KBRI 한국뇌연구원

Press Release

내일을 위한 정부혁신 보다 나은 정부

Identifying the efficacy of suppressing neuroinflammation in leukemia therapy

- Revealing the mechanism of glial cell activity… expected to be used for treatment of dementia

☐ Korea Brain Research Institute (KBRI, President Pann Ghill Suh) said on Nov. 5 that it **was able to discover a substance that suppresses neuroinflammation associated with Alzheimer's dementia**.

○ The findings were published in the October issue of 'Journal of Neuroinflammation', an international journal, and the authors' names and the title of the paper are as follows.

* Paper: Dasatinib regulates LPS-induced microglial and astrocytic neuroinflammatory responses by inhibiting AKT/STAT3 signaling

* Authors: Ka-Young Ryu, Hyun-ju Lee (Co-1st author, KBRI), Hanwoong Woo, Ri-Jin Kang, Kyung-Min Han, HyunHee Park, Sang Min Lee, Ju-Young Lee, Yoo Joo Jeong, Hyun-Wook Nam (co-author, KBRI), Youngpyo Nam (co-corresponding author, KBRI), Hyang-Sook Hoe (corresponding author, KBRI)

☐ There has been a steady stream of reports in the neuroscience community that confirm the fact that neuroinflammamtion is deeply associated with degenerative brain diseases such as dementia. As the excessive activation of glial cells* causes nerve damage and memory degeneration, controlling this is a major concern in the treatment of neurodegenerative diseases.

* Glial Cell: Cells that support tissues of the central nervous system. According to the form, it is divided into astrocyte and microglia.

□ A research team administered a drug(Dasatinib) to treat chronic myelogenous leukemia to an animal model of neuroinflammation for two weeks, and found that both glial cell activity and expression of pro-inflammatory cytokines* were decreased.

* Pro-inflammatory cytokine: The agent that causes neuroinflammation. It is produced primarily by activated macrophage, and is involved in increasing the inflammatory response.

□ In addition, they found that **STAT3* protein signaling, which increase of which has been observed in the blood and brain of patients with Alzheimer's disease, was inhibited in glial cells, thereby inhibiting nueroinflammation.**

