ADIPOSE TISSUE ADAPTATION TO ENVIROMENTAL PRESSURE

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Energy and nutrient fluctuations require finely regulated metabolic systems. Much of the development and evolution of these systems has taken place in the absence of pressures that we now experience as modern humans, including nutrient overload, lack of physical activity, and exposure to thermoneutral conditions and radiations. Overall, these environmental inputs ignite adaptive responses, which persist dramatically due to both increase in life expectancy and chronic lifetime exposure to stress signals. A metabolic pressure is then generated that, if continuous, may lead to metabolic and immunological failure, thus causing reduced tolerance to glucose and infections. In fact, biological responses are unable to cope with these challenges, and homeostatic systems gradually deteriorate.

White adipose tissues (WAT) developed a strong efficacy to buffer energy fluctuations by storing energy excess during postprandial states or release energy rich nutrients to meet the bioenergetics need of high oxidative tissues (e.g., heart, skeletal muscle) during physical exercise or fasting. Differently, brown adipose tissue (BAT) is main thermal rheostat in the body and dynamically adapts its metabolism upon cool temperature exposure. To face this environmental stress, catabolize circulating glucose and fatty acids to produce heat through uncoupled respiration. WAT and BAT are characterized by an heterogenous cell population including adipocytes, stromal cells and immune cells. Although tissue-resident cells synergically participate in maintaining tissue homeostasis, the mechanisms governing the cell crosstalk are still unclear.

Single-cell RNA sequencing (scRNA seq) technologies have greatly advanced the understanding of the cellular complexity and plasticity of many different tissues, as it enables the comparison of the transcriptomes of individual cells. This provides high-resolution maps of the dynamic cellular programs allowing us to answer fundamental biological questions on their function and evolution.
Furthermore, it provides an understanding of context-specific dependencies, namely the behavior and function that a cell has in a specific context, in the case of adipose tissue, understand the role of immune and nonimmune cells in conditions of response to environmental factors which can be crucial to understand some multifactorial disease, such as insulin resistance and type 2 diabetes (T2D).

In order to solve the paradigm of immunometabolic crosstalk in which some cells, such as adipocytes, communicate with immune cells and viceversa to regulate systemic metabolic homeostasis, my PhD project aims to achieve two main targets:

I) In the first two years, I will study the role of immune-non immune cell crosstalk in adipose tissues of mice and human exposed to modern environmental pressure such as overfeeding (db/db mice or high fat diet) and temperature changes (e.g., cold exposure or thermoneutrality);

II) From first to third year of the PhD program, I will create a single-cell atlas of differential gene expression between conditions and cell populations in adipose depots of human and murine samples.