

Master Project Proposal

Title: Deciphering how ovaries talk to other organs to modulate animal physiology

Synopsis:

Within multicellular organisms, different cell populations can have fundamentally different metabolic needs. A challenging task faced by animals is that tissue-specific metabolic requirements need to be coordinated at the whole-organism level. To achieve this task, animals use extensive networks of inter-organ cross-talk, that allow the organism to maintain homeostasis. Inter-organ communication is at the core of most aspects of physiology. Female fertility has emerged as a highly relevant paradigm to study the integration of metabolism, inter-organ communication, and dietary nutrient availability. 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. Furthermore, the production of oocytes by the germline requires a high and balanced nutrient provision. **Which molecular processes in the germline impact animal physiology, what are the signaling molecules underlying the communication between the germline and other tissues, 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, required for the transcriptional regulation of a satiety factor, *fit*, in the fly's adipose tissue, the fat body (FB). In turn, *Fit* acts on the central nervous system (CNS) to regulate the appetite for sugar-rich food, which fuels PPP in the germline.

Communication between organs is often achieved via metabolites or peptides, which are secreted by one tissue into the circulating system to be delivered and act at the organ of destination. The fat body adipokine *fit*, which I showed to be regulated by the metabolic status of the germline, is expressed in the head FB supporting the hypothesis that signaling molecules are secreted from the ovaries into the hemolymph to act at a distance on the FB. The nature of the molecules mediating the communication between these two organs is still unknown. In this project we aim at testing the hypothesis that this communication is carried out by peptides secreted from the germline cells and act hormonally in the adipose tissue. To test this hypothesis we will use the genetic power of the *Drosophila* model system to screen a list of potential secreted peptides for roles in inter-organ communication and regulation of nutrient appetite. For this we will use a combination of approaches, including tissue-specific gene knockdowns and combine that with tissue morphology, and monitoring animal nutrient appetites using state of the art feeding behavior setups and fertility by measuring egg number and quality. The candidate peptides showing the strongest effects in nutrient appetite will be dissected further for their functions in regulating inter-organ communication.

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[Webpage of the group](#)

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.