Universidad de Navarra
Facultad de Ciencias

Propuesta de Trabajo Fin de Máster
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MÁSTER EN MÉTODOS COMPUTACIONALES EN CIENCIAS

Proyecto Nº 4

Título: Endothelial Cell Heterogeneity in Adipose Tissues: Understanding Cell Population Dynamics in Response to Diet Using scRNA Sequencing

Departamento/ Laboratorio: Endothelial pathobiology and microenvironment at the Institut de Recerca contra la Leucèmia Josep Carreras, Barcelona

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Resumen:

The main aim of the Endothelial Pathobiology and Microenvironment Lab, led by Dr. Mariona Graupera, is to research and understand the physiology of blood vessels and their role in disease, with the goal of developing therapeutic strategies to target the vascular compartment. The laboratory focuses on understanding both physiological vessel growth and function, and the critical roles of vasculature in pathological contexts, including vascular anomalies, cancer, and obesity.

The endothelium, the innermost layer of blood vessels, exhibits remarkable heterogeneity across organs, acquiring specific phenotypes to meet each organ's needs. This versatility is crucial for organ homeostasis and regeneration. Adipose tissue, vital for energy storage, insulation, and cushioning, includes white adipose tissue (WAT), which stores energy, and brown adipose tissue (BAT), involved in thermogenesis. Obesity disrupts adipose tissue balance, leading to chronic illnesses such as cardiovascular disease, highlighting the link between blood vessels and adipose function.

Previous studies from our lab have shown that endothelial cells in the white adipose tissue of male mice proliferate after short-term high-fat diet (HFD) exposure (4 days), but not after prolonged exposure (2 weeks). Using a genetic mouse model with endothelial-specific deletion of the gene Pten, we observed enhanced proliferation and resistance to diet-induced obesity. However, the molecular and cellular characterization of these endothelial cells and their diet response is still incomplete. To address this, we will use single-cell RNA sequencing (scRNA-seq) to identify endothelial cell subpopulations and their specific functions, providing high-resolution gene expression profiles and insights into cellular diversity and dynamics.

Objective of the Master Thesis:

This thesis aims to understand endothelial cell dynamics in different adipose depots and how HFD alters these dynamics using scRNA-seq. The specific aims are:

1. Characterize Different EC Subpopulations:
    a. We have isolated ECs from 3 different adipose tissue depots: epididymal white adipose tissue (eWAT), inguinal white adipose tissue (iWAT), and interscapular brown adipose

tissue (iBAT). These 3 depots are to be compared in terms of EC subtypes in normal conditions.

2. Discover Depot-Specific Responses to High-Fat Diet:
    a. Compare EC responses to normal diet, HFD for 4 days, and HFD for 2 weeks, and analyze differential gene expression across the three depots.
3. Study the Effect of Sustained Proliferation:
    a. Investigate how Pten deletion in ECs affects adipose tissue response to diet and contributes to protection against diet-induced obesity.

By addressing these objectives, the thesis aims to provide a comprehensive molecular and cellular map of endothelial cells in various adipose tissues, elucidating their roles and interactions in response to diet and altered proliferative signature. This research will contribute to a deeper understanding of the vasculature of adipose tissues and the overall impact of endothelial cell plasticity in metabolic health.

Student Involvement:

The master student will be involved in the entire process of scRNA-sequencing data analysis, including sequencing quality control, mapping, count matrix production, single-cell quality controls, filtering, clustering, subsetting, population analysis, cell interaction analysis, and pseudobulk RNA-seq analysis. Additionally, the student will develop a comprehensive understanding of scRNA-seq analysis using R libraries such as Seurat, CellChat, NicheNet, and DESeq2. The student will also have the opportunity to work with a high-performance computing (HPC) system based on the Slurm workload manager and bash scripting.

It is important to note that the student will be involved in the computational part of the project but will also need to work closely with laboratory colleagues who develop the wet lab components to understand the underlying biology of the project. This collaboration will help the student develop the specific scientific criteria necessary to advance the project and address research questions. Moreover, the student will be trained and guided by the lab's computational biologist and will work closely with them

OPTATIVAS RECOMENDADAS

1. Análisis e interpretación de datos de alto rendimiento
2. Machine Learning I
3. Machine Learning II
4. Análisis de secuencias y bioinformática estructural