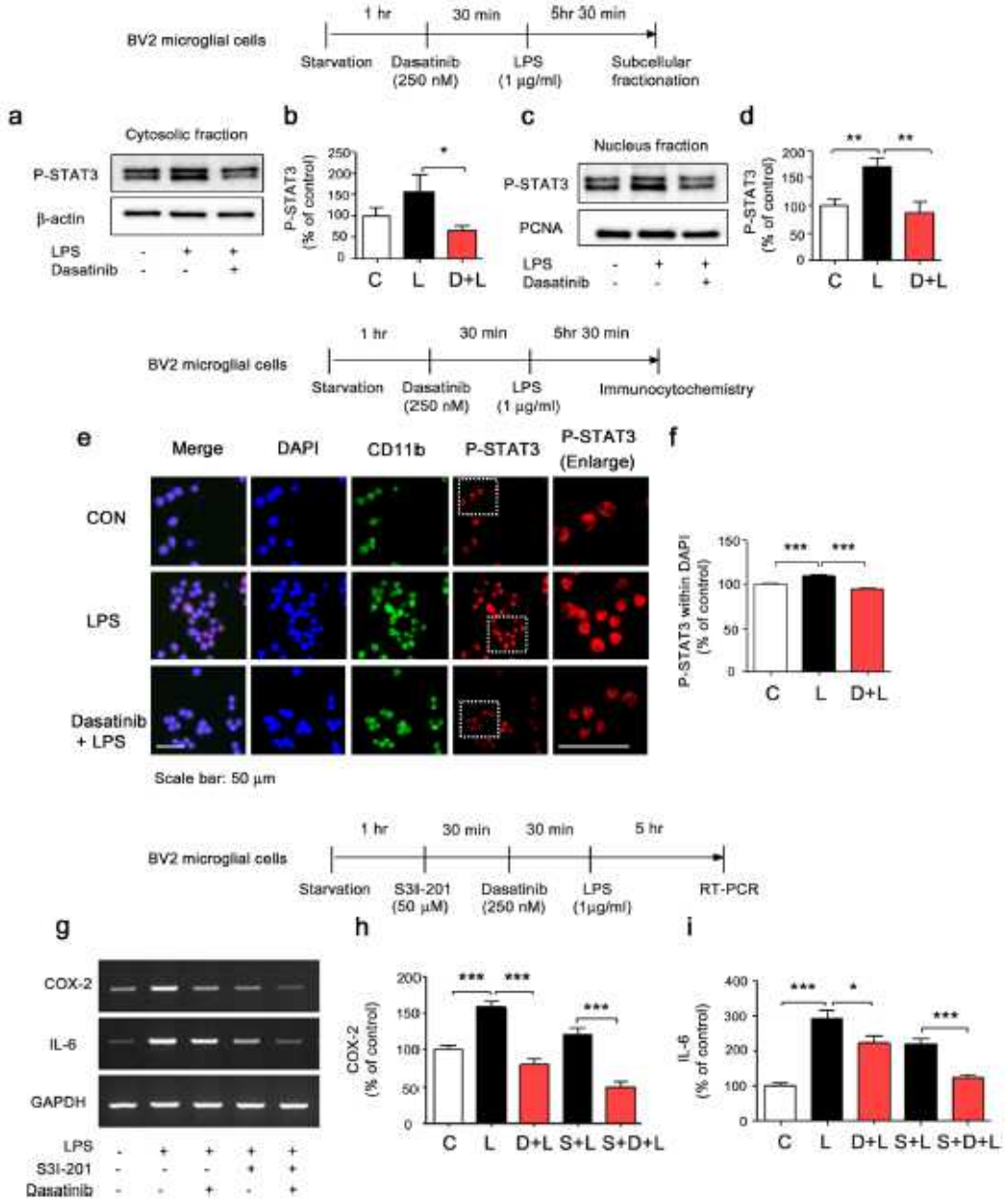
* STAT3: It is a protein that causes autoimmune diseases, and has attracted attention as a therapeutic target of various inflammations.

□ This research is meaningful in that the **KBRI has revealed the efficacy and molecular mechanism by which treatment of leukemia can be used to suppress neuroinflammation through drug repositioning* method.**

* Drug Repositioning: A method to find new efficacy by re-evaluating a drug that failed in clinical trial phase due to lack of efficacy or presence of other drugs in the market.

○ As new targets are set for existing FDA-approved drugs, the use of these drugs in the treatment of inflammatory degenerative diseases will significantly reduce the cost and clinical trial time required for development of new drug.

