PhD Position in Bio/Medicinal inorganic Chemistry

Mechanistic Insights of Cu-based Anticancer Drug Candidates

PhD position for 3 years on the project "Understanding the importance of thiols for biological active copper-ligand complexes" financed by icFRC in the group of Biometals and Biological Chemistry (BCB) headed by Prof. Dr. Peter Faller at the Institut de Chimie, UMR 7177 University of Strasbourg / CNRS; https://bcb.chimie.unistra.fr/

Interdisciplinary and **International** project with several collaborators: Petra Heffeter (Medical University, Vienna, Austria) for biological studies of TSC; Christian Kowol (Inorg. Chemistry, University Vienna, Austria) for the synthesis of Cu-ligands (TSC); Emilia Sicilia (University of Calabria, Italy) for DFT calculations; Bertrand Vileno (UMR 7177, Strasbourg) for EPR measurements.

Project:

Background: Cu-ligand complexes (Cu-L) attracted quite a lot of interest as potential drugs because i) the first Cu-complex entered clinical trials ii) Cu is an essential element for humans and hence Cu-drugs should have less toxic side effects than non-essential metal ions like Pt-drugs and iii) it allows a pro-drug strategy, i.e. the administration of the ligand alone, which forms the active drug by chelation of the endogenous Cu. Latter is of interest in the cases where it could lead to a selective formation of the drug, such as in certain cancer cells, which contain higher Cu-concentrations.

Aim: Thiosemicarbazones (TSC) are a class of Cu-chelators that are intensively developed in multiple clinical trials in cancer research. Most of the proposed targets are proteins with essential thiols. Stability against the very abundant thiol glutathione were related to the biological activity of TSC. The present project aims to understand the chemistry of the interaction of Cu-TSC with thiols. This will give fundamental insights into the structure activity relationships for TSC, the selectivity of the Cu(II)-TSC in terms of affinity and oxidation efficiency towards the different thiols found in biology, and the relevance of Cu-TSC to produce ROS in presence of thiols and dioxygen. This mechanistic understanding is important for the rational improvement of such anticancer drug candidates.

Recent references on the topic from the group:

Santoro A, et al. *Angew. Chem., Int. Ed.* **59**, 7830 (2020)
Santoro A, et al. *Metallomics,* **11**, 994 (2019)

Methods to be used: mainly bioinorganic chemistry with spectroscopy (NMR, EPR, fluorescence, etc), but also some ligand synthesis and inorganic complexation, biochemical techniques (chromatography, …) and cell biology (with partner).

Profile searched: Candidate with a Master degree in chemistry or biology. Preference for a chemist with biological knowledge or a biologist with a (bio)-chemical background. Experience in cell biology, biochemistry or biological inorganic chemistry would be welcome, but are not a prerequisite.

Starting date: September/October 2022
Salary: ca. 1450 net Euros/month (gross ~1850)
Applications: CV with coordinates of scientist able to give a recommendation, and letter of motivation, should be send before the end of May 2022 to pfaller@unistra.fr