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BOOK OF ABSTRACTS

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STEM CELL RESEARCH ITALY

31. SENSITIVITY OF HUMAN GLIOBLASTOMA TO A NEW MONOFUNCTIONAL PT-II COMPLEX BASED ON 8-AMINOQUINOLINE

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OBJECTIVE

Platinum (II) complexes play an important role in cancer treatment. We evaluated the stability and the activity of a new platinum (II)-complex (hereafter called Pt-8AQ) based on 8-aminoquinoline (8-AQ), against four human cancer cell lines. Further studies have been addressed to the human glioblastoma U87-MG, in which Pt-8AQ revealed a significant antineoplastic activity with a mechanism of cytotoxicity different from that reported for cisplatin (CisPt) used as control.

MATERIALS AND METHODS

The *in vitro* antiproliferative activity of Pt-8AQ and CisPt was tested against four tumor cell lines: glioblastoma U87-MG, pancreatic adenocarcinoma CFPAC-1, adenocarcinoma MCF-7 and bi-phasic mesothelioma MSTO-211H by an MTT assay.Their stability was assessed *in vitro* with U87-MG through cytotoxicity assay after 24 h of treatment with fresh drugs or drugs incubated for 24 h at 37°C. The ability of the Pt-8AQ to induce growth arrest was evaluated through cell-cycle analysis and Annexin-V/PI assays by flow cytometry and fluorescent microscope. Real-time PCR or colorimetric assays for specific markers regulating cell proliferation or apoptosis were checked.

RESULTS

The *in vitro* antiproliferative activity highlighted that CisPt activity is always significantly higher with the only exception for U87-MG in which Pt-8AQ showed a higher activity (IC_{50}= 3.68 ± 0.69 µM, $p<0.01$) than CisPt (IC_{50}= 7.27+1.80 µM). The stability of drugs after incubation (37°C, 24 hours) showed that Pt-8AQ still retained a significant pharmacological activity (IC_{50} 8.39 ± 0.79 µM). The effect of drugs (24 h, 10 µM) on cell cycle of U87-MG showed a decrease of the cells in G0/G1 phase and an increase of cells in S phase with CisPt, while Pt-8AQ did not significantly affect the cell cycle pattern. Finally, real-time PCR analysis showed that Pt-8AQ increased the expression of p53.

CONCLUSIONS

Our data reported that Pt-8AQ is a platinum complex endowed with a selectively higher cytotoxic activity than CisPt against U87-MG cancer cell line. The pharmacological activity of this monofunctional platinum complex is related to its ability to trigger apoptosis through a p53 dependent pathway. By considering the prominent stability of Pt-8AQ complex after 24 h incubation at 37°C and the Mesenchymal Stromal Cells (MSCs) resistance to this drug, experiments are in progress to obtain MSCs loaded with Pt-8AQ to consider for advanced cell therapy based on a selective cells' mediated drug delivery.