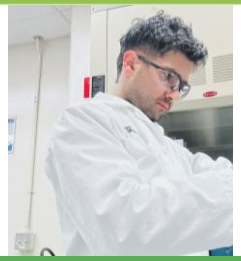
Séminaire

Département des sciences de l'imagerie médicale et des radiations

Enhanced Selectivity and Potency of 64Cu-NOTA-TP-c(RGDfK) for Targeted Glioblastoma Therapy



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Glioblastoma multiforme (GBM) remains one of the most aggressive and treatment-resistant brain tumors, with poor prognosis and limited therapeutic options. Integrin αvβ3, a cell surface receptor overexpressed in GBM, specifically binds to the arginine–glycine–aspartate (RGD) motif, making it a valuable target for tumor-specific delivery. In this study, we evaluated a novel radiotheranostic agent, 64Cu-NOTA-TP-c(RGDfK), designed to combine the diagnostic and therapeutic properties of copper-64 (64Cu), a terpyridine-platinum (TP) complex for enhanced cytotoxicity, and the integrin-targeting peptide c(RGDfK). The agent was compared to 64Cu-NOTA-c(RGDfK), 64Cu-NOTA-TP, natCu-NOTA-TP-c(RGDfK), cisplatin, and temozolomide in U87 MG GBM and SVG p12 astrocyte cell lines. Radiolabeling of NOTA-TP-c(RGDfK) was achieved with >99% purity, and competition assays confirmed high binding affinity to integrin αvβ3 (IC_{50} = 16 ± 8 nM). Cellular uptake, internalization, and retention studies demonstrated significantly higher accumulation of 64Cu-NOTA-TP-c(RGDfK) in U87 MG cells compared to control compounds, with 38.8 ± 1.8% uptake and 28.0 ± 1.0% internalization at 24 h. Nuclear localization (6.0 ± 0.5%) and stable intracellular retention further support its therapeutic potential via localized DNA damage. Importantly, 64Cu-NOTA-TP-c(RGDfK) exhibited the highest cytotoxicity in U87 MG cells (IC_{50} = 10 ± 2 nM at 48 h), while maintaining minimal toxicity in normal SVG p12 astrocytes. These results highlight 64Cu-NOTA-TP-c(RGDfK) as a promising targeted radiotheranostic agent for GBM, warranting further preclinical development.