Center for Integrated Human Brain Science,

Brain Research Institute

Prof. Hironaka Igarashi, M.D., Ph.D.

Most brain degenerative diseases are recognized as pathological protein accumulating diseases. To date, there have been no established treatments that promote clearance of pathological proteins. Enhancing clearance, and thus preventive reduction of accumulation of pathological proteins is an obvious target for new treatment development for this category of brain diseases.

AQP4 is one of the water channel proteins abundant in brain astrocytes, and controls excretion of metabolites from inside the brain parenchyma to the cerebrospinal fluid. It has been reported that a functional decline of AQP4 is one of the causes of intracerebral pathological protein accumulation diseases, such as amyloid-β in Alzheimer's disease, and tau accumulation in head trauma.

Therefore, promotion of AQP4 function can be expected to prevent/ameliorate intracerebral pathological protein accumulation.

Research interests

Applications of Aquaporin4 (AQP4) Facilitator TGN-073

We administer TGN-073, which is small molecules developed by our laboratory and proved the effect facilitating AQP4 function to Alzheimer model 5xFAD mouse against Aβ accumulation.

We are interested in assessments of the effect of AQP4 facilitator, TGN-073, for any other pathological situations.

Materials and methods for collaborations

1. Providing TGN-073.
2. Pre-clinical MRI or pathological assessment for water movement of the brain.

Links to additional info

1) Neuroreport. 2018 Jun 13;29(9):697-703 : Development of TGN-073 facilitates AQP4 https://pubmed.ncbi.nlm.nih.gov/29481527-aquaporin-4-facilitator-tgn-073-promotes-interstitial-fluid-circulation-within-the-blood-brain-barrier-17oh2o-jjvcpe-mri-study/
2) Neurol Res. 2014 Jan 8;25(1):39-43: Water influx into cerebrospinal fluid is significantly reduced in AQP4 knockout but not AQP1 knockout mice. https://pubmed.ncbi.nlm.nih.gov/24231830-water-influx-into-cerebrospinal-fluid-is-primarily-controlled-by-aquaporin-4-not-by-aquaporin-1-17o-jjvcpe-mri-study-in-knockout-mice/
3) Neurol Res. 2014 Dec;36(12):1094-8: Water influx into cerebrospinal fluid is significantly reduced in APP-PS1 mice. https://pubmed.ncbi.nlm.nih.gov/25082552-water-influx-into-cerebrospinal-fluid-is-significantly-reduced-in-senile-plaque-bearing-transgenic-mice-supporting-beta-amyloid-clearance-hypothesis-of-alzheimers-disease/
4) PLoS One. 2015 May 6;10(5):e0123708 : Human PET study proving clearance disturbance in human late onset Alzheimer's disease brain and in brain of cognitively normal seniors. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0123708