Ronald KÜHNLEIN (ORCID: 0000-0003-1448-4117): Identifying the Drosophila Adipokinetic hormone-dependent triacylglycerol lipase

Research interest and scientific background: Swarming migratory locusts are one of the ten Biblical Plagues, with recurrent outbreaks until today. The long-distance flight of these insects is fueled by body fat (triacylglycerol; TG) stores, which become mobilized on demand by lipolysis. Some 50 years ago Adipokinetic hormone (Akh), a functional analogue of mammalian glucagon, was identified to be the key catabolic hormone to trigger insect lipolysis. Until now, however, there is no conclusive *in vivo* evidence concerning the molecular identity of the Akh-dependent TG lipase (Akh-TGL) in any insect species. Our earlier work in the model insect Drosophila demonstrated a dual control of storage lipid mobilization[1]: by the Akh signaling pathway and by the Brummer TG lipase, the fly homolog of the central mammalian Adipose triglyceride lipase (ATGL)[2]. Our characterization of fly mutants, which lack Brummer lipase[3], the Akh hormone[4], or the Akh receptor[1] set the stage for the genetic identification of Akh-TGL and its subsequent characterization. This project will identify a long-standing "missing link" in insect energy homeostasis control and promises to disclose novel targets for intervention with reproduction and physiological fitness of insect pests. As factors and mechanisms of storage lipid breakdown are evolutionarily conserved, identification of Drosophila Akh-TGL bears the potential to provide novel insights in mammalian lipid metabolism.

Approach and methods: The *Drosophila Akh-TGL* gene will be identified by a genetic in vivo RNAi screen. The corresponding Akh-TGL protein will be subjected to structure-function analysis and *in vitro* biochemical characterization. Akh-TGL mutant Drosophila and transgenic flies will be generated for in vivo functional analyses including regulatory network reconstruction. The general validity of this *Drosophila* model in insects will be addressed in migratory locusts.

Affiliation: The student will work at the Institute of Molecular Biosciences at the University of Graz. This project is directly connected to the doc.fund Molecular Metabolism.

References:

1) Grönke, S., Müller, G., Hirsch, J., Fellert, S., Andreou, A., Haase, T., Jäckle, H., Kühnlein, R.P. Dual lipolytic control of body fat storage and mobilization in Drosophila ***PLoS Biology*** 2007, *5* (6), e137. DOI: 10.1371/journal.pbio.0050137
2) Zimmermann, R., Strauss, J. G., Haemmerle, G., Schoiswohl, G., Birner-Gruenberger, R., Riederer, M., et al. (2004). Fat mobilization in adipose tissue is promoted by adipose triglyceride lipase. ***Science*** 2004, *306* (5700), 1383–1386. DOI: 10.1126/science.1100747
3) Grönke, S., Mildner, A., Fellert, S., Tennagels, N., Petry, S., Müller, G., Jäckle, H., Kühnlein, R.P. Brummer lipase is an evolutionary conserved fat storage regulator in Drosophila. ***Cell Metabolism*** 2005, *1* (5), 323-330. DOI: 10.1016/j.cmet.2005.04.003
4) Galikova, M., Diesner, M., Klepsatel, P., Hehlert, P., Xu, Y., Bickmeyer, I., Predel, R., Kühnlein, R.P. Energy Homeostasis Control in Drosophila Adipokinetic Hormone Mutants. ***Genetics*** 2015, *201* (2), 665-683. DOI: 10.1534/genetics.115.178897