

## **In Vitro Exploration of Proton-Based Therapies for the Treatment of Glioblastoma Multiforme**

Glioblastoma multiforme (GBM) is an aggressive brain tumor with an average survival of 15 months due to tumor recurrence or invasion. It accounts for roughly 50% of primary brain tumors. The World Health Organization (WHO) classifies Glioblastoma as a tumor of the Central Nervous System (CNS) of grade 4, the most malignant in the classification scale.

Currently, the standard treatment for patients diagnosed with GBM is surgical removal of the tumor mass, followed by radio and chemotherapy. However, this standard of care is not able to cope with the insidious nature of this tumor.

In this context, this PhD project aims to explore and optimize advanced proton-based therapies that could improve patient outcomes. The study focuses on three main modalities: conventional proton therapy (PT), proton dynamic therapy (ProDT), and proton boron capture therapy (PBCT), with a comparison to photon dynamic therapy (PDT). These approaches leverage the physical advantages of protons for better tumor targeting and normal tissue sparing. In ProDT, protons activate photosensitizers to induce tumor cell death, while PBCT utilizes boron-containing compounds to trigger high-LET alpha particle emissions within tumors, enhancing biological effectiveness.

The project will initially involve in vitro experiments on GBM cell lines to identify optimal irradiation conditions and promising photosensitizers. A potential second phase may include in vivo validation, depending on preliminary results. Ultimately, this research aims to contribute to the development of more effective and less toxic GBM treatments, potentially improving survival rates and patient quality of life.

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