Fernanda Marques et al., J Cancer Sci Ther 2014, 6:10
http://dx.doi.org/10.4172/1948-5956.S1.033

OMICS Group Conferences
Accelerating Scientific Discovery

4th World Congress on
Cancer Science & Therapy
October 20-22, 2014 DoubleTree by Hilton Hotel Chicago-North Shore Conference Center, USA

Ruthenium-based anti-cancer compounds: Insights into their uptake mechanisms and cellular targets

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Ruthenium compounds have shown highly promising anticancer activity and may provide a less toxic and more effective alternatives to platinum-based chemotherapies. Many different ruthenium compounds have been tested for their anticancer properties, however without enough investigation into their mode of action. With the aim to give a contribution to elucidate their mechanism of action we studied a set of structurally related Ru(η^5-C_5H_5) complexes with bidentate N,N´-heteroaromatic ligands as prospective metallodrugs, with focus on exploring the uptake, cell death mechanisms and potential cellular targets. These complexes enter the cells by a temperature-dependent process, probably facilitated by binding to plasma transferrin, present high anti proliferative efficacy in a broad range of tumor cells, preferential localization at the cell membrane and cytosol and the ability to inhibit a lysosomal enzyme, acid phosphatase, in a dose-dependent mode. We have extended these studies to examine the potential of these complexes to target cancer cell metabolism, the energetic-related phenotype of cancer cells. The reliance of glycolytic cancer cells on trans-plasma-membrane electron transport (TPMET) systems for their continued survival raises the question of their appropriateness as a target for anticancer drug development strategies. The results from this study indicated that these ruthenium complexes can inhibit lactate production and TPMET activity in a way dependent on the cancer cell aggressiveness and the concentration of the complexes. *In vivo* antitumor activity of these complexes in a prostate tumor animal model is underway.

Biography

Fernanda Marques is graduated in Chemical Engineering from Instituto Superior Técnico, Universidade de Lisboa and has a PhD in Biochemistry from Faculdade de Ciências, Universidade de Lisboa. She is a Scientific Researcher at Centro de Ciências e Tecnologias Nucleares, Instituto Superior Técnico, Universidade de Lisboa, a Nuclear Tecnological Institute for Research. During the last ten years, she has been involved in the biological evaluation of (radio)metal-based compounds as potential therapeutic agents. She has published more than 50 papers in reputed journals.

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