

ESR 2 position

Project title: Developing the biological potential of organometallic cages

PhD Fellowship in Organic synthesis, Bio-organometallic and Medicinal chemistry

Location: UNIVERSITE de NEUCHATEL (Neuchâtel, Switzerland)

Supervisor: Prof. Bruno THERRIEN (Neuchâtel, Switzerland)

Objectives of the individual project:

The biological side of coordination-driven arene ruthenium metalla-rectangles, metalla-prisms and metalla-cages is a flourishing area of research. These water-soluble metalla-assemblies have been found to possess good anticancer activity, to strongly interact with DNA, to efficiently detect biologically relevant analytes and their cavity has been used to transport and deliver guest molecules to cells. In recent years, we have synthesised a plethora of arene ruthenium metalla-cages in which biologically relevant guest molecules have been encapsulated. We have also synthesised several metalla-cycles and evaluated their anticancer and biological activity. These compounds have opened new perspectives for biological and nano-applications (sensors, drug delivery agents, chemotherapeutics, tweezers) and therefore we would like to add new functionalities to these cages, to better exploit their potential.

To achieve this goal, the main objectives are: 1) Synthesis and characterisation of water soluble arene ruthenium metalla-assemblies for biological applications; 2) Functionalization of the metalla-assemblies with peptides (targeting), large appendages (EPR effect), endoperoxide derivatives (PDT effect), to increase the biological activity and/or the selectivity of the cages; 3) Prepare and characterize stimuli-responsive metalla-assemblies to control the release of the guest molecule (pH sensitive zwitterionic ligands, photoswitchable ligands such as azobenzene or spiropyran derivatives); 4) Perform basic biological tests to identify the most promising systems (high throughput MTT assays, V-propidium iodide double labelling, western blotting with caspase-3 antibody, mitochondrial membrane potential, etc...); 5) Deliver several mg of the best candidates to biologists, to run under collaborations more advanced biological tests.

Planned secondment(s):

Academic Secondment, ISOF-CNR, Italy: To characterise stimuli-responsive metalla-cages and to learn and gain skills from a well experienced photo-chemistry laboratory.

Industrial Secondment, Biolitec, Germany: To test the synthesized arene ruthenium metalla-cages as photosensitizers in photodynamic therapy, or as drug delivery vectors.

Eligibility requirements

EU eligibility criteria for candidates: Candidates of any nationality, but in order to be eligible for the positions the following criteria applies to all applicants:

- The applicant shall at the time of recruitment be in the **first four years of his/her research career** and have **not been awarded a doctoral degree**.
- The applicant must not have resided or carried out his/her main activity in **Switzerland for more than 12 months in the 3 years immediately prior to the recruitment**.



Candidates profile: The candidate should fulfil all requirements listed in the general offer as well as: 1) The applicant must have a master degree (or the equivalent) in organic chemistry, with an interest in medicinal chemistry. A strong knowledge in synthetic organic chemistry is required and some experience in organometallic chemistry is an advantage but not essential; 2) Formation and experience in biological tests in vitro could be an advantage. At least, to be open-minded toward biological study is required; 3) Being a multidisciplinary project, you need to be able to work independently, to have excellent collaborative skills, and to adapt rapidly to different environments.

Questions regarding the recruitment can be sent to: noah@noah-itn.eu.

Questions regarding the project can be sent to: Bruno.Therrien@unine.ch

