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12. The AcMNPV genome: Gene content, conservation, and function

The *Autographa californica* nucleopolyhedrovirus (AcMNPV) was originally described in the early 1970s (1) and research on its genetics began later in that decade. This was stimulated by the facility with which the virus replicated in cells from *Spodoptera frugiperda* (2) and *Trichoplusia ni* (3). Subsequently, this led to the development of technology for the deletion of genes (4, 5), and allowed for targeted studies on the function of specific genes, particularly if the deletion or mutation of the target gene was not lethal to the virus. The publication of the genome sequence of AcMNPV (6) was a landmark in the investigation of this virus because it put all previous and future investigations into context. It also revealed genes that are shared with other organisms, and provided the basis for understanding baculovirus diversity. Subsequently, the development of the bacmid system, which allowed for the production of recombinants via transposition of recombinant plasmids into the AcMNPV genome incorporated into a bacterial artificial chromosome, allowed for manipulation of the whole AcMNPV genome in bacteria (7). The adaptation of this technology to making targeted deletions provided a method for constructing baculovirus gene knockouts in bacteria that could then be investigated via transfection into insect cell lines (8). The modification of this technology using a lambda red recombinant system (9) allowed for the more efficient production of knockouts (10). This has resulted in a proliferation of studies on AcMNPV essential genes that were previously difficult to investigate because knockouts were lethal and they could not be readily generated without the production of complementary cell lines. With bacmid knockouts the function of the target gene can be inferred from the examination of cells transfected with DNA of the mutant. The adaptation of similar bacmid systems for other baculovirus genomes has allowed for parallel studies on these viruses. Concomitant with the development of techniques for investigating gene function has been a proliferation of complete genome sequence data for many baculoviruses. Because of the widespread use of AcMNPV, not only for fundamental investigations on gene function, but also because of its use as an expression vector, I have attempted to annotate the AcMNPV genome in terms of understanding the function of each of the genes.

Adjustments to the AcMNPV genome sequence: There are approximately 150 orfs

This analysis is based on the first AcMNPV genome to be sequence, the C-6 strain (6). Several regions of the AcMNPV genome have been re-sequenced by one or more laboratories. This, in combination with genome sequences of variants of AcMNPV that have become available including the commonly used E2 strain (11), has revealed revisions that should be incorporated into the sequence. The following summarizes the physical corrections to the AcMNPV genome that have been described. The original orfs Ac20/21, 58/59, 106/107 and 112/113 (6) should be combined into single orfs. In addition, resequencing also indicated that Ac17, 52, 131, and

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143 are longer than originally reported (12). The total number of orfs reported for AcMNPV was originally calculated to be 154; this adjustment reduces it by 4. However, the discovery of lef-10 (Ac53a), which was missed in the original annotation because of its significant overlap with the 5' region of an adjacent gene (Ac54) (13), adds an additional orf. Therefore, there appear to be 151 orfs present in the genome based on the original criteria of an orf comprising 50 amino acids. However, Ac85 (53 aa) is only found in two other NPVs that are variants of AcMNPV (PlxyNPV) (14) and RoMNPV (12). Two orfs, Ac97 (56 aa) and Ac140 (60 aa), are only present in AcMNPV. Of these three orfs, only Ac97 was predicted to be preceded by transcriptional regulatory sequences (6). Although these three orfs may not be valid, others may be present that have not yet been detected. Therefore, it would appear that there are 'about' 150 orfs in the AcMNPV genome.

In this review, I have attempted to include pertinent information on the function of all the orfs present in the AcMNPV genome. This is not an exhaustive review, but an attempt to infer function from either actual experimentation on the AcMNPV gene or to homology from related viruses. A significant proportion of the data included comes from the *Bombyx mori* NPV (BmNPV). It is closely related to AcMNPV and is the second most studied NPV and a complete study based on the generation of BmNPV bacmid knockouts of all its open reading frames has been described (15). In addition, comparisons with orfs from Helicoverpa armigera SNPV, a group II alphabaculovirus are also included because it is being intensively investigated in a number of labs. The annotation for this chapter is based on Accession Numbers NC_001623 (AcMNPV C-6 strain - originally L22858), L33180 (BmNPV), and AF271059 (HearSNPV).

Table 1 lists all the genes that have been named in the AcMNPV genome followed by the orf number. It cannot be emphasized enough how important it is to incorporate both orf numbers and the AcMNPV homolog (if present) into any description of a baculovirus gene no matter which baculovirus it is from. Without this reference, it is difficult, if not impossible, to put reports into any sort of perspective. Following the index is a review of what I could find regarding all the genes in the AcMNPV genome. This is not a complete review of these genes but focuses particularly on AcMNPV. When a report of the homolog from another virus is relevant, that material is also included.

Table 1. Index to named AcMNPV genes/gene products from the C-6 strain (6).

