



Title: Stress Out: Promoting Anticancer Activity by Fostering Reductive Stress with Metal Complexes

MSc em Química

Place of work: Departamento de Química e Bioquímica, FCUL; ITQB-NOVA

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Abstract:

In this project, we will develop a new class of anticancer drugs able to disrupt redox homeostasis by promoting reductive stress. We will do so by developing metal complexes able to act as reduction catalysts inside cells. Previous work from our labs has shown that metal complexes can induce reductive stress in cancer cells that ultimately leads to cell death. The main objective is to develop compounds that are able to operate with complementary modes of action to that of existing drugs, to be able to overcome resistance and associated side effects.

To achieve our goal, we plan to fulfil the following tasks:

Task 1. Synthesis of metal complexes based on iridium bearing triazoles ligands (ITQB NOVA). Triazole ligands will be synthesized via click chemistry, using copper and ruthenium catalysts. Synthesized compounds will be characterized by NMR spectroscopy and mass spectrometry, and the stability of the complexes in physiological media will be monitored by NMR.

Task 2. Evaluation of the Metal complexes to promote redox reactions in vitro (FCUL/ITQB NOVA). In this task, we will evaluate the catalytic activity of the metal complexes synthesized in Task 1 in two reactions pivotal to achieve reductive stress: 1) reduction of NAD⁺ to NADH and 2) reduction of GSSH to GSH.

Task 3. Evaluation of the anticancer activity of iridium complexes (FCUL). The antiproliferative activity or cytotoxicity of our metal complexes will be tested in cancer cell lines from different origins, and determine their IC₅₀ values and safety indexes. The mechanisms involved in their antitumoral activity will be analyzed.

Students selected for this project, after thesis registration, are eligible to apply to the BioISI Junior Programme (supporting 8 students with a 6-month Scholarship(BII), being the selection criterium the academic merit of the candidates.