Cis P-tau is induced in clinical and preclinical brain injury and contributes to post-injury sequelae

Xiao Zhen Zhou[1,2,3], Onder Albayram[1,2,3], Asami Kondo[1,2,3], Rebekah Mannix[4], Colin Smith[5], Cheng-Yu Tsai[1,2,3] and Chenyu Li[1,2,3]

[1]Harvard Medical School

[2]Beth Israel Deaconess Medical Center

[3]Center for Life Science

Traumatic brain injury (TBI) is characterized by acute neurological dysfunction and associated with the development of chronic traumatic encephalopathy (CTE) and Alzheimer's disease. We previously showed that cis phosphorylated tau (cis P-tau), but not the trans form, contributes to tau pathology and functional impairment in an animal model of severe TBI. Here we found that in human samples obtained post TBI due to a variety of causes, cis P-tau is induced in cortical axons and cerebrospinal uid and positively correlates with axonal injury and clinical outcome. Using mouse models of severe or repetitive TBI, we showed that cis P-tau elimination with a speci c neutralizing antibody administered immediately or at delayed time points a er injury, attenuates the development of neuropathology and brain dysfunction during acute and chronic phases including CTE-like pathology and dysf-23.9 (y a)8.9 (n)4 (d b)129 (o)7 (log)-23.9 (y a)8.9 (n)4 (d(e(o)12 (f s Ted 8n co(e0 (t)5)8.9 (n)4 (dr9 (t)-5.9 (h)3.9osi)12 gogy ausc4 (en)19(os)3 (a)18 ;5 shraunaxotunctid c3y and cysf(n)19s(r r)13; shfunaxotute a c3edlay and cdysf-23.9 (n)19s(r r)13; th(uid a) or

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