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SBI Pharmaceuticals Co., Ltd.

**Tokyo Institute of Technology Announces Publication of Research Paper on  
5-ALA in an American Scientific Journal PLOS ONE**

**-5-ALA+SFC may suppress the expression of a host receptor for SARS-CoV-2-**

SBI Pharmaceuticals Co., Ltd., (Head office: Minato-ku, Tokyo; Representative Director & President: Yoshitaka Kitao), a subsidiary of SBI Holdings, Inc., engaged in the research and development of pharmaceuticals and medical devices using 5-aminolevulinic acid (5-ALA) (\*1), and Tokyo Institute of Technology (Meguro-ku, Tokyo; President: Kazuya Masu) hereby announce the publication of a research article titled “Suppression of angiotensin converting enzyme 2, a host receptor for SARS-CoV-2 infection, using 5-aminolevulinic acid *in vitro*” in an American scientific journal, PLOS ONE, on February 9, 2023 (local time).

Journal: PLOS ONE

Title : Suppression of angiotensin converting enzyme 2, a host receptor for SARS-CoV-2 infection, using 5-aminolevulinic acid *in vitro*

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Abstract: The receptor angiotensin-converting enzyme 2 (ACE2), which exists on the surface of human cells, is thought to be required for severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) infection (\*2). In this study, we found for the first time that the expression level of ACE2 in host cells was markedly decreased as a result of 5-ALA hydrochloride contacting with cultured cells. In addition, when 5-ALA hydrochloride was combined with sodium ferrous citrate (SFC), the expression level of ACE2 was further reduced and the intracellular heme level was increased. This suggests that the suppression of ACE2 expression by 5-ALA may be mediated through heme production, and we also found that inhibition of heme oxygenase-1 (HO-1), which is involved in heme degradation, also reduced ACE2 expression. Based on the above, we inferred that the combination of 5-ALA and SFC may lead to a decrease in SARS-CoV-2 infectivity via suppression of ACE2 expression.

(\*1) 5-aminolevulinic acid: 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-aminolevulinic acid is contained in food such as shochu lees, red wine and Asian ginseng. It is also known as a material forming chloroplasts in plants.

(\*2) Sungnak W, Huang N, Bécavin C, Berg M, Queen R, Litvinukova M, Talavera-López C, Maatz H, Reichart D, Sampaziotis F, Worlock KB. SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes. Nature medicine. 2020 May;26(5):681-7.

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