Dysregulation of β4 gene transcription in the striatum of Huntington Disease transgenic mice

ハンチントン病モデルマウスにおけるナトリウムチャネルβ4 サブユニットの発現抑制

小山文隆[1)]、宮崎晴子[1)2)]、黒沢大[1)]、玉岡晃[2)]、金子武嗣[3)]、貫名信行[1)]

[1)]独立行政法人理化学研究所脳科学総合研究センター構造神経病理研究チーム
[2)]筑波大学大学院医学系研究科神経内科学
[3)]京都大学大学院医学研究科高次脳形態学研究領域

Dysregulation of β4 gene transcription in the striatum of Huntington Disease transgenic mice

Fumitaka Oyama[1], Haruko Miyazaki[1, 2], M. Kurosawa[1], Akira Tamaoka[2], Takeshi Kaneko[3] and Nobuyuki Nukina[1]

[1]Laboratory for Structural Neuropathology, RIKEN BSI, Saitama, Japan.

[2]Department of Neurology, University of Tsukuba, Tsukuba, Ibaraki, Japan

[3]Department of Morphological Brain Science, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Sodium channel β4 (β4) is a recently identified auxiliary subunit of the voltage gated-sodium channels. We found that β4 is significantly downregulated in the striatum of Huntington Disease (HD) model mice and patients. *In situ* hybridization with β4 probe, followed by immunohistochemistry using anti preproenkephalin (PPE) or anti preprotachykinin A (PPTA) indicated that β4 mRNA is expressed in two groups of striatal neurons projecting to globus pallidus (GP)(marker protein: PPE) and substantia nigra (SN)(marker: PPTA). TaqMan RT-PCR analysis indicated that both β4 and PPE mRNAs are preferentially decreased in striatum at a presymptomatic stage of HD mice, while PPTA mRNA and its peptide are unaltered even at the symptomatic stage. These results indicate that there is a difference in downregulation of mRNA and its product among striatal projection neuron proteins and suggest that loss of β4 in the striatum of HD transgenic mice is due to dysregulation of β4 gene transcription.