

Institute of Zoology and Biomedical Research

Topic: **Interactions between circadian and immune systems in *Drosophila***

Name of supervisor: prof dr hab. Elzbieta Pyza

elzbieta.pyza@uj.edu.pl

Background information

Insects have the innate immune system, which includes several mechanisms protecting them against various pathogens. In *Drosophila* the following eight classes of antibacterial protein have been identified: Defensin (Def), Drosocin (Dro), Cecropins (Cec), Attacin (Att), Dipterocins (Dpt), MPAC (post-translationally modified pro-domain of AttC), Drosomycin (Drs), Metchnikowin (Mtk) and Andropin (Anp). Defensin (Def) is active against Gram-positive bacteria. Drosocin (Dro), Cecropins (Cec), Attacins (Att), Dipterocins (Dpt) and MPAC (truncated post-translationally modified pro-domain of AttC) are active against Gram-negative bacteria. Cecropins are highly effective against most of the Gram-negative strains. It has been speculated that the helix-forming capability of Cec, in contact with lipidic components of the bacterial membrane, results in a general disintegration of the membrane structure and lysis of bacteria. Dro binds to the multi-helical lid above the substrate-binding pocket of bacterial heat shock protein (DnaK) leading to the inhibition of chaperone-assisted protein folding. Dpt increases the permeability of the outer and inner membranes of bacteria. Att interferes with the transcription of *omp* gene that is involved in synthesis of porines, proteins of membrane channels. Drosomycin (Drs) and Metchnikowin (Mtk) are efficient proteins against fungal infection. Andropin (Anp) is the only antibacterial protein that is not induced after pathogen infections, but it is expressed during mating in males to protect the reproductive tract against infection. The expression of these proteins is stimulated during various infection but also by internal and external factors. One of them is an input from the circadian clock. The regulation of antibacterial protein expression will be studied during 24 h period under various light conditions to learn an effect of circadian inputs and light on immune responses. Moreover, disruption of the clock may lead to diseases and may decrease longevity. It is also possible that environmental factors (UV light, temperature) and food (the presence of anti-oxidants) may decrease or increase the effect of the clock on immune responses. The aim of this project is to learn about interactions between the innate immune system, the circadian clock and environmental factors affecting the immune system or the clock. The project will test a hypothesis that the clock, by rhythmic expression of antibacterial proteins at specific time, delays aging and increases survival.

The main question to be addressed in the project:

The effect of the circadian clock on the innate immune system regulation and its possible role in the organism survival.

Information on the methods/description of work:

In the project transgenic lines of *Drosophila* will be used to change expression of genes encoding antibacterial proteins as well as mutants of clock genes. Antibacterial protein and their genes will be studied by Western blotting and RT-PCR, respectively. Survival and behavioral tests will be used to study aging and longevity of flies.

Special requirements from the student – optional

Place/name of potential foreign collaborator – optional:

Dr. R. Costa, University of Padova, Italy

At least one reference to the relevant paper:

Damulewicz, M., Loboda, A., Jozkowicz, A., Dulak J., Pyza E. (2017): Interactions between the circadian clock and heme oxygenase in the retina of *Drosophila melanogaster*.

Mol. Neurobiol. 54:4953-4962. DOI: 10.1007/s12035-016-0026-9.

Damulewicz, M., Loboda, A., Jozkowicz, A., Dulak J., Pyza E. (2017): Haeme oxygenase protects against UV light DNA damages in the retina in clock-dependent manner. Sci. Rep. 7:5197. DOI:10.1038/s41598-017-05418-6.