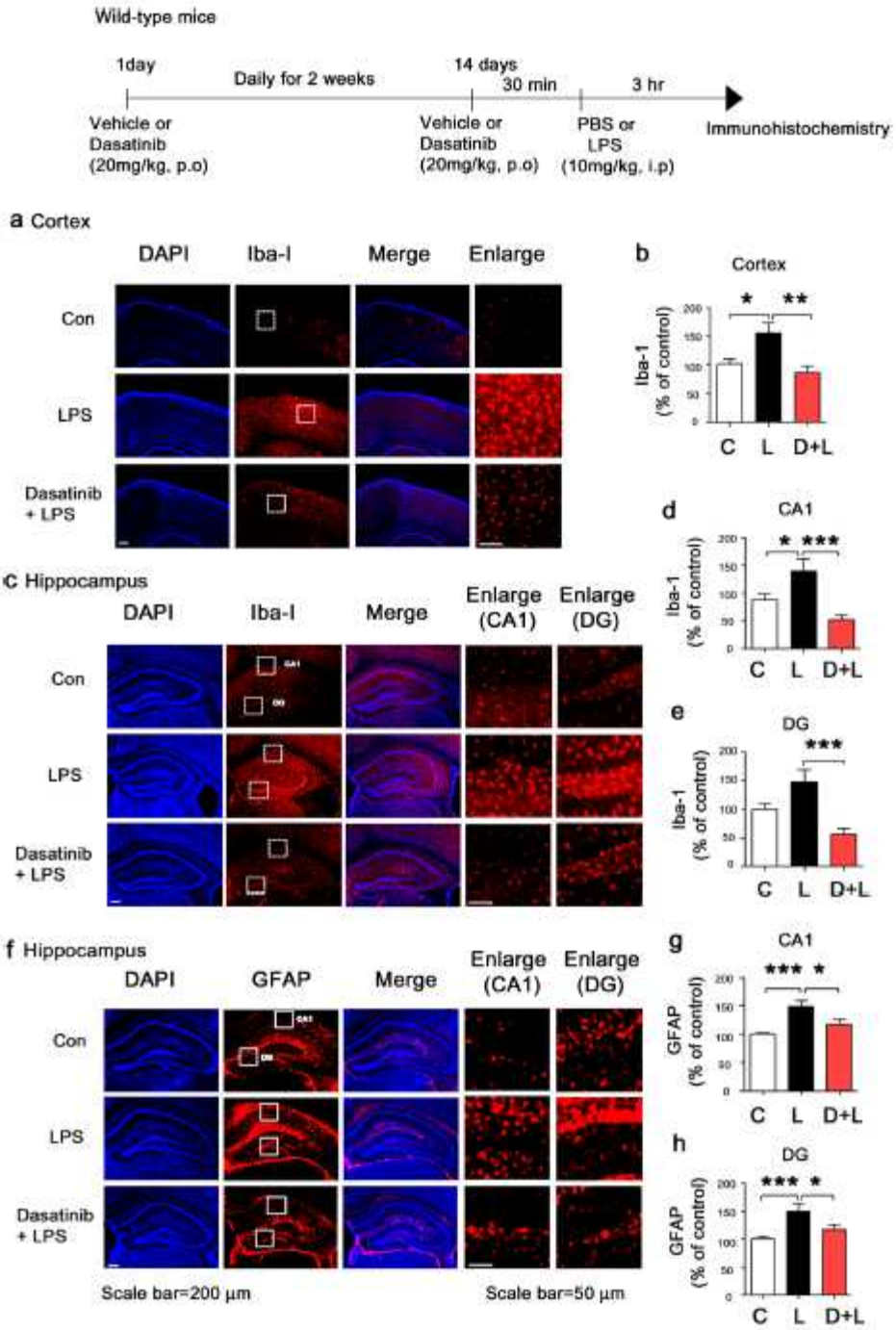
□ Dr. Hyang-Sook Hoe, a corresponding author of the paper (Head of Research HQ of HBRI) said, “in the follow-up research, we will study the possibility of Dasatinib as a multi-target medicine that can simultaneously control several pathologies of Alzheimer’s disease."



[Figure 1] Dasatinib reduces LPS-induced cytosolic and nuclear p-STAT3 levels in BV2 microglial cells.

