（学位第３号様式）

学 位 論 文 要 旨

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題　目	Genetic analysis of virulence in the entomopathogenic bacterium *Photorhabdus luminescens* using model nematode *Caenorhabditis elegans* (モデル線虫 *Caenorhabditis elegans* を用いた昆虫病原性細菌 *Photorhabdus luminescens* が発揮する病原性の遺伝学的解析)

The Gram-negative bacterium *Photorhabdus luminescens* symbiotically associates with entomopathogenic nematode *Heterorhabditis bacteriophora*. Although *P. luminescens* is highly virulent to many insects and nonsymbiotic nematodes, the complete picture of its virulence still remains unclear. The combination of genetically tractable free-living nematode *Caenorhabditis elegans* and pathogens has contributed to our understanding of virulence mechanisms and innate immune systems. The purpose of this study is to demonstrate the virulence mechanisms of *P. luminescens* using model nematode *C. elegans*.

Firstly, the pathogenicity of *P. luminescens* against *C. elegans* has been described in detail. Because of a transparent body, the collapse of the intestinal cells of *C. elegans* was observed when fed on *P. luminescens*. Observation of *gfp*-tagged cells revealed that *P. luminescens* killed *C. elegans* without colonization of the intestinal lumen. Secondly, I examined the activities of conserved signaling pathways involved in innate immunity, including the p38 mitogen-activated protein kinase (MAPK) and insulin/IGF-1 signaling pathways of *C. elegans*, during the ingestion of *P. luminescens*. Using reverse genetic approaches, the p38 MAPK pathway was activated and required for the host defense against *P. luminescens*. In contrast, the innate immune responses via insulin/IGF-1 signaling pathway were rather inactivated by *P. luminescens* through the overexpression of an insulin-like gene. In addition, I obtained virulence-attenuated *P. luminescens* mutants against *C. elegans* through the screening of a transposon-mutagenized library. One of the mutants had a mutation in *pdxB* that encodes erythronate-4-phosphate dehydrogenase, which is required in *de novo* vitamin B_6 biosynthesis pathway. *pdxB* mutants were growth deficient in nutrient-poor medium and less virulent against *C. elegans*. However, when *pdxB* mutants were supplemented with vitamin B_6, their growth in minimal medium and virulence against *C. elegans* were restored. Lastly, I confirmed that the mutation in *pdxB* caused a reduction in insecticidal activity against *Zophobas morio*. These results suggest that production of appropriate amounts of vitamin B_6 is critical for the pathogenicity of *P. luminescens*.

The present study demonstrated the suitability of *C. elegans* as a model host to analyze the pathogenicity of *P. luminescens*, and it is hoped that this model system will contribute to the complete elucidation of the virulence mechanisms of *P. luminescens*.