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

**Project title:** NEW ANTI-INFLAMMATORY AND PRO-APOPTOTIC PHOTOSENSITIZERS AGAINST ARTHRITIS

**Universities involved (Joint Doctorate diploma):**
- UNIVERSITE de NEUCHATEL (Neuchâtel, Switzerland)
- UNIVERSITE de LIMOGES (Limoges, France)

**Employer:** UNIVERSITE de NEUCHATEL (Neuchâtel, Switzerland)

**Research project description and main objectives:** Rheumatoid arthritis (RA) is an inflammatory joint disease characterized by chronic synovitis, synoviocyte proliferation and, in its later stages, cartilage and bone destructions. When persistent, synovitis remains resistant to treatment by anti-inflammatory drugs, disease-modifying anti-rheumatic drugs, and intra-articular corticosteroids. Therefore, surgical removal of synovium is generally required and is not always efficient. In this context, we will design new functionalized arene ruthenium porphyrin or chlorin complexes in RA models. The combination of the photodynamic action of porphyrin with the cytotoxicity of arene ruthenium complexes has shown excellent anticancer activities under light. The main objective of this project is to provide new functionalized arene ruthenium porphyrin or chlorin complexes which will be tested *in vitro* on cultured synoviocytes isolated from fresh synovial biopsies obtained from RA patients undergoing arthroplasty and *in vivo* on rat models. The main task will consist on preparing multifunctional linkers to combine arene ruthenium units and porphyrin or chlorin moieties and to study the chemical and photodynamic properties of the new compounds. 

*In vitro* studies will demonstrate the pro-apoptotic and/or anti-inflammatory properties of the new compounds, as well as giving details on the signaling pathways activated in the treated cells. *In vivo*, collagen-induced RA models will help to demonstrate the safety and efficacy of the new metal-based drugs and to gain a better understanding of the biological distribution and the mode of action of these arene ruthenium photosensitizers in biological environments.

**Required competencies:** The candidate should fulfill all requirements listed in the general offer as well as:
- 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.
- Formation and experience in biological tests *in vitro* and *in vivo* could be an advantage. At least, to be open-minded toward biological study is required.
- Being a multidisciplinary project, you need to be able to work independently, to have excellent collaborative skills, and to adapt rapidly to different environments.

**Starting date:** September 1st 2018

**Duration:** 36 months

**Names of supervisor and contact:**
- Pr. B. Therrien (UNIVERSITE de NEUCHATEL)
- Pr. B. Liagre (UNIVERSITE de LIMOGES)
- Dr. D. Léger (UNIVERSITE de LIMOGES)
- Contact: polythea@unilim.fr