

POSTDOCTORAL POSITION AT THE INTERFACE OF PHOTOBIOLOGY/MOLECULAR CHEMISTRY TO MODULATE ALLOREACTIVE-IMMUNE RESPONSE WITH PHOTOSWITCHES

Job type: CDD (funded by Lorraine Université d'Excellence (LUE))

Period: 24 months

Start date: September 2023

Salary: From 28 to 35 k€ per years

- **Information related to the host laboratories:**

Laboratories:

1. **Laboratoire Lorrain de Chimie Moléculaire** (L2CM, UMR 7053), <http://www.l2cm.univ-lorraine.fr/l2cm/>, Boulevard des Aiguillettes B.P. 70239 - 54506 Vandoeuvre les Nancy Cedex France

The objective of L2CM is to explore and develop synthetic methods for innovative molecules and molecular materials for applications in various domains towards chemistry (drug design, catalysis), physics (energy, materials) and biology (drug delivery, imaging, therapy). Those research activities are conducted within HeMaf and MolSyBio teams and are supported by numerous technics of synthesis and characterization integrated into internal platforms (SynBion, Photons, MassLor) and partnership.

2. **Ingénierie Moléculaire et Physiopathologie Articulaire** (IMoPa, UMR 7365, <https://imopa.cnrs.fr>, Biopôle, Campus Brabois-Santé, 9, avenue de la forêt de Haye BP20199, 54505 Vandoeuvre-lès-Nancy.

TEAM 6 is specialized in projects focusing on immunomodulation by stem cells, including anti-tumoral properties of immune cells. IMoPa has access to animal facilities, and high adding value platforms such as single cell technology or multiparametric flow cytometry. V. Decot belongs also to the Cell Therapy Unit (UTCT; CHRU of Nancy) which has experience in the field of clinical trials (one PHRC closed and 2 open) and has a production platform for prepared advanced therapy drugs currently supported by the ARS of the Greater East Region. In addition, this platform was recently awarded the "industrial integrator" label as part of the Grand Defi Bioproduction program.

Supervisors of the postdoc:

Andreea Pasc (PR, team MolSyBio, L2CM) and Véronique Decot (PU-PH, team 6, IMoPa and UTCT, CHRU of Nancy)

- **Research topic of the postdoc:**

Keywords:

Photobiology, organic chemistry, photophysical characterization, biological chemistry, cell biology, two-photon microscopy, fluorescence imaging, cell dynamics.

Context and research objectives:

Allogeneic hematopoietic stem cell transplantation remains the most effective treatment option for patients suffering from hematological malignancies.¹ The anti-leukemic effect of this cellular therapy relies on immune cells present within the donor stem cell graft, such as T or Natural Killer (NK) cells that can target recipient residual leukemic cells. However, graft vs host disease (GVHD), the most severe complication occurring in 50% of the patients receiving a graft from siblings, is due to donor T cells.² Controlling activation or deactivation of T and NK cells through immune checkpoints such as Tim-3 appears of paramount importance to propose specific, acting on demand, immunomodulating therapeutics for T cell-mediated diseases (*i.e.* GVHD) while maintaining NK-cell anti-tumoral responses. To do so, photoresponsive systems were proposed in the so-called photoimmunotherapy approach³. Among them, photoswitchable azo-benzene PS ligands of Tim-3 were reported to efficiently modulate the function of NK cells upon Z/E isomerization at 365 or 455 nm light.⁴ However, the chromophores

should exhibit significant absorption in the optical biological window, in the 650 to 1350 nm range. To date, only few examples of photoswitches can induce such geometrical change in the NIR region. To overcome this issue, an alternative strategy is based on the exploitation of nonlinear optical properties and in particular two-photon absorption (TPA) to trigger the photochemical events. The attractiveness of TPA in the field of photoswitches is clearly due to the possibility to cover the NIR region, and thus to (1) allow a deeper penetration of biological tissues and to (2) have a low energy per photon, harmless for biological tissues compared to the absorption of UV-Vis light.

In conclusion, the present project aims to design and demonstrate the immunomodulatory properties of new ON/OFF photoresponsive molecular tools on T and NK cells, through phosphatidylserine/Tim-3 binding, targeting thus applications in GVHD and autoimmune diseases. To this aim, the effects of **swPS** will be evaluated on T and NK cells isolated from GVHD patients.

Job description:

We offer a two-years postdoc position to work on organic synthesis of molecular photoswitches to *in vivo* evaluation of their toxicity and impact on T and Natural Killer cells. Within the frame of this project, both photophysical and biological properties will be determined. A good expertise in photobiology/photochemistry will be required and valued by combination with high expertise in immunology, cell biological, chemistry and photophysics and studies of L2CM and IMoPa. As a postdoctoral researcher, you will be attached to both laboratories, which are located in Vandoeuvre-les-Nancy, France. Missions in Tanaka's lab (Heidelberg University) will be planned to perform in live cell imaging and statistical analysis of cell dynamics.

Mission and specific responsibilities: You will be responsible and/or participate to the following tasks:

- synthesis of two photolipids, according to procedures already reported by L2CM
- Encapsulation of photolipids within liposomes and physico-chemical characterization
- Assessment of photophysical properties of resulted liposomes by photophysical technics (spectroscopy, fluorimetry, Z-scan)
- Immune cell phenotyping (flow cytometry) and functional assays (proliferation, multiplex cytokine analyses, cytotoxicity).
- Participation in the supervision of PhDs, engineers, and trainees - restoring the results, communication at international conferences, participation in writing of manuscripts.

- **Candidate profile and application form:**

Applicants should hold a PhD in photobiology with prior experience in cell biology and at the interface with photochemistry/photophysics. Additional experience in organic synthesis or biophysics would be appreciated. Creativity, autonomy and strong reliability are highly required, together with strong interest in multidisciplinary approach. This project will give great opportunities to develop/extend competences in immunology, photophysics, biophysics and associated characterization techniques with cutting-edge equipment. They are expected to be highly motivated and possess great team spirit to take advantages to work in a leading research environment and potentially make breakthrough innovations in immunotherapy. All applicants must be able to communicate fluently in English. Applications should be sent to Andreea Pasc (andreea.pasc@univ-lorraine.fr) and Véronique Decot (veronique.decot@univ-lorraine.fr). It should include a detailed resume and a cover letter highlighting how they meet the criteria.

References:

- (1) Baron, F.; Storb, R. *Springer Semin. Immunopathol.* **2004**, *26*, 71
- (2) Jamil, M. O.; Mineishi, S. *Int. J. Hematol.* **2015**, *101*, 452;
- (3) Hartrampf, N. et al. *Chem. Eur. J.* **2020**, *26*, 4476;
- (4) Yang, X. et al *J. Am. Chem. Soc.* **2022**, *144*, 3863