



## 3-years PhD position open, INSERM U1312 BRIC – Team TRIO2

**Title:** Exploring the energy metabolism necessary for the tumorigenesis of Sézary cell

**Application deadline:** 2023 08 31

### Project

Our team « Translational Research in Oncodermatology and Orphan skin diseases (TRIO2) » within the INSERM U1312 « Bordeaux institute of oncology (BRIC) » is interested in the aggressive forms of primary cutaneous lymphomas (PCL) and specifically in the Sézary Syndrome (SS). To date for SS, neither the oncogenic events present in the initiating cells, nor those involved in their aggressiveness, are known, which limits the development of personalized strategies or innovative therapeutic approaches more efficient and well tolerated, even if the currently available targeted therapies (anti-CCR4, anti-CD30, anti-CD158) are both associated with a better response rates and duration of response.

Numerous data suggest the interest of a therapeutic targeting of cancer cell metabolism. Sézary cell' metabolism is poorly documented. Nevertheless, we have preliminary results, leading us to explore this pathway as a relevant strategy either to increase the efficacy of drugs or to offer new therapeutic targets.

The objective of this research work is to determine the metabolic profile of Sézary cells in relation to their immunophenotype (naive CD4+ T lymphocyte, central memory, memory effector...) through the study of the energy requirements necessary to maintain their tumorigenic capacities and to highlight cell populations with potential differences in sensitivity to drugs.

The first objective is to determine the metabolic pathway preferentially used by Sézary cells. We will start with Sézary cell lines maintained *in vitro* in culture according to the same modalities. We will also work on Sézary cells freshly isolated from blood samples of SS patients (6 patients will be recruited). This number should allow us to reveal divergences linked to inter-individual variability but also convergences linked to tumor cells. To validate this point, it is necessary to have reference values. This will be obtained with healthy CD4+ T cells from the French blood establishment (Agreement AC2019-3713). Healthy donors (6 planned) will be age and sex matched to SS patients. The comparison between healthy and tumor metabolic profiles (cell lines and patient cells) will allow us to define a metabolic signature specific to the Sézary cell.

The second objective is to use the metabolic plasticity of T cells to modulate the metabolism of Sézary cell lines to approximate that of Sézary patient cells. Indeed, knowing that cell metabolism is an adaptive mechanism subject to environmental pressures, variations will probably be revealed by the comparative analysis of data from cell lines and patient cells. Thus, depending on the metabolic profile identified in objective 1, we will treat the Sézary cell lines with different metabolic modulators and examine the effect of this treatment on their immunophenotype (naive, central memory, effector memory...), cell cycle distribution, viability, cell death, tumorigenic capacities *in vitro*.

Having available for research purposes Sézary cell lines, that in addition to an immunophenotype, a cytogenetic and a genotype similar to SS patient cells *in vivo*, will exhibit a metabolism close to that of Sézary cells *in vivo*, will allow us to study the effect of therapeutic molecules in the 3D pre-clinical models developed in our team.

If you are interested in the topic and translational research and if you have knowledge in cell biology, oncology and metabolism you are welcome to apply.

## Profile

- You have a master degree in Cancer Biology, Cell Biology, Biomedical Sciences or equivalent.
- Graduation with distinction (or more).
- Motivation and commitment for pursuing a PhD in the field of oncology.
- Experience in cell biology research, metabolism, molecular biology and/or immunology, FACS and microscopy skills are a plus.
- Very good knowledge of English, both orally and written.
- Other required competences: proactive, communicative, accurate, able to work independently and in team, good organization and coordination skills, eager to learn.

## Offer

- A dynamic environment with opportunities for further development and training, and collaboration with other research groups and core facilities.
- The opportunity to be part of a dynamic team and provide a meaningful contribution to cutaneous lymphoma research.
- Start date: from October 1st, 2023

**Funding:** The PhD is entirely funded for 3 full years.

Interested applicants should contact the **PhD director:** Prof. E Chevret. Mail: [ediith.chevret@u-bordeaux.fr](mailto:ediith.chevret@u-bordeaux.fr)

**Laboratory:** INSERM U1312 – BRIC (Bordeaux Institute in Oncology), team TRIO2 (leaders: Prof. M Beylot-Barry and Dr H Rezavani)