Inserm

Job Offer

Postdoctoral Position in single cell transcriptomics/imaging and Non-Hodgkins Lymphoma, Cancer Research Center of Toulouse, France

Job Profile	
CSS	2/7
Offer description	A postdoctoral fellowship for 2 years is available as early as January 2024 at Cancer Research Center of Toulouse, a biomedical research center in Toulouse (France) affiliated to the Université Paul Sabatier Toulouse III. This project is part of TRANSCAN project entitled "Bispecific antibodies in Lymphoma: Microenvironmental profiling to predict treatment response and uncover immunogenic resistance mechanisms", coordinated by Wolfgang Huber (EMBL Heidelberg, Germany), and integrating six European partners (Sascha Dietrich, Heidelberg University Hospital; Camille Laurent, UMR 1037 and department of pathology, IUCT, Toulouse; Karin Tarte, UMR S 917, Rennes; Peter Horvath, Eotvos Lorand Research Network, Biological Research Center, Szeged, Hungary; Claudio Tripodo, University of Palermo, Palermo, Italy). The general aim of this consortium is to identify and understand lymphoma cell intrinsic and extrinsic signatures of response and resistance to bispecific antibodies by single-cell transcriptomics and multiplex assays, in order to develop strategies to overcome treatment resistance.
Researcher profiles	☐ First-Stage Researcher *(PhD candidate)* X Young Researcher (*with less than 4 years research experience after PhD)* ☐ Established Researcher *(with more than 4 years research experience)* ☐ Senior Researcher
Research Fields (2 max.)	X Biological Sciences ☐ Chemistry X Computer Science ☐ Engineering ☐ Environmental Science ☐ Ethics in Health Sciences ☐ Medical Sciences ☐ Neurosciences ☐ Pharmacological Sciences ☐ Physics ☐ Technology ☐ Other (specify):
Main Activities	**Context -** Non-Hodgkin's lymphoma (NHL) is cancer that arises from lymphocytes and has an age-standardised incidence rate of 17 cases per 100.000 persons. Nearly 90 percent of NHL types develop in B cells. Diffuse large B-cell lymphoma (DLBCL) represents the most common aggressive- and follicular lymphoma (FL), the most common indolent B-cell lymphoma subtype. Although ~60% of DLBCLs are curable with current induction and salvage protocols, a substantial fraction of patients develops recurrent or progressive disease that is often fatal. The recently approved CD19-CAR-T cells can induce remissions in a significant subset of

relapsed and refractory (r/r) DLBCL patients; but many DLBCL patients continue to relapse after this procedure. In contrast, the treatment for advanced FL aims to control the disease but not to cure it. Effective treatments can often control the disease for several years, but there is a substantial proportion of patients who develop standard treatment-refractory FL and run out of treatment options.

Redirection of autologous T cells is an effective therapeutic principle to target B cell malignancies. There are two major approaches: i) genetically modified chimeric antigen receptor (CAR) T cells that can induce complete response (CR) in up to 54 % of patients with refractory aggressive B cell non-Hodgkin lymphomas (B-NHL) (Neelapu et al. 2017) but which is time-consuming and very expensive; ii) bispecific antibodies (BsAb) that are an off-the-shelf approach that redirect T cells against malignant B cells by concomitant binding to CD3 and a target antigen, such as CD19 or CD20. Although some BsAb such as Blinatumomab, the first-in-class anti-CD19 BsAb, exhibits CR up to 37% in r/r B-NHL patients (Goebeler et al. 2016), only a minority of patients shows sustained response. Thus, an improved understanding of the factors contributing to the treatment efficacy of BsAb is urgently needed to predict treatment response.

The different aims will be developed in Pr Laurent's team in collaboration with the consortium are:

Aim 1- Microenvironmental characterization of relapsed and refractory B-NHL (Rennes, Toulouse, Heidelberg University Hospital, EMBL). We will characterize the genetic and transcriptional landscape of microenvironmental and lymphoma cells by single cell RNA sequencing.

Aim 2: Ex-vivo and in-vivo response profiling to understand resistance mechanisms (Heidelberg University Hospital, Szeged, Toulouse, Rennes). We will validate the results obtained of drug screening (more than 60 BsAb) on primary samples (Heidelberg University Hospital) on more sophisticated 2D and patient-derived 3D multicellular spheroid co-culture models taking into account the different cellular components from the microenvironment.

Aim 3: Spatial composition and cellular engagement (Heidelberg University Hospital, Szeged, Toulouse, Palermo). Spatial characterization will be performed in FPPE tissue both by spatial transcriptomics and multiplex imaging.

CRCT provides a highly dynamic scientific life between fundamental and clinical research in Toulouse (https://www.crct-inserm.fr/en/), with around 400 people. The postdoctoral fellow will work in the team of Pr Camille Laurent "Novel Immuno-Therapeutic Strategies for Lymphoma"at the CRCT in close interaction with the department of pathology (IUCT), and will benefit from the support of engineer and the expertise of the state-of-the-art core facilities (Cite seq/Flex technology, spatial phenotyping- Phenocycler).

Associated Activities

The recruited post-doctoral fellow will perform single cell profiling and spatial phenotyping on r/r FL or DLBCL samples. He/She will be involved, in close collaboration with a bioinformatic expert, in the analysis of these data and their integration with clinical data to identify predictive factors of BsAb response.

	The fellow is expected to interpret and criticize his/her own results as well as to write scientific articles and perform oral presentations in local, national and international meetings. Our future strategy is to present the post-doctoral fellow to academic institution (INSERM, CNRS) competition to become a full-time researcher. Particular attention will be given to CVs with a profile likely to be selected for the competition.
Specific Requirements or Constraints	- PhD in Hemato/Immunology-oncology or related field. - Strong experience in Hemato/Immunology-oncology - Experience in cell culture, bulk transcriptomics and computational biology are a plus. - Rigorous, dedicated, innovative and autonomous. Good communication skills that allow productive interactions with an interdisciplinary team (experimental and computational biologist, medical doctors). Ability to communicate in both spoken and written English.
Skills/Qualifications	- Skills in single cell transcriptomics and imaging are required. At least, basic computational skills are necessary.
Required Experience	☐ 0 to 2 years ☐ 2 to 4 years X 4 to 10 years (including PhD) ☐ >10 years **Fields:** Hemato/Immunology-oncology
Required Education Level or Diploma	• PhD
Required Languages	• English, French
Hosting Unit	
Code	U1037
Name	Cancer Research Center of Toulouse
Director	Dr Pierre Cordelier
Composition	CRCT provides a highly dynamic scientific life between fundamental and clinical research in Toulouse (https://www.crct-inserm.fr/en/), with around 400 people.
Address	2 avenue Hubert Curien, 31100 Toulouse
Website	https://www.crct-inserm.fr/en
Contract	
Type	Fixed-term employment (CDD), project funded by TRANSCAN
Duration	24 months
Salary	Salary level determined according to experience following internal guidelines, i.e. according to experience

Envisaged Start Date	January 2024

Application

Applicants must send a CV and a cover letter to:

laurent.Camille@iuct-oncopole.fr and christine.bezombes@inserm.fr

Contact for further information (name, telephone/mail):

Deadline for application: End of October 2023