ARIF1 (Actin rearranging factor1)	**Ac20/21**
Alkaline nuclease	***Ac133**
Apsup	**Ac112/113**
BRO (Baculovirus repeated orf)	**Ac2**
BV/ODV-E26	**Ac16**
BV/ODV-C42	***Ac101**
Calyx, polyhedron envelope	**Ac131**
Cathepsin	**Ac127**
ChaB homolog	**Ac59**
ChaB homolog	**Ac60**
Cg30	**Ac88**
C42	**Ac102**
Chitinase	**Ac126**
Chondroitinase, odv-e66	**Ac46**
Conotoxin like (Ctl)	**Ac3**

Table 1. continued from previous page.

DA26	**Ac16**
DNA primase	**Ac14**
Desmoplakin-like	***Ac66**
DBP (DNA binding protein)	**Ac25**
DnaJ domain protein	**Ac51**
DNA polymerase	***Ac65**
EGT	**Ac15**
ETL (PCNA)	**Ac49**
ETM	**Ac48**
ETS	**Ac47**
Exon-0	**Ac141**
F (fusion protein homolog)	**Ac23**
FGF (fibroblast growth factor)	**Ac32**
FP (few polyhedra), fp-25k	**Ac61**
Fusolin (gp37)	**Ac64**
GP16	**Ac130**
GP37	**Ac64**
GP41	**Ac80**
GP64	**Ac128**
Gta (global transactivator)	**Ac42**
Hcf-1 (host cell factor 1)	**Ac70**
Helicase, p143	***Ac95**
He65	**Ac105**
Histodinol phosphatase	**Ac33**
Homologous regions	**Hrs** (see end of chapter)
Iap-1	**Ac27**
Iap-2	**Ac71**
Ie1	**Ac147**
Ie0	**Ac147-0**
Ie2	**Ac151**
J domain	**Ac51**
Lef1	***Ac14**
Lef2	***Ac6**
Lef3	**Ac67**
Lef4	***Ac90**
Lef5	***Ac99**
Lef6	**Ac28**
Lef7	**Ac125**

Table 1. continued from previous page.

Lef8	***Ac50**
Lef9	***Ac62**
Lef10	**Ac53a**
Lef11	***Ac37**
Lef12	***Ac41**
Me53	**Ac139**
MTase (methyl transferase)	**Ac69**
Nudix	**Ac38**
ODV-E18	***Ac143**
ODV-E25, p25, 25k	***Ac94**
ODV-EC27	**Ac144**
ODV-E56, Pif-5	***Ac148**
ODV-E66	**Ac46**
P6.9	***Ac100**
P10	**Ac137**
P11	**Ac145**
P12	**Ac102**
P15	**Ac87**
P18	**Ac93**
P24	**Ac129**
P26	**Ac136**
P33 sulfhydryl oxidase	***Ac92**
P35	**Ac135**
P40	***Ac102**
P43	**Ac39**
P45, p48	***Ac103**
P47	***Ac40**
P49	***Ac142**
P74, Pif-0	**Ac138**
P94	**Ac134**
P95, p91	***Ac83**
P143 (helicase)	***Ac95**
PCNA	**Ac49**
Pe38	**Ac153**
PEP polyhedron envelope protein	**Ac131**
Pif-0, p74	***Ac138**
Pif-1	***Ac119**
Pif-2	***Ac22**

Table 1. continued from previous page.

Pif-3	***Ac115**
Pif-4 (19K)	***Ac96**
Pif-5, odv-e56	***Ac148**
Pif-6	***Ac68**
Pif-7	***Ac110**
Pif-8, vp91, vp94	***Ac83**
PK1 (Protein kinase 1)	**Ac10**
PK2 (Protein kinase 2)	**Ac123**
PKIP (Protein kinase interacting factor)	**Ac24**
PNK polynucleotide kinase	**Ac33**
PNK/PNL polynucleotide kinase/ ligase	**Ac86**
Polyhedrin	**Ac8**
Pp31;39K	**Ac36**
Pp34, polyhedron envelope	**Ac131**
Pp78/83;orf1629	**Ac9**
Primase	**Ac14**
Primase accessory factor	**Ac6**
Protein tyrosine phosphatase (ptp)	**Ac1**
Single stranded DNA binding protein (SSB)	**Ac67**
SOD superoxide dismutase	**Ac31**
Sulfhydryl oxidase, sox	***Ac92**
TLP telokin-like	**Ac82**
TRAX-like	**Ac47**
Ubiquitin	**Ac35**
VLF-1 very late factor 1	***Ac77**
Vp39, capsid	***Ac89**
Vp80, vp87	**Ac104**
Vp91, p95	***Ac83**
Vp1054	***Ac54**
19K (pif-4)	***Ac96**
38K	***Ac98**
39K, pp31	**Ac36**
49K	***Ac142**

* Core genes

Annotation of the AcMNPV genome

Below is an annotation of the orfs in the AcMNPV genome based on their orf number from (6). An asterisk (*) indicates a core gene with homologs found in all sequenced baculovirus genomes. The orf size in amino acids, followed by the molecular mass in kDa is indicated after each orf as reported by (6, 12). The same information is also included for the BmNPV (16) and *Helicoverpa armigera* (HaSNPV) (17) orthologs of these genes. Both AcMNPV and BmNPV are Group I alphabaculoviruses whereas HaSNPV is a group II alphabaculovirus and lacks some of the genes found in AcMNPV and BmNPV but also has some additional genes. The survey of information regarding each gene was updated in early 2019.

