

GLP-1 AND GLP-1 RECEPTOR CO-LOCALIZATION IN HUMAN GLIOMAS AND CONTROL BRAIN SAMPLES

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Background and aims. Gliomas are the most common primary brain tumours, and glioblastoma (GBM) still has a poor prognosis. Glucagon-like peptide-1 (GLP-1) is an incretin hormone that also acts as a neuropeptide; its receptor (GLP-1R) is expressed in the normal human brain (hypothalamus, brainstem, hippocampus, meninges, neurohypophysis) and is overexpressed in several tumours, including neural and embryonic neoplasms. GLP1R expression is also associated with prognosis in many cancer types, and GLP-1R agonists are increasingly prescribed for type 2 diabetes and obesity. This work aimed to evaluate the expression and co-localization of GLP-1 and GLP-1R in human glioma and control brain samples.

Methods. Samples of glioblastoma (GB, IDH-wildtype, grade: G4), gliosarcoma (GS, IDH-wildtype, G4, GB with sarcomatoid areas), oligodendroglioma IDH-mutant 1p/19q codeleted (ODG, G3) and control tissue were analysed by double immunohistochemistry for GLP-1 and GLP-1R (20x magnification). The positive pixel count and the percentage of $GLP1^{+}/GLP1R^{+}$ co-localizing cells were quantified. Preliminary group comparison comprises: 2 patients GS-affected, 9 GB, 3 ODG, 2 inflammatory controls (INFL). Non-tumoral, non-inflammatory brain samples from largely resected tumoral brain tissue were used as an additional control group (EXTRATUM). Ordinary one-way ANOVA with Tukey's multiple comparison test (GraphPad Prism) were performed; data are mean ± standard deviation.

Results. GLP-1 expression was low and comparable in gliomas and EXTRATUM, whereas it was higher in INFL ($p \leq 0.0001$). GLP-1R expression was higher in EXTRATUM and GB/ODG tumour tissues ($p \leq 0.0001$). The percentage of co-localization was higher in the INFL (15.6±0.7%) and EXTRATUM (9.9±1.2%) controls than in GB/GS samples (5.44±0.6/6.42±0.39) ($p \leq 0.0001$).

Conclusions. GLP-1/GLP-1R co-localization is detectable in glioma tissue and shows a group-dependent pattern, being higher in ODG than in GS and GB samples, and highest in the INFL control. These preliminary findings suggest that GLP-1 signalling is modulated in the glioma microenvironment and support GLP-1R as a candidate molecular target and prognostic biomarker, with potential relevance for the growing population of patients treated with GLP-1R agonists.