Internship proposition
One page max
M2 I3/0HNU 2024-25

Lab: CRCI²NA
Team: reMoVE-B / #11

Name and position of the supervisor: Tessoulin Benoit / Chiron David
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Candidate: Data Analyst
Title of the internship: Unraveling the tumor immune microenvironment of B-cell lymphoma using single-cell RNA-seq and deconvolution of bulk data

Summary of the internship proposal:
Mantle cell lymphoma (MCL) is a rare but aggressive and still incurable mature B-cell malignancy. New strategies are therefore needed to counteract this resistance and associated systematic relapses. Over the last 2 decades, most studies have focused on the structural and functional genomic abnormalities of this disease, leading to the characterization of its molecular origin, the factors involved in its heterogeneous clinical course and markers of resistance to different treatments (*Sarkozy et al, Blood 2024*). In contrast to these abnormalities intrinsic to tumor cells, the dialogue between MCL and its microenvironments was, until recently, largely ignored. Our previous results show an impact of immune ecosystems in the biology of MCL (*Chiron et al Blood 2016, Decombis et al Blood 2023, Decombis et al Haematologica 2022, Tessoulin et al Front Oncol 2019*). However, we still have very little information on the precise nature and composition of the different ecosystems of MCL. Although scRNA-seq strategies have been democratized for the study of ecosystems, their use remains limited in terms of the number of tumor samples that can be analyzed and is impossible to apply to old samples. This is why the development of tools capable of generalizing some of the discoveries made by scRNA-Seq on 'bulk' sequenced samples (the whole tumor, with all the cell types) is necessary to the development of our knowledge of this microenvironment.

In order to better characterize these lymphomas, we are currently sequencing MCL samples at single-cell resolution within their bone marrow (n=6) or lymph node (n=8) ecosystem (10X Genomics). The main objectives of this internship will be:
1) To analyse these scRNA-seq datasets using standard pipelines (Bird Architecture, Seurat, Metacell, ….).
2) Define transcriptomic signature matrices for immune populations (lymphoid and myeloid) associated with MCL.
3) Define the best deconvolution granularity by cross-validation with cytometry data and apply these signatures to larger cohorts using the bulk RNA-seq deconvolution technique (*CibersortX, https://cibersortx.stanford.edu/, Newman et al. Nat Biotech 2019*). Particular attention will be paid to datasets associated with clinical annotations in order to define their prognostic impact (*e.g. LyMa trial*).

This project is at the interface between fundamental research (Dr Chiron, CNRS) and translational research (Dr Tessoulin, CHU). It will be carried out in close collaboration with a PhD student (Candice Madiot), the team's in-house bioinformatics support for scRNA-seq (Céline Bellanger) and Dr Tessoulin's support for deconvolution strategies.

Option(s) linked to the project:

Clinical Research Profile
X Data Analyst Profile
Experimental Biology Profile