Ac1 (168aa:19.3kDa), (Bm130:168aa:19.3kDa), (protein tyrosine phosphatase (ptp); baculovirus phosphatase (bvp)).

Ac1 homologs are present in the genomes of all lepidopteran Group I NPVs, but not those of other baculoviruses. Closely related orfs are found in a variety of invertebrates, e.g., *Drosophila* (E = 7e-30) and vertebrates, e.g., human (E = 2e-27). It is expressed from a late promoter (18). It was originally identified because of its relatedness to protein tyrosine phosphatases and its ability to dephosphorylate proteins at ser, thr and tyr residues (19). However, it was later found that Ac1 is an RNA 5'-triphosphatase and hydrolyzes the gamma phosphate of triphosphate-terminated poly(A) and also hydrolyzes ATP to ADP and GTP to GDP (20, 21). The crystal structure has been determined (22). Ac1 is predicted to have one of the same enzymatic activities of LEF-4 (Ac90) that is involved in preparing RNA for cap formation. Although deletion is not lethal, AcMNPV mutants are partially defective in occluded virus production in Sf-21, but not Tn-368 cells (23). I addition, it was found to be required for AcMNPV replication in in *S. exigua* larvae (24), but not for replication of BmNPV in *B. mori* larvae (25). A host *B. mori* ptp was shown to be induced by BmNPV infection and RNAi knockdown reduced viral replication (26). Although not reported to be associated with AcMNPV ODV by proteomic analysis, it was detected in BV preparations (27). It was reported to influence BmNPV infected larval wandering late in infection in one study (28), but had no effect in another (29).

Ac2 (328aa:38.8kDa), (Bm131:349aa:40.1kDa, Bm22:317aa:35.4kDa, Bm80:239:27.5kDa, Bm81:318aa:35.9kDa, Bm132:241aa:27.8kDa), (Ha59:244aa:28.2,Ha60:527aa:59.7kDa,Ha105:501aa:58.3kDa) (Baculovirus repeated orf—BRO).

Derivation: In American inner-city dialect 'bro' means 'brother', but not necessarily a close relationship.

Homologs of Ac2 have a widespread distribution in lepidopteran NPVs and GVs and are also found in the dipteran, but not hymenopteran NPV genomes. Related orfs are also found in double-stranded DNA phage, prokaryotic class II transposons, and a variety of DNA viruses pathogenic for insects, including entomopox viruses, iridoviruses and ascoviruses (30). Twenty-three copies of *bro* genes have been reported in a *Heliothis virescens* ascovirus genome sequence (31). Although there is only one copy of the *bro* gene in AcMNPV, the number can vary in different baculoviruses from none in the closely related *Rachiplusia ou* MNPV — its orfs are 96% identical in sequence to AcMNPV (12), two in the more closely related PlxyNPV (14) (orfs are 98.5% identical to AcMNPV), to up to 16 copies in LdMNPV (32). AcMNPV Ac 2 deletion mutants are viable, but some differences in polyhedron production in infected cells were noted (30). One of the major differences in gene content between BmNPV and AcMNPV is the presence of 3-5 copies of *bro* genes in BmNPV vs. a single copy in AcMNPV (16). The BmNPV *bro* genes are present in three locations with duplicate genes in two of the locations. In contrast, another BmNPV strain only shows 3 copies of the gene, one at each of the three locations (33, 34). This suggests that duplication/loss of these genes might be common. In the strain with five genes, individual mutants of four of the genes were isolated in BmNPV, but a mutant of one gene (*bro-d*) could not be

isolated. Also, a double mutant of *bro-a* and *bro-c* could not be produced, suggesting that they complement an essential function and that *bro-d* has a unique essential function (35). BmNPV BRO proteins have DNA binding activity (36), and all the BmNPV *bro* genes appeared to be expressed as early genes and are distributed in both the nucleus and cytoplasm (35). One of the *bro* gene products was found to interact with laminin, a glycoprotein that is a major constituent of the basal lamina and is involved in cell attachment (37). In BmNPV infections, BRO proteins were found to be phosphorylated (36) and BRO-D was found to be highly phosphorylated (38). In AcMNPV, *bro* was highly expressed in T. ni midguts throughout infection (39).

Ac3 (53aa:5.6kDa) (Conotoxin-like (*ctl*) genes).

Conotoxins are small disulfide-rich ion channel antagonists isolated from snails (genus *Conus)* (40). Homologs of *ctl* are found in about half of the sequenced Group I and Group II lepidopteran NPV genomes and two GVs (Xcni- and HaGV). Although in AcMNPV a single *ctl* gene is present, several other viruses, e.g., OpMNPV and LdMNPV, encode two *ctl* genes of different lineages (*ctl-1* and *ctl-2*). Homologs are found in the *Amsacta moori* entomopoxvirus (E = 0.006), a few mosquito species, a funnel web spider, a wasp, and a bacterium. The EPV (*A. moori* gene falls within the baculovirus *ctl-2* lineage. In a study examining the AcMNPV *ctl* (*ctl*-1) gene, no differences in mortality, motility, or weight gain were observed when either neonate or late instar *Spodoptera frugiperda* larvae were infected with an AcMNPV mutant deleted for *ctl-1*, compared with infection with wt virus (41). It was found to inhibit melanization and when conjugated to gfp, it localized to cell membranes (42).

