Title	**Translational studies for the preclinical development of an innovative 2 in 1 small molecule technology towards advanced Hepatocellular carcinoma**
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Project description:

Aggressive tumors are still incurable and only an interdisciplinary approach can solve this transversal problem. Among major neoplasia, hepatic carcinoma (HCC) is the fifth most common form of cancer in the world and is characterized by high cell proliferation and high resistance to chemotherapeutic treatments. Although it is the second leading cause of cancer death, no drug is actually effective for the treatment of primary HCC and Sorafenib (approved in 2007) is the only one currently available for the treatment of patients in advanced stages of the disease, but also leads to appearance of serious side effects, such as thrombocytopenia, anaemia, rash, fatigue and gastrointestinal bleeding.

In this context, our rational design of unconventional drugs has been taking into account that the real breakthrough is not simply finding new compounds to treat cancer, but also improving their cellular absorption while minimizing unwanted toxicity. On the basis of these considerations, the PhD student will be requested to run a research project mainly concerned with the design, synthesis and characterization of a new generation of metal-dithiocarbamato derivatives able to selectivity exert their antitumor activities toward the malignant cells. In particular, these new potential drugs, obtained by conjugation of the Au(III), Ru(III) and Cu(II) metal centers to a dithiocarbamato-functionalized biomolecule, will be designed as carrier-mediated delivery systems exploiting specific membrane-receptors to selectively transport the cytotoxic metal cargo into the tumor site. After the synthesis and physico-chemical characterization of the new compounds, some in vitro experiments will be carried out against the hepatocellular carcinoma cells. If possible, specific inhibitors will be also used to check whether the antiproliferative activity is really mediated by as the selective interaction between the targeted-compounds under investigation and the corresponding membrane receptors.

Since the new compounds might be scarcely soluble in water and hence, in physiological environment, we will start to study new bio-compatible vehicles to better solubilize selected complexes, by incorporating them in supramolecular aggregates.

The PhD student will acquire experience in the above mentioned application field as well as in the functionalization of the biomolecules with the dithiocarbamato group, in the synthesis of the metal derivatives , and in the techniques for their purification and characterization.

Publications:

1) *DALTON TRANS.*, 2018, 47, 15477-15486. 2) *Chem.Med.Chem.* 2018, 13, 1131-1145.
3) *European J. Med. Chem.*2017, 138, 115-127. 4) *J. Inorg. Biochem*.2016, 65, 159–169

Collaborations/Network:

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