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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 announces 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.

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| Journal | <i>Cell</i> |
| 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 | <p>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.</p> <p>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.</p> <p>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</p> |

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| | <p>suppress the G4 assembly, thereby inhibiting α-synuclein aggregation and preventing the decline of nerve function.</p> <p>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.</p> |
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(*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) Synucleinopathy 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.

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