Ac4 (151aa:17.6kDa), (Bm133:151aa:17.7kDa).

Homologs of Ac4 are found in most Group I, and a few Group II and GV genomes, but not in other lineages. Ac4/Bm133 is likely to be nonessential because when it was deleted the virus appeared normal (15, 43, 44). However, in BmNPV, Bm133 and 134 were found to be distributed throughout the cell during infection and deletion of either gene appeared to reduce the number of occluded virions(45).

Ac 5 (109aa:12.4kDa), (Bm134:109aa:12.4kDa).

Homologs of Ac5 are found in most Group I NPV genomes. Ac5/Bm134 is likely to be nonessential because when Bm134 was deleted, the virus appeared normal (15, 28). However, in BmNPV, Bm133 and 134 were found to be distributed throughout the cell during infection and deletion of either gene appeared to reduce the number of occluded virions and Bm134 appeared to localize to polyhedra(45, 46). Although Ac5 was suggested to form a complex with PIF proteins (47), this was not observed by others (46, 48).

*Ac6 (210aa:23.9kDa), (Bm135:210aa:23.8kDa) (Ha117:241aa: 27.8kDa)(Lef-2)(DNA primase accessory factor).

LEF-2 is a DNA primase accessory factor and is encoded by all baculovirus genomes. It interacts with LEF-1 (49), the baculovirus DNA primase. It has homology to the large subunit of DNA primase in several archaea. It is required for transient DNA replication (50, 51). It is an essential gene as AcMNPV or BmNPV bacmids deleted for *lef-2* were unable to produce infectious virus (15, 52).

Based on limited amounts of DNA synthesis by a *lef-2* bacmid knockout in transfected cells, it was suggested that Lef-2 is not required for the initiation of DNA replication. This was in contrast to a bacmid with the helicase gene deleted that showed no synthesis (52). However, the transfected DNA is likely nicked and therefore the ends of the nicks could act as primers, resulting in limited amounts of leading strand DNA synthesis in the absence of an active primase complex. Elution profiles of LEF-1 and LEF-2 from ssDNA cellulose and DEAE resin, suggested that LEF-2 may bind to both DNA and LEF-1 (53). LEF-2 mutants have been characterized that appear to affect very late transcription, indicating that it may have roles in both replication and transcription (54). In addition, BmNPV LEF-2 was shown to activate late transcription (55).

Ac7 (201aa:23.6kDa) (Orf 603).

This gene is only found in three baculovirus genomes in addition to AcMNPV, including ClbiNPV, PlxyNPV and RoMNPV. Deletion from AcMNPV did not affect replication in cell culture or in *T. ni* larvae (56).

Ac8 (245aa:28.6kDa), (Bm1:245aa:28.8kDa) (Ha1:245aa: 26.7kDa) (polyhedrin, occlusion body protein).

Homologs of polyhedrin (called granulin in GVs) are found in all baculovirus genomes, except for that of the dipteran virus (CuniNPV). Surprisingly, CuniNPV has an occlusion body protein unrelated and about three times as large as polyhedrin of other baculoviruses (57, 58). Because of unexpected patterns of phylogeny of AcMNPV polyhedrin, it has been suggested that it is a chimera derived from both Group I and II sequences (59). It is generally thought that polyhedrin serves to stabilize baculovirus virions in the environment allowing them to persist indefinitely. The polyhedrin gene is nonessential in cell culture, and occlusion-positive and negative plaques can be readily be distinguished. This, in combination with the strength of the polyhedrin promoter, led to the use of the polyhedrin locus as the site for the production of recombinant baculoviruses (4, 5). The crystal structure of AcMNPV polyhedra and Cydia pomonella GV granula have been described (60) (61).

Ac9 (543aa:60.7kDa), (Bm2:542aa:60.9kDa) (Ha9:413aa:45.9kDa), (pp78/83, Orf1629).

Homologs of pp78/83 are found in all lepidopteran NPV (I and II) genomes. It is an essential gene. Because it is located adjacent to the polyhedrin gene, it was originally manipulated via complementation to elevate the frequency of obtaining recombinant baculoviruses at the polyhedrin locus (62). It is phosphorylated (63) and is a structural protein located at one end of nucleocapsids (63, 64). Ac9 is a Wiskott-Aldrich syndrome protein (WASP)-like protein involved in nuclear actin assembly during the baculovirus infection that leads to movement of virions through the cytoplasm of the infected cell (65, 66).

Ac10 (272aa:32kDa), (Bm3:275aa:32.4kDa) (Ha10:267aa:31.5kDa), (Protein kinase-1 (PK-1)).

