

PACAP and VIP counteract glioblastoma cells invasiveness

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Glioblastoma multiforme (GBM) is an aggressive brain tumor characterized by hypoxic areas. The low oxygen supply induces expression of hypoxia-inducible factors (HIFs) leading to overexpression of epidermal growth factor receptor (EGFR) [1]. It is well known that pituitary adenylate cyclase-activating polypeptide (PACAP) and vasoactive intestinal peptide (VIP) are involved in human tumors, however, their role on GBM invasiveness has not been well elucidated [2]. To this end, we have investigated, for the first time, the anti-invasive effect of PACAP or VIP on GBM cells following exposure to hypoxia, by using desferrioxamine mesylate salt (DFX), an hypoxia-mimetic agent. The results have shown that under low oxygen tension, both PACAP and VIP reduce cells migration by modulating HIFs and EGFR expression. This effect is mediated through the inhibition of phosphoinositide 3 kinase (PI3K)/Akt and mammalian mitogen activated protein kinase/Erk kinase (MAPK/ERK) signaling cascades, which, as previously demonstrated, interfere with HIF-1 α and HIF-2 α expression. In conclusion, our data suggest that PACAP and VIP might be good candidates to modulate GBM invasiveness exacerbated by hypoxic microenvironment.

This work was supported by grants from MIUR FIRB 2010 and MIUR PRIN-2009.

References

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Keywords

PACAP; VIP; glioblastoma multiforme invasiveness; hypoxia; HIFs; EGFR.