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Neuropeptides of the VIP family inhibit glioblastoma cell invasion through interaction with the VPAC1 receptor

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Vasoactive intestinal peptide (VIP) and pituitary-adenylate cyclase activating polypeptide (PACAP) are neuropeptides widely distributed in both central and peripheral nervous systems. These neuropeptides modulate numerous functions in cancer cells including proliferation and migration of glioblastoma (GBM) cell lines. Because the highly invasive nature of GBM is a major therapeutic problem in these tumors, we evaluated here the involvement of VIP and PACAP and their receptors (referred as the VIP-receptor system) on cell invasion in two cell lines, M059K and M059J, derived from a same human GBM. In Matrigel invasion assays, M059K cells that express more the VIP-receptor system than M059J cells were less invasive. In both cell lines, VIP decreased cell invasion. To optimize the effects of VIP on the M059J cells which express a low level of the VPAC1 receptor compared to M059K cells, this VIP/PACAP receptor was overexpressed in the M059J cells. This overexpression led to morphological changes associated with a decrease in cell invasion compared to control transfected cells. This decrease was more important in the presence of VIP. Addition of the antagonist VIP_{10-28} or a polyclonal anti-PACAP antibody to the culture medium of M059K cells showed that endogenous neuropeptides of the VIP-receptor system reduced the invasive capacity of these cells. These results indicate that the more the VPAC1 receptor is expressed and activated by endogenous or exogenous agonists in these human GBM cells, the less these cells are able to invade *in vitro*.