Homologs of pk-1 are found in lepidopteran NPV and GV genomes, but not in other lineages. AcMNPV PK-1 shows significant relatedness to some insect orfs, e.g., *Anopheles gambiae* (E = 3e-18). Purified PK-1 was able to phosphorylate histone substrates (67). A bacmid with a knockout of pk-1 produced no viral progeny, although DNA replication was unaffected. It was also found that the kinase catalytic domain was required for infectivity. Cells transfected with the mutant bacmids showed extensive arrays of tubular structures that appeared to lack DNA suggesting that the phosphorylation of one or more proteins was required for capsid morphogenesis (68). Ts mutants characterized for defects in very late gene expression contained mutations in *pk-1* (69). In addition, inactivation of pk-1 mRNA using DNAzyme technology caused a reduction in the expression from the polyhedrin promoter (70). PK-1 also may be associated with a very late transcription complex and be involved in the phosphorylation of LEF-8 (71). PK1 of SpltNPV-I and AcMNPV may interact with the polyhedrin promoter, suggesting that it might act as a very late gene transcription factor (72) (73).

Ac11 (340aa:40.1kDa), (Bm4:340aa:39.8kDa).

Homologs of Ac11 are found in all lepidopteran Group I NPV and in one Group II (LdMNPV) genomes, but not in other lineages. Although it was suggested that Bm4 was nonessential (15), an examination of Ac11 suggested that it was required for BV production and ODV envelopment (74). In addition, it was reported that Ac11 interacts with components of the ESCRT-III complex and may be involved in the release of nucleocapsids at the nuclear membrane(75).

Ac12 (217aa:25.4kDa).

Homologs of Ac12 are found in many alphabaculoviruses and a few betabaculoviruses. It has an F-box domain and interacts with S phase kinase associated protein1 and may be involved in ubiquitin pathways, but is a non-essential gene (76). It shows limited similarity to the tryptophan repeat gene family proteins of *Amsacta moorei* entomopoxvirus (E = 0.12) (see also Ac30).

Ac13 (327aa:38.7kDa), (Bm5:331aa:39.3kDa)(Ha123:385aa:44.5kDa).

Homologs of Ac13 are found in all Group I, II, and GV genomes, but not in other lineages. Analysis by HHpred (77) predicts that it contains coiled-coil regions and has some structural similarity to some membrane proteins. Ac13/Bm5 may be nonessential because when it was deleted, the virus appeared normal (15). However, Bm5 appears to encode a late expressed protein not associated with BV or ODV (78) and it was also found that Bm5 localizes to the nuclear membrane and its inactivation caused lower titers of BV, fewer occlusion bodies, and seemed to interfere with the expression of some very late genes, and resulted a delay in larval death (79). In another investigation, Bm5 was termed BION (baculovirus protein associated with both the inner- and outer nuclear membranes) because it was found to be present in both the inner- and outer nuclear membranes (80).

*Ac14 (266aa:30.8kDa), (Bm6:270aa:31.1kDa), (Ha124:245aa:29kDa) (Lef-1, DNA primase).

LEF-1 is a core gene present in all baculovirus genomes. Purified LEF-1 has DNA primase activity (53). It interacts with Ac6 (LEF-2) (49), the baculovirus DNA primase accessory factor and is required for transient DNA replication (50, 51). Lef-1 is likely an essential gene as a deletion/insertion mutant in the BmNPV homolog (Bm6) could not be isolated (15, 81).

Ac15 (506aa:57kDa), (Bm7:506aa:57.0kDa), (Ha126:515:58.9kDa), EGT.

Ac15 encodes ecdysteroid UDP-glucosyltransferase (82) and homologs are found in all Group I, II, and most GV genomes, but not in other lineages. Homologs are found in a variety of insects, e.g., *B. mori* (E = 3e-50). The function of EGT is to block molting and pupation in infected larvae by catalyzing the transfer of glucose from UDP-glucose to ecdysteroids, thereby inactivating these insect molting hormones (83, 84). This is thought to prolong the feeding stage of infected larvae, thereby allowing the virus to replicate over a longer period in larger larvae, resulting in a higher yield of virus. AcMNPV and BmNPV mutants in which the *egt* gene is inactivated are viable (84) but their survival time is reduced (44, 85). Spontaneous deletions of the *egt* gene commonly occur in cell culture (86).

Ac16 (225aa:25.9kDa), (Bm8:229aa:26.2kDa) (BV/ODV-E26).

Homologs of Ac16 are found in all lepidopteran Group I NPV genomes, but not in other lineages. Ac16 interacts with fp25 (Ac61), forms a complex with cellular actin (87) and is palmitoylated (88). It was found to be associated with the envelopes of both BV and ODV and was called BV/ODV-E26, and was also identified as being associated with ODV by mass spectrometry analysis (89). However, in BmNPV, the homolog of AcMNPV Ac16 (Bm8) was not identified as a virion structural protein (90). It was suggested that the difference in the results was due to the source of the antibody (91). In BmNPV, Bm8 directly interacts with IE-1 (92). Similar observations were made in AcMNPV with Ac16 interacting with both IE-1 and IE-0 (93). In addition, Bm8 was found to interact with cellular membrane-bound proteins or secreted proteins (94). A mutant, in which AcMNPV orf16 (called DA26) was insertionally inactivated was viable and showed no difference from wt in *T. ni* or *S. frugiperda* cells or larvae (95). Initial attempts at isolation of null mutants of BmNPV (Bm8) were not successful, but a C-terminal deletion mutant was viable (90), although this mutant was unable to produce BV titers as high as wt. However, a bacmid deleted for Bm8 was viable (15). It was also found that Bm8 appears to

