CRCL CENTRE DE RECHERCHE EN CANCÉROLOGIE DE LYON

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

"Immune impact of the expression of human endogenous retroviruses in hematological malignancies"

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Project 's rationale:
Human Endogenous Retroviruses (HERVs) represent 8% of the human genome. Most HERV genes are non-functional due to DNA recombination, mutations, and deletions, but some produce functional proteins including group-specific antigen (gag), polymerase (pol) with reverse transcriptase, and the envelope (env) surface unit. A major function of DNA methylation in humans is silencing of HERVs and other viral sequences in the human genome. HERV genes can be unmethylated and expressed in embryonic stem cells (Santoni et al, Retrovirology 2012 : *9*, 111) and in some tumors (Stengel et al, Genes Chromosomes Cancer 2010, *49* : 401–411). HERV retroviral gene products may act as tumor associated antigens activating both T-cell and B-cell responses (Wang-Johanning et al, Cancer Res 2008;68(14):5869–77 ; Rycaj et al, 2014, Clin Cancer Res; 21(2); 471–83). Our group has developed new bioinformatics-based methods to identify HERV-derived epitopes that induce high avidity T cells against tumor cells. After validation in solid tumors (one submitted manuscript, several patents, founding of ErVaccine Technologies), our group has also identified HERV-derived antigens that characterize leukemic cells.

Objectives of the post-doctoral research project:

1. To characterize HERV expression in chronic myelomonocytic leukemia (CMML) and analyse the effects of epidrugs on their expression in several hematogical malignancies (collaboration Françoise Porteu, INSERM U1287, Gustave Roussy)
2. To assess the antileukemic effect of HERV specific T cells
3. To assess the role of HERV-directed immune response in allogeneic stem cell transplantation
4. To develop antibody and cell therapy-based approaches targeting HERV antigens

The project will be based both on primary tumors from patients and patient-derived primary tumors (PDX) developed in immunodeficient mice. The project will involve the following technics: RNAseq transcriptomic, *in silico* epitope prediction (collaboration with bio-informaticians), *in vitro* immune cell assays, multiparametric flow-cytometry, and contribution to patient monitoring.

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 ideally hematology should address their CV and contact information of 3 referees via e-mail to Stéphane DEPIL, MD, PhD, at stephane.depil@lyon.unicancer.fr