Metabolism research using the Drosophila model organism (Lab projects in Molecular Biosciences)

ELIGIBILITY: 2.5 CGPA and 2+ years of study
DURATION: 8 weeks, 40h/week, *dates tbc*
LAB COST: 600 EUR
CREDITS: 12 ECTS
APPLICATION: Transcript of Records, Resume and, Motivation letter addressed to project supervisors. The documents must be uploaded on CIE's Student Exchange Portal (SEP) by **December 3, 2019**.

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We use obese and diabetic fly models to address the molecular mechanisms of energy metabolism in development, health, and disease. In this framework we offer three summers student projects:

Project 1: Developmental roles of storage lipid metabolism

The most commonly used energy storage form of living cells is the incorporation of free fatty acids into neutral lipid molecules, namely triacylglycerols and steryl esters. These molecules are then stored in specific organelles called lipid droplets, the fat depots of the cell (1–3). In order to balance energy demand and excess energy during various stages of growth or development, cells mobilize or synthesize storage lipids in a highly controlled manner. The life cycle of Drosophila melanogaster is characterized by two non-feeding developmental stages i) embryogenesis i.e. from a single cell to the larval stage and ii) metamorphosis i.e. from the larval to the adult body plan (4). During these states of development, the organism completely relies on internal reorganization events and autonomous energy supply.

Our research focuses on storage lipid breakdown, that is mainly conducted via the Drosophila Brummer lipase (5), homolog of the mammalian ATGL lipase. We combine in vivo experimental approaches such as food intake measurements, microcalorimetric analyses, starvation and aging experiments with biochemical approaches that include lipase activity assays, state of the art lipidomics and immunoblotting. Using light sheet microscopy, we will perform life cell imaging during embryogenesis to visualize potential lipid metabolism checkpoints pivotal for development and confirm potential developmental derailments via immunofluorescence confocal laser scanning microscopy.

The summer student will be introduced into Drosophila lipid metabolism and will perform fly genetics and a variety of the aforementioned methods under supervision to enhance the understanding of pivotal roles of storage lipid mobilization during the life cycle of Drosophila.

Further reading:

1. Welte, M. A. Expanding roles for lipid droplets. Curr. Biol. 25, R470-81 (2015).
2. Walther, T. C. & Farese, R. V. Lipid Droplets and Cellular Lipid Metabolism. Annu. Rev. Biochem. 81, 687–714 (2012).
3. Heier, C. & Kühnlein, R. P. Triacylglycerol metabolism in drosophila melanogaster. Genetics 210, 1163–1184 (2018).
4. Hales, K. G., Korey, C. A., Larracuente, A. M. & Roberts, D. M. Genetics on the fly: A primer on the drosophila model system. Genetics 201, 815–842 (2015).
5. Grönke, S. et al. Brummer lipase is an evolutionary conserved fat storage regulator in Drosophila. Cell Metab. 1, 323–330 (2005).

Project 2: Functional diversification of organ-associated fat depots

Lipids are a multifaceted class of molecules with pivotal functions in cell biology and physiology. Lipids serve as energy reserves, as building blocks of biological membranes and as hormones. Disturbed lipid metabolism underlies a plethora of human diseases, e.g. obesity, type 2 diabetes, and neurodegeneration. We use Drosophila melanogaster as a model system to study central aspects of lipid biology. In this summer student project we will examine functional differences of distinct storage lipid depots in Drosophila.

The major storage lipid is triacylglycerol (TAG). TAG is sequestered in globular cellular organelles termed lipid droplets. Specialized cells termed adipocytes accumulate large amounts of lipid droplets and store the majority of organismal TAG. Collectively, adipocytes form the so-called insect fat body, which is equivalent to the mammalian adipose tissues. Fat body is found in all major body segments of Drosophila and constitutes distinct TAG depots in the vicinity of organs such as brain, intestine or ovaries. However, if these depots have different functions is largely unknown.

We will use a combination of state-of-the-art techniques to characterize possible functional differences between different TAG stores. In the first phase of the project we will examine (1) the molecular lipid composition, (2) the lipid turnover rates, and (3) the morphology of different TAG depots. The second phase will focus on genetics and aims to elucidate the role of different enzymes in the metabolism of different TAG depots. The applicant will be introduced to lipidomics approaches, confocal laser scanning microscopy, genetic tools and metabolic tracer studies.

Project 3: Mechanisms of insulin resistance

We use Drosophila larvae that are fed a high-sugar diet to model obesity and type 2 diabetes (6-7). It is well established that caloric excess increases the risk for developing metabolic disease, but little is known about the molecular links between the two. We use Drosophila to study the signaling network underlying obesity-driven type 2 diabetes.

Further reading:

1. Musselman, L. P.; Fink, J. L.; Narzinski, K.; Ramachandran, P. V.; Hathiramani, S. S.; Cagan, R. L.; Baranski, T. J., A high-sugar diet produces obesity and insulin resistance in wild-type Drosophila. Dis Model Mech 2011, 4 (6), 842-9.
2. Pasco, M. Y.; Leopold, P., High sugar-induced insulin resistance in Drosophila relies on the lipocalin Neural Lazarillo. PLoS One 2012, 7 (5), e36583.