STUDENT INTERNSHIP

Topic: Scientific Pipeline creation for multimodal single-cell and spatial transcriptomics data analysis
Duration: 3 to 6 months start on February
Location: Oncodesign HQ – Dijon
Benefits: Monthly indemnity + meal Ticket

Our Company

OPM is a technological company specialized in precision medicine. OPM's mission is to bring innovative therapeutic and diagnostic solutions to treat therapeutic resistance and metastasis evolution. The patient is at the center of our reflection, of our unique innovative model, and our investments. For OPM "our collective success is paramount", there can be no value creation without exchange, without dialogue. The value creation resulting for us from reciprocity, i.e. balanced and fair exchanges at all levels, whether between internal collaborators, or with our partners, therapists, patients, experts and investors.

Context

All the cells in your body are made up of the same genome. What makes the difference is the expression of the genes in RNA or "transcriptome". This is the set of messenger RNAs (**mRNA**s) transcribed in the cell, the translation of which in proteins that is responsible for the cellular phenotype. One method to assess the transcriptome is messenger RNA sequencing or RNA-seq. However, the main problem with RNA-seq technology is that it measures the average expression of a tissue and not the expression of a cell. But, another method allows the sequencing of the transcriptome of a single cell. This is called Single Cell RNA Seq (**scRNA-Seq**) and have become increasingly widespread since 2013 when it was chosen as Nature's Method of the Year.

Over the last few years, single cell methods have enabled the monitoring of gene and protein expression, genetic, and epigenetic changes in thousands of individual cells in a single experiment – the single cell multimodal omics became Nature's Method of the Year 2019. With the improved measurement and the decreasing cost of the reactions and sequencing, the size of these datasets is increasing rapidly. The critical bottleneck remains the analysis of the wealth of information generated by single cell experiments [1].

But, despite the ongoing success of scRNA-seq, a crucial practical obstacle exists: the need to isolate viable cells from whole tissue without inducing stress, cell death, and/or cell aggregation. Immunologists have perhaps benefitted the most from scRNA-seq because many immune cells (particularly T and B lymphocytes) are relatively easy to isolate from circulating blood, lymphoid organs, peripheral tissue, and even tumors [2][3][4][5]. Therefore, purely from a technological standpoint, there has been an impetus to conduct transcriptomics on intact tissue. Since spatial information is preserved by studying intact tissue, these methods have been referred to as spatially-resolved transcriptomics, or simply 'spatial transcriptomics' (Nature's Method of the Year 2020).

Furthermore, it is becoming increasingly apparent that sub-cellular localization of mRNAs varies according to gene function, regulating for example where a protein product is produced and trafficked in cells [6]. This is a common phenomenon, affecting an estimated 70% of transcript species [7]. In past decades, these inferences were made by targeted screens of specific mRNAs but are beyond the current capabilities of scRNA-seq. Emerging spatial transcriptomics techniques promise to profile simultaneously hundreds to thousands of genes at subcellular resolution allowing scientists to measure all the gene activity in a tissue sample and map where the activity is occurring. This technology is already leading to new discoveries that are instrumental in helping scientists gain a better understanding of biological processes and disease [8].

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However, the data generated by spatial transcriptomics technologies are inherently noisy, high-dimensional, sparse, and multi-modal (including histological images, count matrices, etc.), thus requiring specialized computational tools for accurate and robust analysis.

The objective of this internship is to implement a first pipeline regarding single-cell multimodal data analysis dedicated to new therapeutic target identification. Then, the development of a second pipeline based on spatial transcriptomics data will be addressed.

Missions & activities of the internship

- State of the art of single cell multimodal data analysis (bibliography)
- State of the art of spatial transcriptomics (bibliography)
- Assessment of all the biases induced by single cell multimodal and spatial transcriptomics
- Identification of algorithms to deal with single cell multimodal and spatial transcriptomics data
- Public datasets retrieval
- QC of the datasets as requested by the both methodologies
- Pipeline development of single cell multimodal data analysis
- Pipeline development of spatial transcriptomics data analysis
- Results validation

Student expected background/Knowledge

M2 or Engineer in Computer Science / Bioinformatics with programming skills.

- A good knowledge of the R language is required, a knowledge of the Python language is an advantage
- Strong interest in molecular biology and oncology
- Knowledge of pipeline management is a plus (Snakemake).

References

[1] Michael S. Balzer, Ziyuan Ma, Jianfu Zhou, Amin Abedini and Katalin Susztak, How to Get Started with Single Cell RNA Sequencing Data Analysis. JASN June 2021, 32 (6) 1279-1292; DOI: https://doi.org/10.1681/ASN.2020121742
[2] Haque A, et al. A practical guide to single-cell RNA-sequencing for biomedical research and clinical applications. Genome Med. 2017;9(1):75.
[3] Stubbington MJT, et al. T cell fate and clonality inference from single-cell transcriptomes. Nat Methods. 2016;13(4):329–32.
[4] Shalek AK, et al. Single-cell RNA-seq reveals dynamic paracrine control of cellular variation. Nature. 2014;510(7505):363–9.
[5] Mahata B, et al. Single-cell RNA sequencing reveals T helper cells synthesizing steroids de novo to contribute to immune homeostasis. Cell Rep. 2014;7(4):1130–42.
[6] Holt CE, Bullock SL. Subcellular mRNA localization in animal cells and why it matters. Science. 2009;326(5957):1212–6.
[7] Lecuyer E, et al. Global analysis of mRNA localization reveals a prominent role in organizing cellular architecture and function. Cell. 2007;131(1):174–87.
[8] https://www.10xgenomics.com/

How apply?

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