L-Glutamate acts as intracellular transmitter in the central nervous system and some peripheral tissues. L-glutamate is stored in secretory vesicles and then secreted from the cells through exocytosis. VGLUT is a transporter responsible for vesicular storage of L-glutamate. However, very little is known about the molecular nature of the VGLUT moiety. In this study, membrane topology of VGLUT2 and functional role of carboxyl terminal were investigated. Results revealed new topology model with carboxyl-terminal region facing to cytoplasm. To assess the role(s) of carboxyl terminal, mutations were introduced and the effect of mutations on the expression and localization of VGLUT2 was examined. Localization and expression were analyzed. In addition to localization, glutamate uptake activity of these mutants were analyzed. Results indicated that C-terminal region is important for localization but not for transport activity.
論文審査結果の要旨

Vesicular glutamate transporter (VGLUT) はグルタミン酸の能動輸送体でありグルタミン酸の化学伝達に本質的に重要である。しかしながらその重要性にもかかわらず、その構造と機能は不明である。我々はVGLUTのトポロジーとターゲッティングにかかわるアミノ酸残基を生化学的手段を用いて研究した。そしてトポロジーを決定し、特にカルボキシル末端部分はシナプス胞とのターゲットティングに必要な事を証明した。一連の発見はVGLUT研究を大いに進歩させた。Ph.D.論文としてまことにふさわしいものである。