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Development of new antibodies against glioblastoma (Rome Technopole, FP7)

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Glioblastoma (GBM) is the most diffuse and aggressive neoplasm of the nervous system. It is characterized by aggressive growth and high rates of recurrence. Despite the advancements in conventional therapies, the prognosis for GBM patients remains poor. ErbB receptor tyrosine kinases are involved in several cellular processes, such as proliferation, differentiation, cell survival, migration, and invasion. Among them, ErbB3 is overexpressed in GBM tissue and, after binding with its specific ligand, Neuregulin-1 (NRG1), phosphatidylinositol 3-kinase (PI3K)/AKT pathway is activated, contributing to the motility of cancer cells and cancer metastasis [1-2]. That's why a promising new GBM therapeutic approach has considered ErbB3 as a target. In fact, recent studies show how the use of anti-ErbB3 monoclonal antibodies can have positive effects in fighting tumors [3]. There is a consideration to be made regarding the complicated physiological characteristics of intracranial tumors. These include the presence of the blood-brain barrier (BBB), which leads to insufficient penetration of therapies. For these reasons the aim of this project is to evaluate the effective BBB crossing of new anti-ErbB3 monoclonal antibodies, using different approaches. First, we use an *in vitro* model of the BBB composed of murine bEnd.3 endothelial cells and primary murine astrocytes. This co-culture system creates a barrier that reaches a trans-endothelial electrical resistance (TEER) measured in the absence or presence of murine GBM cells GL261. For *in vivo* experiments we will test the best administration route of new anti-ErbB3 monoclonal antibodies to reach the brain in GBM-bearing, by labeling and visualizing anti-ErbB3 and by evaluating its efficacy on tumor volume and mice survival.

References

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