

**2-YEARS POST-DOCTORAL POSITION OPEN
IN TUMOUR IMMUNOLOGY
IN LYON, FRANCE**

**“Development of T cell-based immunotherapies
targeting HERV-derived epitopes in hematology”**

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Project rationale:

Hematological malignancies are characterized by a low mutational burden. There is therefore a major need to identify tumor-specific antigens beyond those associated with mutations to develop innovative T cell-based immunotherapies. Human Endogenous Retroviruses (HERVs) represent 8% of the human genome. HERVs are silenced by epigenetic mechanisms in normal cells but are aberrantly expressed by tumor cells. Given their viral origin, HERV products may represent tumor antigens relevant for cancer immunotherapy. We have developed new bioinformatics-based methods to identify tumor-specific HERV-derived epitopes that induce high avidity T cells against tumor cells. After validation in solid tumors (Bonaventura et al, Sci Adv 2022), our group has also identified HERV-derived antigens that characterize leukemic cells (Alcazer et al, Am J Hematol 2022).

Objectives of the post-doctoral research project:

1. To characterize HERV expression in chronic myelomonocytic leukemia (CMML) (collaboration with Françoise Porteu, INSERM U1287, Gustave Roussy, and bioinformatics team)
2. To validate the presence and the immunogenicity of new HERV-derived epitopes in CMML and acute myeloid leukemia (AML)
3. To assess the role of HERV-directed immune response in Graft-versus-Leukemia (GVL) effect after stem cell transplantation
4. To generate HERV-specific engineered TCR-T cells and evaluate their antileukemic activity in *in vitro* and *in vivo* models

The project will be based both on primary tumors from patients (collaboration with Hematology Department - University Hospital Lyon Sud) and leukemia models developed in immunodeficient mice. The project will involve the following techniques: RNAseq transcriptomic, *in vitro* immune cell assays, multiparametric flow-cytometry, T cell therapy using TCR engineering.

Working language: English and French (not necessarily)

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Candidates holding a PhD or an MD-PhD with a solid experience in immunology and hematology should address their CV and 2 reference names via e-mail to Dr Vincent ALCAZER, MD, PhD, at vincent.alcazer@chu-lyon.fr and Prof Stéphane DEPIL, MD, PhD, at stephane.depil@lyon.unicancer.fr