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ORAL PRESENTATION

Oral presentations

OP 1

Development of potential anticancer agents by coordination of bioactive molecules to organometallic fragments

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Ru(II)-arene complexes are promising alternatives for the clinically applied platinum-based chemotherapeutics. One approach is the attachment of bioactive molecules to organometallic moieties, leading to compounds with potential multi-targeted character which are able to interact with different biological targets [1,2]. [1,4]-Naphthoquinones are known for its broad range of biological activities such as antibacterial, anti-inflammatory and anticancer activities and the mode of action is supposed to be related to reactive oxygen species (ROS) formation. [1,3]-Dioxoindan-2-carboxamides have shown promising topoisomerase inhibiting properties and this compound class can be easily obtained by rearrangement of the [1,4]-naphthoquinone backbone. With the aim to develop novel metallodrugs with potential multi-targeted properties, these bioactive scaffolds were coordinated to organometallic fragments. The synthesized ligands and the corresponding Ru(II), Os(II) and Rh(III) complexes were characterized by standard analytical methods and their behaviour under physiological conditions, binding affinity towards biomolecules, cytotoxicity in human cancer cell lines, ROS generating ability and further mode of action studies will be discussed.

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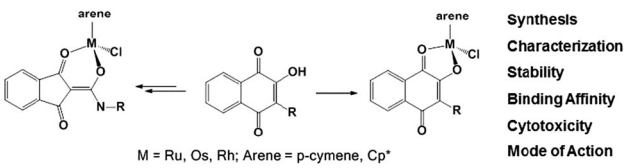

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OP 2

Effect of a hexacationic ruthenium complex as potential anticancer drug on the cell metabolome studied by ^{1}H HR-MAS NMR spectroscopy

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A water soluble hexacationic Ruthenium complex $[(p\text{-cymene})_6Ru_6(tpt)_2(dhnq)_3](CF_3SO_3)_6$ with tri-pyridyl-triazene (tpt) and dihydroxy-naphthoquinone (dhnq) as bridging ligands was prepared and tested for its anticancer activity and interaction with potential biological targets [1]. The complex was found to be highly cytotoxic against human ovarian carcinoma cells (A2780) with an IC_{50} value of 0.45 μM. To learn more about the specificity and the mechanism of action, the effect of the complex on the metabolic profile of three different human cell lines was studied by high resolution magic angle spinning (HR-MAS) NMR spectroscopy. HR-MAS NMR allows obtaining well resolved ^{1}H NMR spectra from living cell suspensions [2] well suited for chemometric analyses.

Cisplatin-sensitive and -resistant cancer cells (A2780 and A2780cisR) as well as human embryonic kidney cells (HEK-293) as healthy model cells were each incubated with the Ru-complex for 24 and 72 h, respectively. The corresponding cell suspensions were submitted to HR-MAS NMR yielding a total of 104 ^{1}H NMR spectra of control and drug treated samples. Multivariate statistical analysis (PCA and PLS) of the spectra indicated clear metabolic changes between control and drug-treated cells for all 3 cell lines, as shown in the Figure for $t_{incub} = 24$ h. The changes were most pronounced for A2780 cancer cells mainly due to lipids and choline containing compounds indicating potential drug-induced membrane breakdown. The single components responsible for the discrimination between all control and drug treated groups are discussed in more detail in this presentation.

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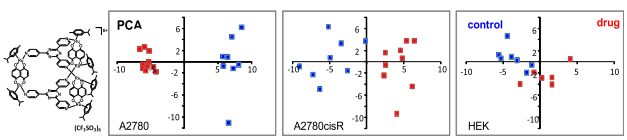

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