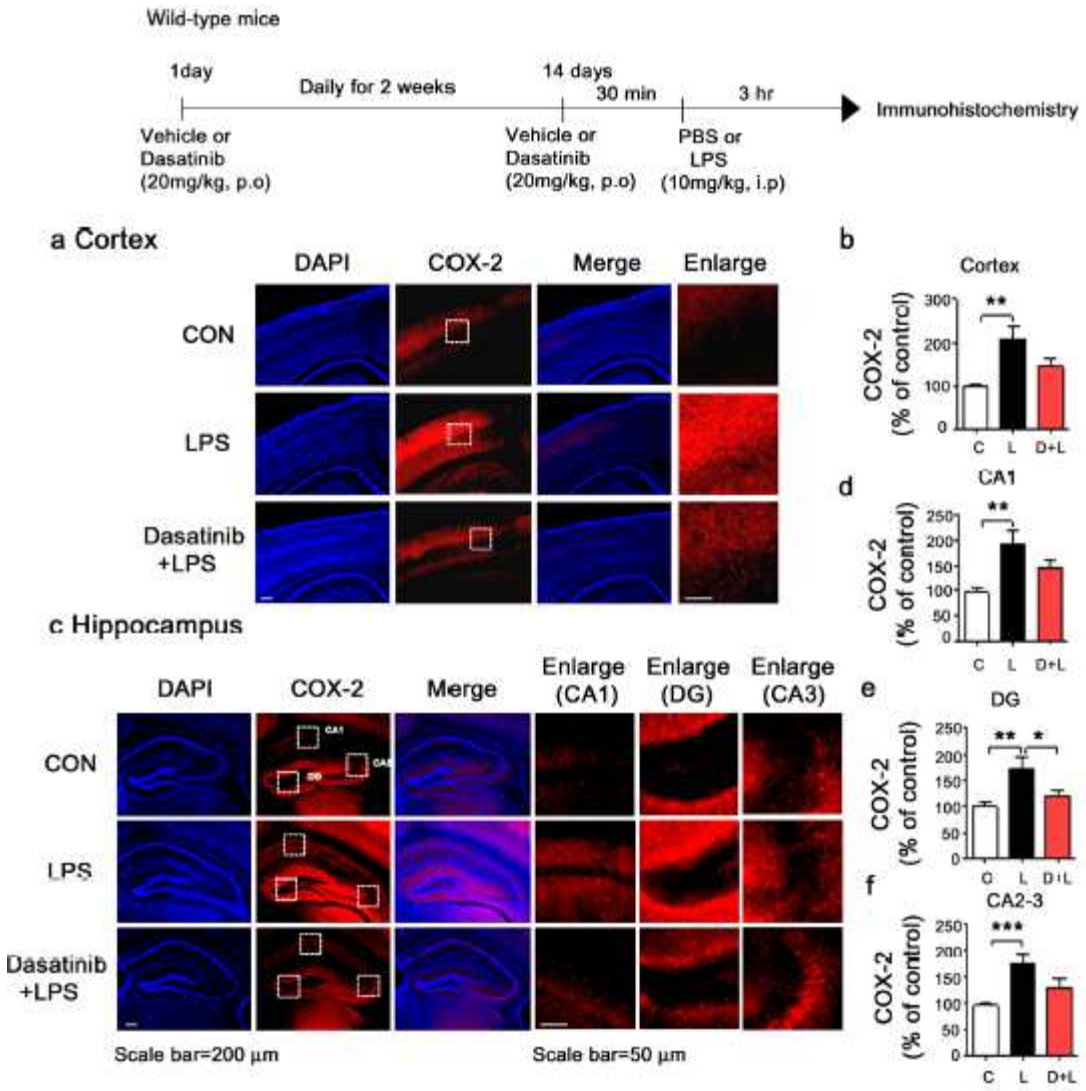
(g-i).

LPS-induced increment of pSTAT3 level was significantly reduced by tretment of Dasatinib in the BV2 microglial cells (a-f). Dasatinib inhibits LPS-induced COX-2 or IL-6 mRNA levels by partially regulating STAT3 signaling (g-i).



