BACE1 cleavage mediates neurite morphology induced by sodium channel β4 subunit

Haruko Miyazaki[1, 2], Fumitaka Oyama[1], Hong Kit Wong[1], Kumi Kaneko[1], Takashi Sakurai[1] Akira Tamaoka[2], and Nobuyuki Nukina[1]

[1]Laboratory for Structural Neuropathology, RIKEN BSI, Wako, Saitama, Japan; [2]Department of Neurology, University of Tsukuba, Tsukuba, Ibaraki, Japan

β-cleavage of amyloid precursor protein (APP) by β-site APP cleaving enzyme-1 (BACE1) is crucial for pathogenesis of Alzheimer disease (AD). Recently, we identified sodium channel β4 (β4) that is significantly downregulated in the striatum of HD model mice and patients and found that β4 is a substrate for BACE1. β4 is a member of the IgCAM superfamily and serves as an auxiliary subunit of the voltage-gated sodium channel. To examine the functional roles of β4 processing, Neuro2a cells were transfected with β4 and BACE1. Overexpression of β4 caused neurite extension and increased number of filopodia-like protrusions. Coexpression of β4 and BACE1 extended neurite and decreased number of filopodia-like protrusions compared with β4 expressing cells. These results suggest that BACE1 cleavage regulates β4-mediated neurite outgrowth activity. Our findings may provide new insights into the underlying pathology of HD as well as AD.