Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: How do ovarian tissues turn dietary sugars into eggs?

Synopsis:

Because it is critical for animal fitness, the function of the germline needs to be tightly regulated, ensuring the reliable and timely production of high-quality oocytes. The production of oocytes by the germ line requires a high and balanced nutrient provision. Consistently I have previously shown that the gremline has an instructive role in regulating appetite for sugars, a nutrient required for oogenesis and oocyte production. When entering cells, dietary nutrients fuel a variety of metabolic pathways. Furthermore, the metabolic identity of cells is tightly linked to their functions, so different cell populations can have fundamentally different metabolic needs. **Which metabolic processes in the ovary impacts cell, tissue and animal physiology, namely reproduction and nutrient appetite, and how these are modulated by nutrient availability, are key questions that our lab will approach.**

Using Drosophila as a model organism, I have recently described the activity of the metabolic pathway pentose phosphate pathway (PPP) in the germline as a novel integration node in the regulation of animal physiology and reproduction. In early oogenesis the germline undergoes metabolic rewiring through the upregulation of the PPP, a process that is critical for oogenesis and requires the provision of dietary sugars. Furthermore, the PPP in the germline defines a new axis of communication with the fly's adipose tissue, which relays the information to the central nervous system (CNS) to regulate the appetite for sugar-rich food, which fuels PPP in the germline.

The ovaries are composed of a variety of different tissues, including germline and somatic cells. Somatic cells include muscle which surround the developing oocyte chains, trachea tubes that direct gas exchange close to the tissue and, in close contact with the germline, there are epithelial cells. These cells have very prominent roles in directing and assisting the development of the oocyte. If and how dietary sugars are also metabolized by these cells and whether this impacts oocyte development as not been investigated. The hypothesis which we aim to test is that specific populations of somatic cells have specific metabolic identities according to the functions they carry out within that tissue and that this is required for female fertility. To test this hypothesis we will investigate which molecular pathways involved in carbohydrate metabolism are active in the somatic tissues of the female reproductive system. Computational approaches and available datasets of single cell RNA sequencing will be used to investigate the expression levels of enzymes from different metabolic pathways. The functional relevance of these enzymes and metabolic pathways in female fertility will be evaluated experimentally by tissue-specific gene knockdowns combine d with tissue morphology visualization, and monitoring fertility by measuring egg number and quality.

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Bibliography: Carvalho-Santos, Z.; Cardoso-Figueiredo, R.; Elias, A. P.; Tastekin, I.; Baltazar, C.; Ribeiro, C. Cellular Metabolic Reprogramming Controls Sugar Appetite in Drosophila. Nat Metab. 2020, 2 (9), 958–973.