inhibit occlusion body production in middle silk glands and its deletion accelerated the death of infected insects (44). In another investigation with BmNPV, inactivation of Bm8 resulted in reduced levels of BV and more occlusion bodies in both cultured cells and larvae and appeared to accelerate viral infection in various tissues suggesting that it might be involved in tissue tropism (96). In AcMNPV, deletion of Ac16 resulted in a delay in full levels of DNA synthesis and BV production in one study (97), but had lesser effects in another (93). Analysis by HHpred (77) predicts that it contains a coiled-coil region.

Ac17 (209aa:23.9kDa), (Bm9:210aa:24.1kDa), (Ha128:266aa:30.4kDa).

Homologs of Ac17 are found in most Group I and II NPV genomes. It is an early expressed gene with a product of about 19 kDa that localizes to the cytoplasm (98). A homolog of Ac17 in HearNPV (He128) is expressed late and was found in the cytoplasm (99). Deletion of Ac17 did not affect DNA synthesis, although BV production was reduced by up to a factor of 10 to 100 (97). Deletion of both Ac16 and Ac17 was similar to the Ac17 deletion although there were more significant delays for DNA replication and BV titers to reach levels similar to the Ac17 deletion alone (97). Similar results were reported for a BmNPV bacmid knock out. In addition, the mutant BmNPV took significantly longer to kill larvae and required higher titers BV to achieve an LD_{50} (100). The predicted size of Ac17 is longer than previously reported (12).

Ac18 (353aa:40.9kDa), (Bm10:356aa:41.5kDa).

Homologs of Ac18 are found in all Group I and II NPV genomes. An AcMNPV bacmid deleted for Ac18 was infectious with an LD50 in *T. ni* larvae similar to wt, but took somewhat longer to kill larvae (101). It was observed that Ac18 was upregulated about 2 fold by AcMNPV-miR-1 and was suggested that Ac18 interacts with fp25 and Ac18 upregulation may affect the function of fp25(102). Analysis by Hhpred (77) suggested that it was related to nucleotidyl transferase with over 80% probability.

Ac19 (108aa:12.2kDa), (Bm11:110aa:12.5kDa), (Ha115:129aa: 15.3kDa).

Homologs of Ac19 are found in all Group I and most Group II NPVs. Ac19 is likely to be nonessential because when it a BmNPV Bm11 deletion was viable (15, 44). However, more recent investigations on Bm11 indicated that it is a late gene, localized to the ring zone, and its inactivation reduced OB production and the occlusion of ODV (103).

Ac20 (Ac20/21 (417aa:47.7kDa), (Bm12:440aa:50.0kDa), (Ha131: 265aaa:30.4kDa)(arif-1).

The two orfs, Ac20/21, were likely caused by a sequencing error in the original C6 sequence. This region has been re-sequenced in several AcMNPV strains including C6 and in all cases it was found that Ac20 and 21 are a single orf (104), see also (12). Homologs of arif-1 are present in all Group I and most Group II genomes. AcMNPV orf20/21 is called actin-rearrangement-inducing factors (arif-1). It is expressed as an early gene and transfection of a plasmid containing this gene into Tn-368 cells is able to induce actin rearrangement (105). Arif-1 was found to colocalize with F-actin at the plasma membrane and deletion mutants showed a loss of actin concentration at the plasma membrane. Deletions of the C-terminal half of the gene or insertion of the LacZ gene near the center of the orf resulted in constructs that showed no significant loss of infectivity in Tn-368 or Sf cells (104). Arif-1 was more highly expressed in midgut than cultured cells suggesting it may be important in establishing the infection (39). Defective mutants of BmNPV Arif-1 caused a significant delay in the infection in several tissues including trachea, fat body, suboesophageal ganglion and brain (106).

*Ac22 (382aa:43.8kDa), (Bm13:382aa:43.8kDa), (Ha132:383:44.5kDa) (PIF-2).

This gene is a member of the per os infectivity factor (PIF) (107) gene group. These genes can be deleted and the mutants are still infectious for cultured cells, but are not orally infectious for insects (108). It is present in all baculovirus genomes and is also present in a nudivirus (109) and an *Apis mellifera* filamentous virus genome (110). For more information see Ac138 (p74) and Chapter 3.

Ac23 (690aa:79.9kDa), (Bm14:673aa:78.0kDa), (Ha133:677aa: 78.2kDa), F (Fusion) protein.

