Behavioral Genetics of Pain Sensation in Fruit Flies

Karen Sanford（筑波大学 生物学類）　　指導教員：古久保-徳永 克男 (筑波大学 生命環境系)

Background and Purpose

Nociception is the response of the nervous system to noxious or potentially damaging stimuli. In this process, sensory neurons called nociceptors are activated by chemical, mechanical, or thermal stimuli. This detection and processing of information alerts organisms of possible threats and results in the sensation of pain in humans. While nociception is essential for survival, persistent pain has adverse effects on life. Therefore, studying the mechanisms behind nociception is important to better understand sensory response systems and treat pain.

Drosophila melanogaster is an excellent model system due to its simple structure and genetic likeness to humans; fruit fly nociceptors have been shown to be functionally and morphologically similar to those of vertebrates[1]. Neuropeptides are short amino acid sequences associated with numerous physiological processes, including pain modulation. Their systems are evolutionarily well-conserved, and past studies suggest that neuropeptides may play significant roles in mammalian nociception. However, little is known about how neuropeptides regulate nociception.

This study aims to characterize and elucidate the mechanism of action of three neuropeptides which may be implicated in nociception in *Drosophila* larvae. In this paper, the mutant larvae will be referred to as mutants (M) 1, 2, and 3.

Methodology

Thermal Nociception Assay

Drosophila larvae exhibit a highly stereotypical rolling response to harmful stimuli, known as nocifensive escape locomotion (NEL)[2]. This avoidance behavior is specific to noxious stimuli and thus can be used as an indicator of nociception. In this behavioral assay, wandering third instar larvae were collected from vials using distilled water. Larvae were placed on a dish with a thin layer of water. Using a thermal probe, heat was applied to the abdominal regions (A4-A6) of larvae and latency until complete lateral rolling (360° or more) was recorded. The thermal probe was set to 42°C for M1 and M2 larvae as they were previously found to be hypersensitive to heat, and 45°C for M3a and M3b larvae, which were insensitive to heat. All experiments were carried out at 25°C room temperature.

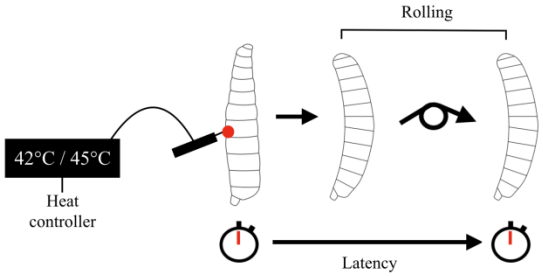

Fig. 1: Diagram of methodology

Results and Discussion

Results were consistent with previous findings that M1, M2, and M3a/b larvae exhibit abnormal behavior in response to noxious heat. M1 and M2 larvae are hypersensitive, and M3a/b larvae are insensitive. Lower latency was seen in M1 and M2 larvae compared to control larvae at 42°C, and higher latency was seen in M3a/b larvae compared to control larvae at 45°C.

To confirm that the hypersensitivity and insensitivity to noxious heat was due to the mutations, deficiency experiments were conducted. Unfortunately, no deficiency larvae were available for M2. Deficiency tests showed that the hypersensitivity of M1 and insensitivity of M3a/b were due to the genetic mutations. Graphs and remaining findings will be discussed in the presentation.

Conclusion

Results raise the possibility of these neuropeptides' association with thermal nociception. Research is required to further reveal the mechanisms behind nociception, including the possible roles of other neuropeptides in the regulation of nociception.

References

1. Milinkeviciute, G. Drosophila as a tool for studying the conserved genetics of pain. *Clinical Genetics*: 82. October 2012. Pages 359-366.
2. Tracey et al. painless, a Drosophila Gene Essential for Nociception. *The Cell*: 113. 18 April 2003. Pages 261-273.