J2326: A neurotrophic and fibrillar β-amyloid dissolution molecule for Alzheimer's disease

Ji-Wang Chern, PhD

(陳基旺)

School of Pharmacy and
Center for Innovative Therapeutics Discovery
National Taiwan University

Alzheimer's disease is a neurodegenerative disorder characterized by progressive neurite loss and fibrillarβ-amyloid deposition. However, none of the clinically approved anti-Alzheimer's agents has been reported on either these two pathological processes. Here, we show that an alkyl alcohol-substituted quinoline (J2326) created by joining an 11-carbon alkyl alcohol to 5-chloro-8-methoxyquinoline, stimulates neurite outgrowth and dissociates β -amyloid fibrils. We observed that J2326 triggered ERK-dependent neurite outgrowth and regrowth accompanied by enhanced synaptic function in vitro. In addition, J2326 attenuated β -amyloid aggregation and stimulated the dissociation of pre-existing aggregates. We also demonstrated that J2326 binds to β -amyloid fibrils. Moreover, J2326 exhibits neuroprotective function associating with its anti-oxidant and anti-caspase effects. Animal studies showed that J2326-stimulated regrowth of dystrophic neuritesare pivotal for the improvement of memory in mice with fibrillarβ-amyloid-induced lesions. J2326 has pluripotent effects on neuroprotection and neuritogenesis and stands for a novel compound for the development of anti-Alzheimer's agents.