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SBI Holdings, Inc.

SBI Pharmaceuticals Co., Ltd.

## **Curative and Protective Effects of the Combined Treatment of 5-aminolevulinic Acid and Iron against Malaria Infection was Confirmed in Animal Model.**

SBI Pharmaceuticals Co., Ltd. (Head office: Minato-ku, Tokyo; Representative Director and CEO: Yoshitaka Kitao; “SBI Pharmaceuticals”), a subsidiary of SBI Holdings, Inc., engages in research and development of pharmaceuticals, health foods and cosmetics using 5-aminolevulinic acid (“5-ALA”) (\*1) announced in *Antimicrobial Agents and Chemotherapy* published on October 21 that the combined use of 5-ALA and sodium ferrous citrate (SFC) (\*2) had the effect to cure the mice infected with malaria parasites and protect them from re-infection. This was confirmed in the joint research with the University of Tokyo, a national university (Location: Bunkyo-ku, Tokyo; President: Makoto Gonokami; “University of Tokyo”)

While malaria is the most widespread infection in terms of the annual numbers of patients and deaths, the conventional medicines cause strong side effects. In addition, many parasites having resistance to these medicines have emerged in recent years. Although safer antimalarial drugs have been developed and are being used more extensively, drug-resistant malaria parasites have already spread. Therefore, urgent development of new malaria remedies is globally required.

In the joint research with Professor Kiyoshi Kita (Graduate School of Medicine, The University of Tokyo), SBI Pharmaceuticals clarified in *in vitro* study that the combined use of 5-ALA and SFC could induce growth inhibition of the most pathogenic malaria parasite to human. This time new findings were announced with respect to the effects caused by combination of 5-ALA and SFC on the dynamic mechanism of malaria parasites *in vivo*.

Using the mice infected with the lethal strain of rodent malaria parasite, a potential of the combined treatment was evaluated as an antimalarial drug. As a result, curative effects were observed in 60% of the mice that received combination of 5-ALA and SFC. In addition, it became clear that the cured mice showed resistance to re-infections of the same parasite for even more than 230 days after the recovery from the primary infection, acquiring long-term immunity to the malaria parasites. An increase in the antibody specific to these parasites was observed in the sera from the cured mice, attributing to the resistance.

Both 5-ALA and SFC are the compounds that are currently in use for foods and pharmaceuticals, and the safety of using them for human has been established. With fewer side effects than the existing antimalarial drugs, the combination has a high potential to become very effective and revolutionary antimalarial drug. Future

development toward the clinical application is expected.

Journal carrying the paper:

Name : Antimicrobial Agents and Chemotherapy  
Title of the paper : *In vivo* curative and protective potential of orally administrated  
5-aminolevulinic acid plus ferrous ion against malaria  
Authors : Shigeo Suzuki, Kenji Hikosaka, Emmanuel O. Balogun, Keisuke  
Komatsuya, Mamoru Niikura, Fumie Kobayashi, Kiwamu  
Takahashi, Tohru Tanaka, Motowo Nakajima, Kiyoshi Kita  
DOI number : 10.1128/AAC.01910-15.  
Abstract URL : <http://aac.asm.org/content/59/11/6960.abstract>

(\*1) 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 radish sprouts. It is also used as an ingredient of health foods, and has been approved as an intraoperative diagnostic agent for brain tumor by utilizing its specific characteristics to be metabolized to protoporphyrin IX and accumulate in cancer cells.

(\*2) Sodium ferrous citrate (SFC)

SFC is an effective compound for the treatment and prevention of anemia, and has been extensively used for pharmaceuticals and health foods for a long time.

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