a disease that lowers the production of ATP that is a source of energy in body. It is caused by lowering the activity of mitochondrial respiratory chain complex due to the genetic disorder. However, there was no definitive therapy exist but only symptomatic therapies were applicable for mitochondrial disease.

5-aminolevulinic acid (5-ALA) metabolizes in cells, and becomes "heme" by bonding with iron. Heme becomes a part of a mitochondrial respiratory chain complex to help ATP production. A combination of 5-ALA and iron has been expected to be used as a treatment drug for mitochondrial disease, since the acceleration of mitochondrial function was observed from the animal study.

This collaboration study used dermal fibroblast from patients diagnosed as mitochondrial disease to confirm efficacy of the combination of 5-ALA and iron (sodium ferrous citrate, SFC). It resulted in a significant increase of mitochondrial respiratory chain complex and ATP production - Which revealed that 5-ALA and SFC improve mitochondrial function on dermal fibroblast of mitochondrial disease patient for the first time in the world.

This study result suggests a possibility of definitive therapy against mitochondrial disease by "enzyme reinforcing treatment" that reinforces activity of remaining mitochondrial respiratory chain enzymes to improve mitochondrial function. Currently, an investigator-initiated phase III trial that uses 5-ALA and SFC as investigational drugs mainly targeting Leigh's Syndrome (one of the examples of mitochondrial disease) is on-going in Japan, mainly handled by this research group, and it is highly expected as a new treatment drug for mitochondrial disease in future.

† 5-aminolevulinic acid (5-ALA): An amino acid produced in mitochondria. It is an important substance that serves as a functional molecule related to energy production in the form of heme and cytochromes, and its productivity is known to decrease with age. 5-ALA is contained in food such as shochu lees, red wine and Asian ginseng. It is also known as a material forming chloroplasts in plants.

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