S6

Baculovirus Host Specificity and Cellular Antiviral Response against Baculoviruses: Identification of a Baculovirus Gene That Restricts *Bombyx mori* Nucleopolyhedrovirus Replication in a Permissive *B. mori* Cell Line

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Nucleopolyhedroviruses (NPVs), members of the family Baculoviridae, are enveloped, rod-shaped, large insect-specific viruses that contain a double-stranded, covalently closed circular DNA genome of 80-180 kbp. NPVs have been isolated from more than 520 insect species spanning eight different orders, and respective NPVs isolated from different species of insect generally exhibit a very narrow host range property, causing the lethal infection only in insect species from which the NPVs are originally isolated and closely related insect species.

We have employed five different NPVs and eight different insect cell lines in combination and characterized the interactions between NPVs and cell lines. On the basis of our data on viral DNA replication, viral structural protein synthesis, budded virion (BV) yield, polyhedrin synthesis and cytopathology, it was demonstrated that each of these different NPVs established unique interactions with different cell lines. These interactions include productive replication leading to cell lysis and varying types of abortive replications that result from the defects in certain biological events relevant to viral replication, including defective viral DNA replication and defective viral gene expressions that are temporally distinct. Alternatively, abortive NPV replications are attributed to apoptosis induction and global protein synthesis shutdown, which represented two major cellular defense responses against baculovirus infection.

We have previously found that co-infection of BmN-4 cells (*B. mori*) with *B. mori* NPV (BmNPV) and *Hyphantria cunea* NPV (HycuNPV) results in restricted replication of BmNPV that is able to replicate to a high titer in BmN-4 cells. Employing such experimental system, we have recently identified a HycuNPV-encoded gene, *hycu-ep32*, that is responsible for the

restricted BmNPV replication in permissive BmN-4 cells. HycuNPV mutant defective in *hycu-ep32*, vHycu ep32, is readily generated, indicating that *hycu-ep32* is nonessential for HycuNPV replication in permissive SpIm cells. In non-permissive BmN-4 cells, on the other hand, infection with HycuNPV results in severe global protein synthesis shutdown, while vHycu ep32 did not cause any specific protein synthesis shutdown. These results indicate that Hycu-EP32 serves as a signal that triggers cellular defense response mediated by protein synthesis shutdown during HycuNPV infection of non-permissive BmN-4 cells.