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Targeting cancer with selective and potent ruthenium compounds

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Statement of the Problem: The discovery of new active and selective anticancer agents, able to reduce the noxious side effects of the chemotherapeutics in clinical use, and able to overcome resistance mechanisms, is the main goal for the research in this field.

Methodology & Theoretical Orientation: We have been developing new of [Ru(η^5 -C₅H₅)(2,2'-bipyridine-R)(PPh₃)]⁺ based compounds through structure-activity studies, endowed with specific targeting components to take advantage of the singular characteristics of tumor cells and tissues, such as their permeability to macromolecules and overexpression of several receptors. Thus, when in the structure of our compounds R is a biodegradable and biocompatible polymer and/or a biomolecule recognized by cancer cells, passive and/or active targeting can be achieved, respectively.

Through a wide set of biological assays that involved spectroscopic, imaging and proteomic techniques, we show that this family of ruthenium metallodrugs possess very attractive features.

Conclusion & Significance: These compounds show high cytotoxicity against several cancer cell lines with different degrees of aggressiveness (eg. hormone dependent vs triple negative breast cancer) and strong inhibition of key proteins known for their role in mechanisms of cell resistance. Their targets seem to be the proteins that regulate the microtubule or actin dynamics leading to cell death by apoptosis. In vivo studies in a zebrafish model revealed that the compounds are well tolerated. Thus, in this presentation the potential of new ruthenium(II) compounds for the targeted therapy of metastatic and resistant cancers is disclosed.

Biography

Andreia Valente is an assistant researcher at Centro de Química Estrutural at Faculdade de Ciências da Universidade de Lisboa. Presently, she leads the drug discovery and delivery systems research line at FCUL that has formed several undergraduate students (through their final Graduation Project), 15 MSc and 4 PhD (ongoing). She was granted with a Royal Society of Chemistry Research Fund Grant in 2015 and she is at the present PI of a funded project in the area of medicinal chemistry and a WG Member of the COST action CA17104 "New diagnostic and therapeutic tools against multidrug resistant tumors", having participated in the last years in 8 funded projects and/or Transnational Cooperation Programmes.

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