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学 位 論 文 の 内 容 の 要 旨

Dissertation Abstract

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(学位論文のタイトル) Title

Comparative study of neuron-specific promoters in mouse cerebral cortex
transduced by intravenously administered AAV-PHP.eB

(AAV-PHP.eB の静脈投与によるマウス大脳皮質における複数のニューロン特異
的プロモーターの比較研究)

(学位論文の要旨) 2,000 字程度、A4 判

Adeno-associated virus (AAV)- PHP.B (PHP.B) and AAV-PHP.eB (PHP.eB), capsid variants of AAV serotype 9, efficiently penetrate the mouse blood-brain barrier and predominantly infect neurons. Thus, PHP.B / PHP.eB capsid and a neuron-specific promoter is a reasonable combination for effective neuronal transduction. However, the transduction characteristics of intravenously administered PHP.B / PHP.eB carrying different neuron-specific promoters have not been studied systematically. Herein, using an intravenous infusion of PHP.eB in mice, a comparative study of the ubiquitous CBh and three neuron-specific promoters, the Ca²⁺/calmodulin-dependent kinase subunit α (CaMKII) promoter, neuron-specific enolase (NSE) promoter, and synapsin I with a minimal CMV sequence (Syn I-minCMV) promoter was performed. Three neuron-specific promoters' expression levels of a transgene were almost comparable to or higher than those by the CBh promoter. Among the promoters examined, the NSE promoter caused the highest transgene expression. All neuron-specific promoters transduced neurons exclusively. The CaMKII promoter, which is generally believed to work exclusively in excitatory neurons, transduced both excitatory and inhibitory neurons without bias. In contrast, the NSE and SynI-minCMV promoters transduced neurons with a significant predominance of inhibitory neurons. These results are useful in neuron-targeted broad transgene expression through the systemic infusion of blood-brain-barrier-penetrating AAV vectors carrying the neuron-specific promoter.