

論 文 要 旨

PCP4/PEP19 downregulates neurite outgrowth via transcriptional regulation of
Ascl1 and NeuroD1 expression in human neuroblastoma M17 cells

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Abstract

Purkinje cell protein 4/peptide 19 (PCP4/PEP19) is 7.6 kDa peptide originally found in Purkinje cells. PCP4/PEP19 is a differentiation maker of Purkinje cells, where it functions as an antiapoptotic factor. Cerebral neuronal cells also express PCP4/PEP19, which may be related to neuronal cell survival. However, evidence suggests that PCP4/PEP19 may also be involved in neuronal differentiation. Here, we investigated the effects of PCP4/PEP19 expression on neuronal differentiation by analyzing neurite outgrowth, and expression of neuronal differentiation markers in cultured human neuroblastoma M17 cells. When PCP4/PEP19 expression was reduced by siRNA-mediated knockdown, neurite outgrowth was significantly increased. Among many differentiation markers tested, expression of NeuroD1 was increased, while that of Ascl1 was decreased upon PCP4/PEP19 knockdown. Furthermore, luciferase reporter assays revealed that PCP4/PEP19 knockdown upregulated NeuroD1 and downregulated Ascl1 expression, at the transcriptional level. These results suggest a new function of PCP4/PEP19, which suppresses neurite outgrowth and neuronal differentiation through the regulation of NeuroD1 and Ascl1 expression in M17 cells. Furthermore, immunohistochemical studies showed that PCP4/PEP19 localizes in the nuclei of human neuroblastoma cells. Therefore, PCP4/PEP19 may also be an intranuclear negative regulator of neuronal differentiation and may thus be a potential therapeutic target to promote cellular differentiation in human neuroblastoma.