

**$^1\text{H}$  HR-MAS NMR based metabolomics of cells lines responding to treatment with the diruthenium trithiolato complex  $[(p\text{-MeC}_6\text{H}_4\text{iPr})_2\text{Ru}_2(\text{SC}_6\text{H}_4\text{-}p\text{-Bu}^t)_3]^+$  (DiRu-1)**

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The diruthenium trithiolato complex  $[(p\text{-MeC}_6\text{H}_4\text{iPr})_2\text{Ru}_2(\text{SC}_6\text{H}_4\text{-}p\text{-Bu}^t)_3]^+$  (DiRu-1) is highly toxic against human ovarian cancer cells A2780 and the corresponding cisplatin resistant variant A2780cisR in vitro with  $\text{IC}_{50}$  value of 0.03  $\mu\text{M}$  [1]. In vivo experiments showed that the survival rate of mice could be significantly prolonged using DiRu-1 compared to cisplatin, and proved presence of ruthenium in cancer cells. In vitro measurements revealed inhibition of mitochondrial respiration and decrease in glutathione levels [2], and showed that DiRu-1 causes increased levels of reactive oxygen species (ROS) in cells and induces caspase-driven apoptosis in estrogen-responsive breast adenocarcinoma (MCF-7) cells as well as necrosis, mitotic catastrophe, necrosis and autophagy [3].

In order to gain more insight into its modes of action,  $^1\text{H}$  high resolution magic angle spinning (HR-MAS) NMR spectroscopy was employed to analyze the metabolic profile of ovarian cancer cells A2780, A2780cisR, and Human embryonic kidney cells HEK-293, used as a model for healthy cells treated with 0.03  $\mu\text{M}$  and 0.015  $\mu\text{M}$  of DiRu-1, respectively, for 24 h. The data have been analyzed using a classical principal component analysis (PCA) and partial least squares discriminant analysis (PLS-DA) to evaluate the effects of the treatment by DiRu-1 on the metabolic profile and to provide a hint on metabolites or groups of metabolites correlated with the cellular response, as shown previously for a ruthenium hexacationic metallaprism [4].

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