脳下垂体アデニル酸シクラーゼ活性化ポリペプチドによる ラット知覚神経細胞株 ND7/23 での プロテインキナーゼ A 依存的サブスタンス P 発現誘導

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Protein kinase A-dependent substance P expression by pituitary adenylate cyclase-activating polypeptide in rat sensory neuronal cell line ND7/23 cells

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ABSTRACT: The neurotrophic effects of pituitary adenylate cyclase-activating polypeptide (PACAP) on the rat sensory neuronal cell line ND7/23 cells were investigated. PACAP caused a concentration-dependent increase in the number of neurite-bearing cells and the expression of the substance P precursor (PPT) mRNA during 24 hours. The effects of PACAP were mimicked by vasoactive intestinal polypeptide (VIP) with lower potency and dibutyryl-cyclic AMP (dbcAMP), and inhibited by inhibitors of protein kinase A, ERK kinase or p38 kinase, KT5720, U0126 or SB203580, respectively. In a PPT promoter luciferase reporter assay, the increase of PPT mRNA was the result of an increase in PPT gene transcriptional activity by PACAP. The increasing effects of PACAP on PPT mRNA were similarly observed in primary cultured rat dorsal root ganglion (DRG) cells. Thus, PACAP could induce differentiation-like phenomena in sensory neurons in a cAMP-, protein kinase A-, ERK kinase- and p38 kinase-dependent manner. These results provide evidence of the neurotrophic action of PACAP, which may function to rescue damaged neurons or to switch the neuronal phenotype in injured or inflamed sensory neurons.

抄録　一次知覚神経において、脳下垂体アデニル酸シクラーゼ活性化ポリペプチド (PACAP) は、神経突起伸長を促進し、神経伝達物質サブスタンス P の mRNA 転写活性を増加させた。この作用は、血管作用性小腸ペプチド (VIP) およびジブチリル cAMP によっても同様に発現し、各種阻害薬を用いた検討の結果、PKA、ERK および p38 MAPK に依存することが示された。

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