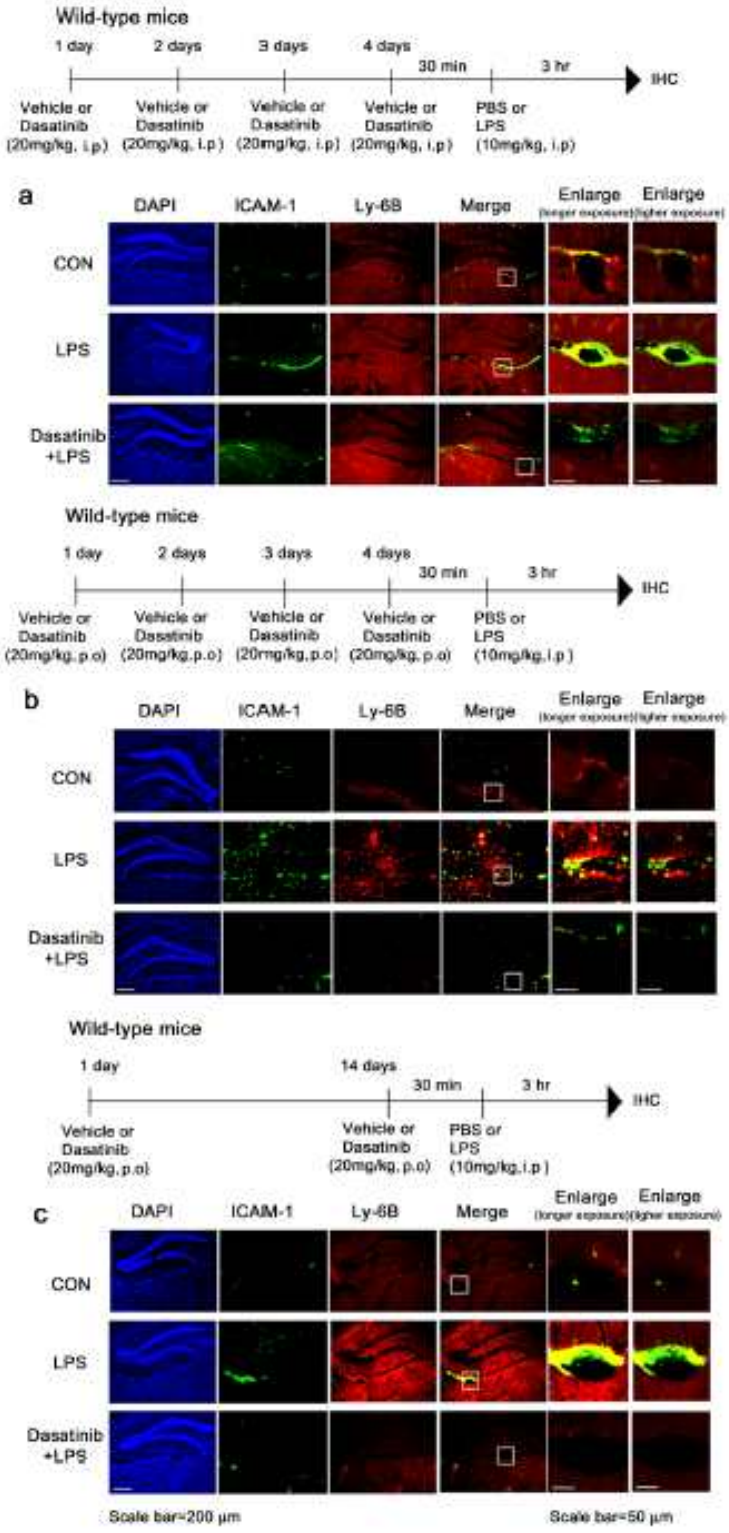
[Figure 2] Dasatinib reduces glial activation in the animal model of neuroinflammation

Oral administration of dasatinib (20 mg/kg) daily for 2 weeks significantly decreases the LPS-induced increment of microglial activation (Iba-1) and astrocytic activation (GFAP) immunoreactivities in the cortex and hippocampus of the wild-type mice.



[Figure 3] Dasatinib reduces pro-inflammatory cytokine levels in the animal model of neuroinflammation

Oral administration of dasatinib (20 mg/kg) daily for 2 weeks significantly decreases the LPS-induced increment of COX-2 expression in cortex and hippocampus of wild-type mice.



[Figure 4] Dasatinib decreases LPS-stimulated ICAM-1-interacting neutrophil rolling.

Administration of dasatinib (20 mg/kg) significantly decreases the LPS-induced increment of neutrophil rolling in the wild type mice.