Drosophila melanogaster is considered as a model organism in the research aimed at understanding the genetic and molecular basis of organism development from the unicellular zygote to the mature multicellular form. This is due to the fact that many of the basic mechanisms and pathways controlling development have been preserved during the evolution. Therefore, many of the genes playing the key role for *D. melanogaster* development, are also present in human genome (including 75% of genes responsible for human diseases). It is worth to emphasize, that previous studies carried out on the *D. melanogaster* organism have contributed to key achievements in biology and medicine. One of good examples is the explanation of the molecular mechanisms controlling the circadian rhythm (awarded with The Nobel Prize 2017). Further studies on the molecular mechanisms of development in *D. melanogaster* will certainly contribute to new achievements. It underlines the importance of this project for science and medicine.

Insect development is controlled by the coordinated action of two hormones: 20-hydroxyecdysone (20E) and juvenile hormone (JH). The 20E receptor and the mode of its action are well known. The identity of the JH receptor has been sought for a long time. In 2011 it was reported, that JH receptor is the Methoprene tolerant (Met) protein. Met binds JH and is important for the function of JH in preventing the precocious differentiation during *D. melanogaster* development. The deletion of *met* gene is lethal to most studied species of insects. What is interesting, in *D. melanogaster* exists Met paralog, known as Germ cell-expressed protein (Gce), ensuring the survival of *met* gene null mutants. It was shown, that the functions of Met and Gce are not fully redundant and proteins exhibit tissue specific distribution. This fact has become the main inspiration for our project.

Bioinformatic analyses assign Met and Gce to the family of bHLH-PAS (*basic helix-loop-helix/Per-Arnt-Sim*) transcription factors. The bHLH-PAS family members contain three characteristic and highly homologous domains, bHLH, PAS-A and PAS-B. The similarity between the Met and Gce primary structures is limited to these defined domains, while their long C-terminal fragments (MetC, GceC, respectively) show significant differences. This fact seems to be very significant, since the C-termini of bHLH-PAS transcription factors play a crucial role in regulation of these proteins activity and the action of their complexes. It is worth to emphasize, that there are no available reports (except of our publication concerning MetC) concerning bHLH-PAS proteins structure and the relationship between the structure and the function.

The results of *in silico* analysis indicate that the MetC and GceC may exhibit properties of intrinsically disordered regions (IDRs). Currently, inherently disordered proteins (IDPs) and IDRs focus a great interest of researchers. Both are characterized by the lack of the stable tertiary structure. Despite this they are still fully functional. The structural lability and the possibility of adopting different conformational states seems to be advantageous in molecular recognition processes and allows IDPs to interact with several partners.

The main research hypothesis of the project is based on the assumption, that the structural differences between the C-terminal fragments of Met and Gce are crucial for the distinction between their functions and subcellular localization during *D. melanogaster* development. The aim of our studies is to analyze the structure of the GceC fragment and to refer the obtained results to the published structural data for MetC [Kolonko M. et al., 2016]. We plan to verify GceC and MetC ability to interact with potential partners (FTZ-F1 nuclear receptor and regulatory protein 14-3-3). Such interactions could significantly affect functions of these proteins, defining their subcellular location, structure, and activity.

The results of this project can contribute to a better understanding of the molecular basis of the functions of Met and Gce C-terminal fragments. The molecular characterization of GceC as an IDR and the evaluation of the results in the light of the data published for MetC, allow us to define structural properties, that may be responsible for the functional distinction of these closely related transcription factors. The obtained results will give a better insight into the structure-function properties, as well as the function and regulation of IDR.

Confirmation of the research hypothesis will require the application of several stages. First stage will be the obtainment of the homogenous GceC sample. The aim of following analyzes will be the structural characterization of GceC. These studies will include hydrodynamic analysis, structure disordered analysis and structure modeling. Obtained results will be compared with the published structural data for MetC. All similarities and differences will be thoroughly studied. In the next stage of the research, the ability of MetC and GceC to interact with potential protein partners: FTZ-F1 and 14-3-3 will be examined. The obtained results will allow to connect the differences in Gce and Met structure and possible interactions with partners, with the differences in their functions.