A12

# Host Range Factor 1 (HRF-1) from *Lymantria dispar* Nucleopolyhedrovirus (NPV) is an Essential Viral Factor Required for NPV Productive Infection of Ld652Y Cells Derived from *L. dispar*

**Hiroki Ishikawa[1], Motoko Ikeda[2] and Michihiro Kobayashi[1]**

*[1]Laboratory of Biodynamics and [2]Laboratory of Sericulture and Entomoresources, Graduate School of Bioagricultural Sciences, Nagoya University, Chikusa, Nagoya 464-8601, Japan*

Nucleopolyhedroviruses (NPVs), members of the family Baculoviridae, generally exhibit a narrow host range property. Molecular mechanisms underlying the host specificity determination of NPV have not been well-defined. Recent studies have identified several viral genes that are involved in host specificity determination of *Autographa californica* multicapsid NPV (AcMNPV) in insect cell systems. One of these genes, *hrf-1*, from MNPV of the gypsy moth, *Lymantria dispar*, (LdMNPV) was identified as a factor that promoted AcMNPV replication in a nonpermissive cell line *L. dispar* Ld652Y. HRF-1 precludes global protein synthesis shutdown in Ld652Y cells that is triggered by AcMNPV infection. Analysis of whole genome sequences from several NPVs revealed that *hrf-1* was specifically encoded by the genomes of LdMNPV and *Orgyia pseudotsugata* MNPV that were able to replicate to high titers in Ld652Y cells.

We have found that Ld652Y cells infected with *Hyphantria cunea* NPV (HycuNPV) undergo severe apoptosis, displaying apoptotic bodies, characteristic DNA fragmentation and increased caspase activity. In HycuNPV-infected Ld652Y cells, a considerable amount of viral DNA was synthesized, yielding no detectable budded virions (BVs) and polyhedrin. Studies with a pancaspase inhibitor, Z-VAD-FMK, demonstrated that restricted HycuNPV replication in Ld652Y cells was not due to apoptosis but was likely due to global protein synthesis shutdown that could be restored by HRF-1. Our data showed that HRF-1 precluded global protein synthesis shutdown and promoted progeny BV production in HycuNPV-infected Ld652Y cells. Furthermore, it was found that *Bombyx mori* NPV and *Spodoptera exigua* MNPV, which produced viral DNA in nonpermissive Ld652Y cells, were able to replicate with the aid of HRF-1, while replication of *Spodoptera litura* MNPV, which produced no detectable amount of viral DNA in Ld652Y cells, was not rescued by HRF-1. These results suggest that

HRF-1 is required for an event(s) that occurs after viral DNA replication to yield progeny virions in NPV-infected Ld652Y cells.

It is thus concluded that global protein synthesis shutdown is the major factor that restricts NPV replication in Ld652Y cells and that HRF-1 is a crucial viral factor that copes with this antiviral mechanism operating in NPV-infected Ld652Y cells.