



RESEARCH FINAL REPORT

Effect of ethaRAPTA complex on *BRCA1* defective breast cancer cells

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ABSTRACT

The ethaRAPTA or RAPTA-EA1 complex [ruthenium(II)-arene 1,3,5-triaza-7-phosphaadamantane (pta) complex with an arene-tethered ethacrynic acid ligand] has been reported to overcome drug resistance that has developed due to the current platinum-based treatments. However, the exact mechanism of action of RAPTA-EA1 remains largely unexplored. Here we have further studied the effect of RAPTA-EA1 on *BRCA1*-defective HCC1937 breast cancer cells in comparison to its effects on *BRCA1*-competent MCF-7 breast cancer cells. Differences in cytotoxicity were correlated with the differential accumulations of ruthenium and the induction of apoptosis. The ruthenium complex caused dramatically more damage to the *BRCA1* gene in the *BRCA1*-defective HCC1937 cells than to the *BRCA1*-competent MCF-7 cells. It decreased the expression of *BRCA1* mRNA in the *BRCA1*-competent cells, in contrast, it increased in the *BRCA1*-defective cells. However, the expression of the BRCA1 protein was significantly reduced in both breast cancer cells. The results presented here have demonstrated a differential cellular response for the *BRCA1*-defective and *BRCA1*-competent breast cancer cells induced by RAPTA-EA1. These findings provided an insight into the development of the ruthenium-based compound used for breast cancer treatment.