



Dysregulation of ERV genes in human pituitary adenoma and glioblastoma multiforme: Possible functional role in giant-cell glioblastoma

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Hormone producing cells of the adenohypophysis (AH) represent the origin of the diverse group of pituitary adenomas (PA). Dysregulation of hypothalamic hormone receptors, growth factors and cAMP signaling have been implicated in the molecular etiology of PA. Glioblastoma multiforme (GBM) are the most common primary brain tumors and very heterogeneous, with glioma (WHO grade IV) being the most malignant grade. The giant cell GBM is rare and characterized by multinucleated giant cells.

The expression of Syncytin-1 protein was analyzed in normal AH (n=15) and compared to five PA subtypes (n=117) as well as of GBM (n=13), giant cell GBM (n=5) and normal cortex (n=3) by immunohistochemistry. Absolute gene expression of 20 ERV functional envelope genes and ERVW-5 gag was also measured. Primary human PA cells were isolated and treated with different hormones.

Syncytin-1 protein co-localized with corticotropic cells of the AH. In contrast, all PA demonstrated significant Syncytin-1 protein overexpression, supporting deregulation. All other ERV functional genes showed significant up-regulations in different PA subtypes. Cultivation of primary PA cells with ACTH or CRH resulted in induction of the respective receptors and ERV genes. Syncytin-1 protein co-localized mostly homogeneously with GBM, however accumulated signals in the multinucleated cells of the giant cell GBM were found. Gene expression of the different ERV genes showed high stimulation for Syncytin-1, Syncytin-2, envK and env-Fc2 in GBM compared to control cortex. On the other side, giant cell GBM showed even higher inductions of Syncytin-1, Syncytin-2, env-3, ERVW-5 gag and esp. envK. We are currently investigating the role of Syncytin-1 and p53 in giant cell GBM and its correlation with cell fusion and endomitosis using cell lines.

ERV genes play an essential role in PA and GBM, where Syncytin-1 could be one main factor contributing to the multinucleated cells in giant cell GBM.