Computational biologist in single cell OMICS applied to immuno-oncology

The CISTAR Laboratory " **C**ancer **I**mmune **S**urveillance and **T**herapeutic t**AR**geting"
<u>Head</u>: Dr Christophe Caux, Cancer Research Center of Lyon (CRCL)

Position Summary

We are seeking a highly motivated and scientifically driven computational biologist/bioinformatician. The candidate will bring his/her expertise to contribute to the team objective in identifying key immune surveillance pathways operating in tumors using **a unique strategy,** based on the team **advanced expertise on DC subsets**, combining **single-cell transcriptomic** and **spatial analyses** of innate immune cells **at preneoplastic stages** in breast and colon environment.

Using both human tissue samples and spontaneous sporadic mouse tumor models, the team has generated datasets along 2 axes:

- Deep single-cell RNA-sequencing of innate immune (DC, MΦ, neutrophils, NK) and epithelial/stromal cell compartments comparing normal, preneoplastic lesions and established tumors in order to define cell trajectories during tumor progression and identify specific pathways activated at preneoplastic stage and contributing to prevention of tumor development.

- Tissue localization of each innate immune cell population and identification of its neighbors by deep *in situ* multi-IF spatial analysis with the aim to define the spatio-temporal crosstalk between innate and epithelial/stromal cells.

The successful candidate will **take the lead** to integrate these 2 approaches through deep machine-learning techniques representing a breakthrough strategy to pinpoint key cell/cell interactions and immune surveillance pathways activated at early stage and interrupted in advanced tumors.

Contract: **3 years** private-law contract with salary based on experience.
The team is ready to support the candidate to apply to an INSERM/CNRS researcher position, with possibility to develop new research lines.

Recent publications from the lab related to the field

- Di Roio et al (2023), MDR1-expressing CD4+ T cells with Th1.17 features resist to neoadjuvant chemotherapy and are associated with breast cancer clinical response. Journal of ImmunoTherapy of Cancer, in press
- Voissiere et al (2023), The CSF-1R inhibitor Pexidartinib impacts dendritic cell differentiation through inhibition of FLT3 signaling and may antagonize the effect of durvalumab in patients with advanced cancer – results from a phase 1 study. Science Translational Medicine, in press
- Hubert et al. (2020), IFN-III Is Selectively Produced by cDC1 and Predicts Good Clinical Outcome in Breast Cancer. Science Immunology 5(46).
- Small M et al. (2018), Genetic alterations and tumor immune attack in Yo paraneoplastic cerebellar degeneration. Acta Neuropathol. 135(4):569-579.

Responsibilities

The **three** main objectives of the candidate will be to:

- Use and adapt existing pipelines and develop novel computational methods and tools to analyze complex scRNAseq datasets to identify features/pathways in immune cells, tumor cells and/or stromal cells activated at the pre-cancer stage

- Implement computational methods to calculate cell-cell proximity metrics and infer cell neighborhoods from raw data of multiplex-immunofluorescence tumor tissue staining as well as spatial transcriptomics data
- Explore existing and/or develop tools to integrate scRNAseq data with spatial data and to infer networks of ligand/receptor interactions

The duties also include:
- Keep abreast of emerging methods in computational biology/bioinformatics
- Interact with the immunologists of the team to optimize the design of dry experiments and best adapt the analysis pipelines
- Drive the bioinformatics expertise in the team and provide mentorship for PhD students, with possibility to manage a group of 2 to 3 persons according to experience
- Contribute to data synthesis and to the writing of papers
These responsibilities will be adapted to the candidate' background and experience

Skills and qualifications
- PhD with a solid background in Bioinformatics, Computational Biology or Systems Biology (>2 years of postdoctoral experience would be a plus)
- Experience in utilizing Python and R programming languages as well as bioinformatics pipeline development (prior experience in working with high dimensional single cell omics datasets is a plus)
- Ability to be inventive, to solve problems and to present novel ideas in method development and data analysis
- Ability to work independently while being able to communicate effectively and to evolve in a multidisciplinary research environment
- Knowledge of tumor immunobiology will be considered as an advantage

Host Lab
The team "Cancer Immune Surveillance and Therapeutic Targeting" (CISTAR) is part of the Cancer Research Center of Lyon (CRCL, www.crcl.fr) and is composed of researchers, clinicians, technicians and PhD students all devoted to identify new tumor immune surveillance and escape networks to improve cancer treatment. It already hosts 2 bioinformaticians, PhD students with bioinformatics skills and collaborate with the CRCL Gilles Thomas bioinformatics platform since several years. The team benefits from long-standing interactions with clinicians of Centre Léon Bérard and Hospice Civil de Lyon and is part of various networks/consortiums, including **European IMI Immucan consortia** and the **ITMO program prenoplasia DESTINE 3.0**, which fund the position. The CRCL is a renowned and dynamic research center which benefits from state-of-the-art technological facilities for flow cytometry, cell and molecular biology, bulk and single cell sequencing, spatial transcriptomics, spatial tissue imaging and *in vivo/ex vivo* models.

The candidate will benefit from ongoing international collaborations with the teams of J Hausser (Karolinska Institute, Sweden) and M Claassen (Tubingen University, Germany) for spatial data analysis.

Application
Interested candidates should submit a motivation letter, CV and contact details of 2 references to Christophe Caux (Christophe.Caux@lyon.unicancer.fr). The position is to be filled as soon as possible. **The closing date for applications is December 15th 2023.**

CRCL - Cancer Research Center of Lyon - INSERM-1052, CNRS-5286, Université de Lyon, CLB
Team "Cancer Immune Surveillance and Therapeutic Targeting" – Dir. C. Caux
Centre Léon Bérard – Cheney D 3ème étage
28 rue Laennec – 69008 Lyon FRANCE