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BOOK OF ABSTRACTS

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Cationic Pt(II) complex based on 8-aminoquinoline: *in vitro* activity against human glioblastoma.

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Cancer is undoubtedly one of the most diffuse and challenging arrays of diseases in the modern era, accounting for millions of deaths per year. Glioblastoma multiforme (GBM), in particular, is a highly malignant and aggressive primary brain tumor. Despite of an arsenal of therapeutic interventions, the prognosis of glioblastoma remains very poor. Cisplatin (CisPt) based therapy is one of the most important chemotherapy treatments for GBM and it is repurposed as the second line against GBM, albeit its efficacy is limited by drug resistance and undesirable side effects. 8-aminoquinoline (8-AQ) and its derivatives are heterocyclic compounds that are drawing attention as ligands in the field of bioorganometallic chemistry due to their metal-binding ability along with a variety of biological effects making them as a privileged framework for the preparation of new metallodrug candidates. Our research group have recently reported a series of cationic triamine platinum complexes in which the addition of an alkylated imidazole ligand to the dichloro neutral precursor led to charged platinum complexes eliciting a novel cytotoxic profile involving mechanisms of action not related to a simple DNA crosslinking as established for CisPt. Among the synthetized complexes, Pt-8AQ was tested on three glioblastoma cell lines showing higher antiproliferative activity than the clinically approved CisPt (U87-MG IC_{50} = 3.68 ± 0.69 μM; U373-MG IC_{50} = 11.53 ± 0.16 μM; U138-MG IC_{50} = 8.05 ± 0.23 μM for Pt-8AQ *vs* U87-MG IC_{50} = 7.27 + 1.80 μM; U373-MG IC_{50} = 22.69 ± 0.05 μM; U138-MG IC_{50} = 32.1 ±4.44 μM for CisPt). Moreover, an NMR investigation of Pt-8AQ interaction with 9-EtG, GSH, and Mets7 supported by cell cycle analysis might exclude DNA as the main target, suggesting a novel mechanism of action. Its high stability in solution, indeed, paves the way for an advanced cell chemotherapy strategy using MSCs to deliver the drug.

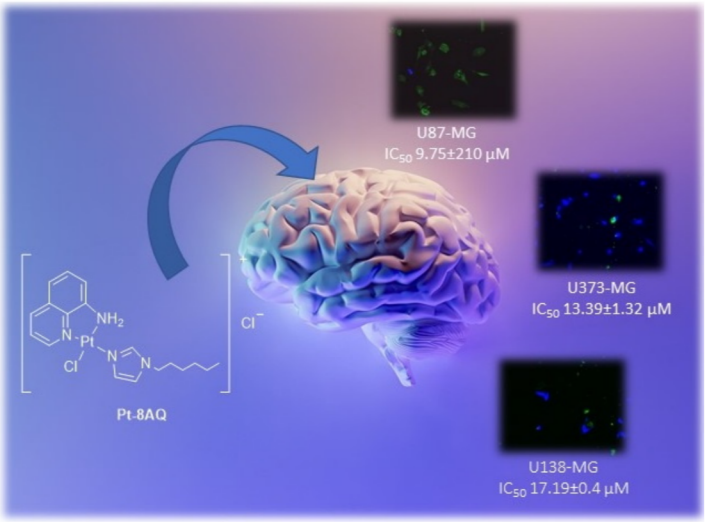

Figure 1. Pt-8AQ active on GBM.

References

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