Ac23 is a homolog of the predicted fusion protein (F) of Group II lepidopteran NPVs, GVs, and the dipteran virus (CuniNPV). Homologs are found in all baculoviruses except the hymenopteran viruses. In Group II viruses such as LdMNPV and HaSNPV, Ac23 homologs (*ld130, Ha133*) encode low pH-activated fusion proteins. In Group I viruses, they appear to be inactive as fusion proteins and have been replaced by *gp64*, which is not found in the Group II viruses, GVs, or hymenopteran or dipteran viruses. Orthologs of the F gene are also found as the env gene of insect retroviruses (111), and are also present in some insect genomes (112). They also appear to be related to the fusion (F) proteins of the paramyxoviridae (see Chapter 2). Although inactive in Group I viruses, the Acorf23 homolog is glycosylated and associated with the envelope of BV and with the membranes of OpMNPV-infected cells (113). In AcMNPV, Ac23 is also associated with BV membranes and its deletion from the genome results in infectious virus, but the time to kill larvae was somewhat extended (10). Ac23 was found to be associated with ODV as was the homolog in CuniNPV (89, 114). Ac23 increases viral infectivity and may be involved in cell binding (115, 116). In BmNPV, deletion of Bm14 had a variety of effects including reduced production of BV, a delay in the lethal time in infected larvae, reduced production of OB, fewer virions in OBs, and irregular OB with pitted surfaces(117).

Ac24 (169aa:19.2kDa), (Bm15:169aa:19.4kDa), Protein kinase interacting protein (PKIP).

Homologs are found in all Group I and II NPV genomes, however, they are not very closely related suggesting that they may be of different lineages. PKIP was found to interact with AcMNPV protein kinase I (see Ac10) in a yeast two-hybrid assay. It stimulates PK-1 activity in vitro. PKIP appears to be essential as attempts to isolate a deletion mutant were unsuccessful (118). Ts mutants in PKIP are defective in very late transcription, show a delay in shutoff of host protein synthesis, and produce few, if any, BV (119). BmNPV bacmids deleted for Bm15 were viable, but the infection spread slower than wt in cultured cells (15).

Ac25 (316aa:36.6kDa), (Bm16:317aa:36.7kDa),(Ha25:324aa:37.6kDa), DNA binding protein (DBP).

Ac25 encodes a single-stranded DNA binding protein called DBP. Homologs are found in all sequenced baculovirus genomes, except that of the dipteran (CuniNPV) (although an orf is present with ~50% identity over 22 aa) and in some instances, multiple copies of the *dbp* gene are present. It has properties similar to the other baculovirus SSB, LEF-3 (Ac67), in that it interacts with itself and is capable of both unwinding and annealing DNA (120). It is an essential gene, as bacmids lacking Ac25 are noninfectious and appear to produce defective nucleocapsids. Although not a virion structural protein, DBP exhibits a tight association with subnuclear structures, suggesting that it is a component of the virogenic stroma (120), and when DBP was deleted from an AcMNPV bacmid, cells transfected with this construct appeared to lack a virogenic stroma. This suggested that *dbp* is required for the production of nucleocapsids and the virogenic stroma (121). In BmNPV, it was also essential as deletion mutants failed to produce virions(122).

Ac26 (129aa:14.6kDa), (Bm17:129aa:14.5kDa), Ha26:133aa:15kDa).

Homologs of Ac26 are found in the genomes all Group I, and most Group II NPV genomes. Bm17 is expressed as a late gene and is localized to both the nucleus and cytoplasm (123, 124). When Bm17 was deleted from a BmNPV bacmid, the virus was viable, but the infection spread slowly in cell culture (15).

Ac27 (286aa:33.3kDa), (Bm18:292aa:34.0kDa), iap-1.

Ac27 is a member of the inhibitor of apoptosis (*iap*) gene family. Up to 6 *iap* homologs are found in baculovirus genomes (125) (126), however AcMNPV has two copies, *iap-1* and *-2*. Unlike *iap-2*, which is found in both Group I and II NPVs, *iap-1* appears to be confined to Group I lepidopteran NPVs and is a member of a lineage distinct from the other iap homologs. Deletion mutants of *iap-1* were similar to wt in their replication in cells lines and larvae of *T. ni* and *S. frugiperda*. However, when they were co-infected with wt virus in Tn-368 (but not Sf-21) cells, the mutants appeared to out compete wt virus (127). Evidence suggested that transfection of AcMNPV iap-1 into T. ni cells suppressed apoptosis by HearNPV infections, although a recombinant HearNPV expressing iap-1 also suppressed apoptosis, BV production was not rescued (128). In another investigation in EppoMNPV, The iap-1 gene was able to delay apoptosis onset caused by inducing agents such as actinomycin but was not able to prevent apoptosis upon prolonged exposure of the cells to the inducer (129). In another study, transient expression of iap-1 from a variety of viruses induced apoptosis and it was suggested that this might facilitate dissemination of the virus (130). For a review see (126).

Ac28 (173aa:20.4kDa), (Bm19:173aa:20.3kDa), (Ha24:187aa:22.2kDa), Lef-6.

Homologs of lef-6 are found in the genomes of all lepidopteran NPVs and GVs. It was originally identified because it was required for transient transcription of late genes (131). A bacmid deleted for lef-6 was infectious, but the virus was severely compromised. The major effect appeared to be reflected in a delay in the onset of late transcription (132). Using the HHpred program (77), AcMNPV LEF-6 showed over 80% probability of being related to the retroviral mRNA export factor TAP (133). BmNPV LEF-6 is highly phosphorylated during infection (38).

