Exploring the transcriptional landscape of gonadotroph tumor microenvironment with single cell RNA-seq

Benoît ALIAGA[1,2], Julie RIPOLL[1], Marie CHANAL[3], Hector HERNANDEZ-VARGAZ[3], Emmanuel JOUANNEAU[3,5,7], Alexandre VASILJEVIC[3,4,7], Gerald RAVEROT[3,6,7], Eric RIVALS[1] and Philippe BERTOLINO[3]

[1] Laboratoire d'Informatique, de Robotique et de Microélectronique de Montpellier, UMR 5506, Univ. Montpellier et CNRS, 161 rue Ada, 34095, Montpellier, France

[2] Master Sciences et Numérique pour la santé, Faculté des Sciences, Univ. Montpellier, Campus Triolet Place Eugène Bataillon, 34095, Montpellier, France

[3] Centre de Recherche en Cancérologie de Lyon, INSERM U1052, CNRS UMR5286, Université Claude Bernard Lyon1, 28 rue Laennec, 69008, Lyon, France

[4] Centre de Pathologie Est, Groupement Hospitalier Est, Hospices Civils de Lyon, 69677, Bron, France

[5] Université de Lyon1, Service de Neurochirurgie, Hôpital Neurologique, Hospices Civils de Lyon, 69677, Bron, France

[6] Fédération d'Endocrinologie, Groupement Hospitalier Est, Hospices Civils de Lyon, 69677, Bron, France

[7] Faculté de Médecine Lyon Est, Université de Lyon1, 69677, Lyon, France

Corresponding Authors: philippe.bertolino@lyon.unicancer.fr, rivals@lirmm.fr

Pituitary is a small endocrine gland located at the base of brain. The anterior part of the gland produces and secretes several hormones which play important roles in the growth, the development and the functions of numerous organs. Different subtypes of endocrine pituitary tumors exist. While somatic mutations, copy number alterations, cell-cycle dysregulations and epigenetics changes have been identified in most pituitary tumor-subtypes, the transformation and tumor-driving mechanisms in the gonadotroph subtype remain unknown [1]. Here, we want to explore whether the implication of the tumor microenvironment plays a role in gonadotroph adenoma based on its emerging roles as candidate actor and therapeutic target in pituitary tumors [2]. To that extent, our main objective is to characterize the composition and transcriptional landscape of gonadotroph tumors microenvironment through the use of single cell genomics.

To address our objective, we performed single cell RNA sequencing (scRNAseq) on surgically resected gonadotroph tumors. Single cells dissociated from tumors were encapsulated using a chromium controller (10X Genomics) prior to library generation and sequencing. During my internship, I develop a single cell RNA-seq (scRNA-seq) pipeline with conda and snakemake [3] to ensure an automatized and reproductible pipeline. The latter comprises three steps: (i) data acquisition (reads quality check, read trimming, demultiplexing and mapping with StarSolo), data cleaning (cells quality check, batch effect correction, and normalization) and cell subpopulation identification both with Seurat.

Here, we aim (i) at optimizing a scRNA-seq pipeline to explore the cellular composition of gonadotroph tumors, (ii) at determining if the microenvironment influences the tumorigenesis or if tumor cells have a genetic origin, and (iii) at pointing out new tumorigenesis factors/biomarkers in gonadotroph adenoma.

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