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Nelonemdaz, a promising breakthrough neuroprotectant for the treatment of stroke

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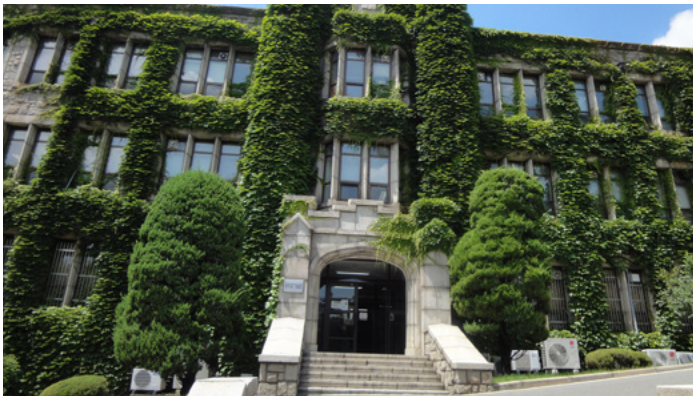
Abstract

Neuronal and glia cells undergo widespread degeneration over time following stroke attack, which results in devastating neurological deficits. Cellular and molecular mechanisms have been delineated underlying pathological brain cell death. Accumulation of extracellular glutamate can cause fulminant neuronal death through excess activation of N-methyl-D-aspartate (NMDA) receptors and subsequent calcium overload after ischemic brain injury. In addition, free radicals contribute to slowly evolving brain cell death after ischemic-reperfusion brain injury. Timely administration of NMDA antagonists and antioxidants significantly prevented brain cell death and functional deficits in preclinical studies. Unfortunately, more than 200 clinical trials of neuroprotectants including NMDA receptor antagonists and antioxidants had failed in showing beneficial effects for acute ischemic stroke patients. Such translational failure of neuroprotectants from preclinical studies to clinical trials are attributable to (1) difference between animal models and human stroke patients, (2) poor quality of preclinical studies, and (3) serious adverse events of NMDA antagonists in human. We discovered nelonemdaz from the structure of sulfasalazine that prevented both NMDA and free radical neurotoxicity. Nelonemdaz is a novel, multi-target neuroprotectant that acts as a modest NR2B-selective NMDA receptor antagonist and a potent spin trapping agent. Nelonemdaz showed promising beneficial effects in animal models of stroke and traumatic spinal cord injury. Safety of nelonemdaz has been verified through two phase I clinical trials for 165 healthy subjects in the US and China. Two phase II trials of nelonemdaz for acute ischemic stroke patients have been conducted in South Korea (SONIC trial) and China (ENIS trial). The SONIC trial is the first clinical study for acute ischemic stroke patients receiving endovascular treatment within eight hours of onset, has enrolled 203 patients, and its enrollment is expected to complete in February 2020. The ENIS trial has been successfully completed for 238 patients within 8 hours of ischemic stroke onset.

Biography

Byoung Joo Gwag received his PhD degree in Neuroscience from Drexel University School of Medicine in 1993, had trained postdoctoral training at Dr. Dennis W. Choi's lab of Washington University School of Medicine, and served as professor at Department of Pharmacology, Ajou University School of Medicine for 1995-2011. He had served as director of Research Institute for Neural Science and Technology, Center for the Study of Interventional Therapy of Stroke and Alzheimer's disease, and Anti-Alzheimer's Drug Development Research Center. He has published more than 90 papers in high impact journals including Science, Journal of Cell Biology, and Journal of Neuroscience. He founded GNT Pharma with his colleagues in 1998 and has led several drug development programs for the treatment of stroke, neurodegenerative diseases, and inflammatory diseases, with more than 70 issued patents worldwide.



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