（学位第３号様式）

学 位 論 文 要 旨

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題　目	Analysis of stress response in insects (昆虫のストレス応答性の解析)

All organisms are exposed to a variety of environmental stresses. These stressors often cause critical damages to organisms, and sometimes kill them. Organisms have evolved various mechanisms to overcome stresses and survive under stressful environments. Acclimation is one of potential mechanisms in the development of tolerance to various environmental impacts. Although this mechanism is very important for all living organisms including human, the molecular mechanisms underlying its induction largely remains ambiguous.

I first focused on reactive oxygen species (ROS) to analyze insect stress responses using armyworm *Mythimna separata* because the recent research outcomes concerning the role of ROS in cellular functions has changed the last few decades: the importance of ROS has been well acknowledged although ROS had been recognized for a long time as a negative agent that causes toxic impacts on biomolecules such as proteins, lipids, and nucleic acids. Measurement of plasma ROS concentrations showed a small peak (at about 70 μM) after lethal heat stress in armyworm larvae previously acclimated to high temperatures. In contrast, lethal stress-induced continuous increase in ROS was observed in non-acclimated larvae. I showed that microinjection with 0.44 μmol/larvae H_2O_2, which brings the plasma ROS concentration up to approximately 70 μM, induced thermotolerance in armyworm larvae. Microinjection with 0.44 μmol/larvae H_2O_2 also increased expression levels of stress related genes such as *SOD*, *Catalase*, and *heat shock protein 70* (*HSP70*) in armyworm larvae, indicating that only a moderate increase in plasma ROS level has positive physiological effects on insects. I found that two insect cytokines (growth blocking peptide (GBP) and stress responsive peptide (SRP)) regulate each other: GBP upregulates SRP expression and SRP exert negative feedback control on GBP expression, which contributes to maintaining homeostasis under stress conditions. Furthermore, I found that stress conditions increased N-acetyltyrosine (NAT) concentrations in the plasma of armyworm larvae. NAT was demonstrated to induce acclimation-like states in armyworm and *Drosophila melanogaster* even without pre-stress treatment. NAT induced FoxO translocation into the nuclei, which elevates expression of antioxidant enzyme genes. Thus, it was strongly suggested that NAT plays an important role in inducing acclimation in insects as a trigger.

I finally studied the molecular mechanism underlying organismal death induction using *Drosophila melanogaster*. Comprehensive gene expression analysis (RNAseq) showed a specific up-regulation of *Phaedra1* (*Phae1*) during induction of organismal death under lethal stress. Ubiquitous *Phae1* overexpression using *actin-Gal4* driver resulted in embryonic lethality without larval hatching. Central nerves system (CNS) specific knockdown of *Phae1* showed enhanced thermotolerance, suggesting that *Phae1* is a gene closely associated with the induction of stress-dependent organismal death. I demonstrated stress-induced elevation of fluorescence in the transgenic fly larvae carrying *Phae1 promoter*-GFP gene, which suggests that this transgenic fly line must be powerful tool for basic researches revealing a precise mechanism of dying process of organism and for applied researches that hunts novel anti-stress supplements as well as new insecticidal agents.