November 27th, 2024

SBI Pharmaceuticals Co., Ltd.

Announces Publication of a Research Paper on 5-ALA from Kumamoto University in *Cell* -5-ALA may prevent neurodegeneration in Parkinson's disease and other synucleinopathies-

SBI Pharmaceuticals Co., Ltd. (Head office: Minato-ku, Tokyo; Representative Director & President: Yoshitaka Kitao; "SBI Pharmaceuticals"), a subsidiary of SBI Holdings, Inc., engaged in research and development of medical devices and pharmaceuticals using 5-aminolevulinic acid (5-ALA) (*1) hereby announce the publication of a research article entitled "RNA G-quadruplexes form scaffolds that promote neuropathological α-synuclein aggregation" from the team, led by Professor Norifumi Shioda and Associate Professor Yasushi Yabuki at Institute of Molecular Embryology and Genetics (IMEG), Kumamoto University in an international scientific journal, *Cell*. This publication includes the joint research findings between Kumamoto University and SBI Pharmaceuticals.

Journal	*Cell*
Title	RNA G-quadruplexes form scaffolds that promote neuropathological α-synuclein aggregation
Authors	Kazuya Matsuo, Norifumi Shioda, Yasushi Yabuki et. al., Institute of Molecular Embryology and Genetics (IMEG), Kumamoto University, Japan
doi	10.1016/j.cell.2024.09.037
URL	https://doi.org/10.1016/j.cell.2024.09.037
Abstract	Synucleinopathy is a neurodegenerative disease which is caused by the harmful protein aggregates of α-synuclein (*2), such as Parkinson's Disease. However, this mechanism of α-synuclein aggregation has been unknown for a long time. The team identified for the first time that unique RNA structures called G-quadruplexes (G4s) (*3) play a central role in promoting the aggregation of α-synuclein, a protein associated with neurodegeneration. G4s assembly is the first key for neurodegenerative diseases after the increase of intracellular calcium ions. Then, α-synuclein directly binds to G4s as a scaffold to form clusters and converts its conformation into a harmful aggregate-prone state. They discovered that 5-aminolevulinic acid hydrochloride (5-ALA), a compound that metabolites bind to G4s, prevented α-synuclein aggregation and suppressed the progression of motor symptoms in the model mice of Parkinson's diseases. These results suggested that the metabolites of 5-ALA, porphyrins, bind to G4s and

	suppress the G4 assembly, thereby inhibiting α-synuclein aggregation and preventing the decline of nerve function. This innovative finding addresses that “the inhibition of G4 assembly” may prevent neurodegenerative diseases, including synucleinopathy such as Parkinson’s disease, multiple system atrophy and Lewy body dementia.

（*1）5-aminolevulinic acid is 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.

(*2) Sinucleinopathy is a general term for progressive neurodegenerative diseases, including Parkinson's disease, multiple system atrophy and Lewy body dementia. In synucleinopathy, “α-synuclein” protein aggregates within nerve cells, causing neurological disorders. However, the mechanism of α-synuclein aggregations had not yet been elucidated.

(*3) Guanine quadruplexes (G4s) are a type of higher-order structure in DNA and RNA. This structure overlaps two or more faces of four guanine tetramers (G-quartets). In this publication, G4s were reported to be formed as a scaffold for α-synuclein aggregation.

This new release is an introduction to the research publication. It does not recommend the use of unapproved drugs.

****

For further information:

SBI Pharmaceuticals Co., Ltd.

E-mail: info_ala@sbigroup.co.jp