A NEW Ru(II) COMPLEX: DNA/HSA-BINDING, ANTI-MIGRATION AND BIOLOGICAL PROPERTIES IN A HUMAN BREAST TUMOR CELL LINE

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ABSTRACT

Breast cancer is the most common cause of cancer deaths among women worldwide. Triple-negative breast cancers (TNBC) do not express estrogen or progesterone receptors nor do they contain an amplified HER2/Neu gene and they account for about 15–20% of all breast cancers; no specific molecular targets or effective vulnerable chemotherapies have been identified so far [1]. For these reasons, new therapies to treat this dangerous disease are urgently needed [2]. A new metal complex with the formula $[RuCl(CTZ)(\eta^6\text{-}p\text{-cymene})(PPh_3)]PF_6$ (CTZ: clotrimazole and PPh_3: triphenylphosphine) was synthesized and fully characterized. This complex presented groove-binding interaction with DNA, as supported by UV-vis titration, viscosity, circular dichroism, gel electrophoresis and Hoechst 33258 displacement assay and a spontaneous static quenching mechanism with HSA protein through electrostatic interactions. The *in vitro* biological screening in prostate, lung and breast tumor cell lines showed more cytotoxic effects than free ligand CTZ and the positive controls cisplatin and doxorubicin; in TNBC MDA-MB-231 cells, the complex induces morphological changes, cell cycle arrest in the sub-G1 phase, cell death by apoptosis and inhibition of colony formation and migration. In order to investigate the metal uptake in MDA-MB-231 cells, single-cell Laser Ablation-Inductively Coupled Plasma-Mass Spectrometry (LA-ICP-MS) was applied by individual ablation of cells from a monolayer exposed to the ruthenium complex for 24 h, after fixation and dehydration. The results obtained from this study demonstrated the feasibility of the strategy to coordinate a transition metal with an organic molecule with the desirable biological property -to improve the efficacy of the latter.

Acknowledge: Brazilian foundations CAPES, CNPq, FAPESP (Grant #2017/23254-9)

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