Ac29 (71aa:8.6kDa), (Bm20:71aa:8.6kDa), (Ha23:67aa:8.3kDa).

Homologs of Ac29 are found in all Group I and most Group II and GV genomes. A BmNPV bacmid deleted for Bm20 was viable (15). Using the HHpred program (77), Ac29 showed over 80% probability of being related to the amphiphysin BAR domain from Drosophila. These are sensors of membrane curvature.

Ac30 (463aa:54.7kDa), (Bm21:472aa:55.8kDa).

Homologs of Ac30 are present in the genomes of all Group 1 NPVs. It has homology to a family of genes that encode tryptophan repeat gene family proteins (see also Ac12) that are also found in entomopox viruses. e.g., *Melanoplus sanguinipes* entomopoxvirus (E = 1e-11). These proteins contain 3 to 12 copies of a 23-amino acid sequence containing tryptophan, leucine and isoleucine residues (134). Ac30 is likely to be nonessential because when the ortholog (Bm21) was interrupted by insertional/deletion mutagenesis in BmNPV, the virus appeared to be normal, although it resulted in a longer survival time suggesting that the mutant was less virulent that wt (135).

Ac31 (151aa:16.2kDa), (Bm23:151aa:16.3kDa), SOD.

Ac31 has homology to super oxide dismutase (136). Homologs are found in the genomes of almost all lepidopteran baculovirus genomes (it appears to be absent only in EppoNPV, a member of Group II, and SpliGV). It has a high degree of similarity to SOD from a variety of insects, including *B. mori* (E = 8E-49). Insect

hemocytes are phagocytic cells similar to neutrophils and can destroy invading pathogens by the production of superoxide (137). Superoxide can be inactivated by SOD by converting it to hydrogen peroxide, which is also toxic, but can itself be inactivated with catalase yielding water and O_2. Many baculoviruses may infect hemocytes and in this manner can spread an infection throughout an insect. The expression of viral SOD might mitigate the effects of superoxide production by hemocytes. An enzymatic activity could not be confirmed for AcMNPV SOD and AcMNPV deleted for *sod* replicated normally in cultured cells and insect larvae. The *sod*-deleted viruses showed no reduction in replication when grown in the presence of paraquat, a superoxide anion inducer (136). In one study, deletion of the *sod* gene from BmNPV (Bm23) indicated that it was essential for replication in BmN cells (138), however, another report indicated that a Bm23-deleted bacmid was viable (15).

Ac32 (181aa:20.6kDa), (Bm24:182aa:20.8kDa), (Ha113:301aa: 34.4kDa) fgf.

Ac32 has homology to fibroblast growth factor (FGF). Orthologs are found in the genomes of all lepidopteran baculoviruses and may reflect several independent lineages. AcMNPV *fgf* is most closely related to a non-baculovirus gene in *D. melanogaster* called *branchless* (E = 3e-24). In contrast, a Group II *fgf* homolog from LdMNPV is less closely related to the insect homologs (e.g. *D. melanogaster* branchless E = 2e-10) and the GV homologs show only limited similarity to NPV *fgf* homologs (e.g., AcMNPV vs CpGV FGFs = ~10% identity). It has been suggested all of the NPV *fgf*s are monophyletic, however the possibility of at least two capture events of fgf in the GVs has not been ruled out (139). AcMNPV FGF is a secreted protein that stimulates insect cell motility (140). In BmNPV, the FGF homolog is glycosylated, which is essential for its (141, 142) and binds to an insect receptor of FGF/*branchless* called *breathless* (141). Although the deletion of *fgf* in AcMNPV showed no differences from wt on cultured cells (143), the time of death was delayed when fed to two insect species (144). Similar results were observed for a BmNPV *fgf* (145) and HearNPV (146) *fgf* deletion mutants. vFGF was more highly expressed in midgut than cultured cells suggesting it may be important in establishing the infection (39). It has been suggested that FGF may play a role in dissemination of the virus within the host insect (144). vFGF appears to initiate a cascade of events that may accelerate the establishment of systemic infections. This involves two processes. vFGF from virus infected midgut cells diffuse through the basal lamina and attract tracheal cells so that they are adjacent to infected midgut cells but separated by the basal lamina. vFGF then activates FGF receptors located on the tips of tracheal cells. This leads to the activation of matrix metalloproteases located in the same subcellular region via a MAP kinase or NFkB pathway. Matrix metalloproteases subsequently activate effector caspases that move extracellularly so that they are positioned for the degradation of the basal lamina by digestion of the laminin component. The delaminated tracheal cells are then susceptible to virus infection. This allows the transit of the virus through tracheal cells to other tissues and results in the systemic infection (147). This theory is supported by evidence for the activation of matrix metalloproteinases, the activation of effector caspases, and the degradation of laminin after the per os infection of midgut cells.

Ac33 (182aa:20.8kDa) (polynucleotide kinase (PNK)).

Orthologs of Ac33 are found in most Group II and a few Group I and GV genomes. Homology searches indicate that it has significant similarity to polynucleotide kinase-3'-phosphatase of *Apis mellifera* (E = 9e-36) and somewhat lesser to the human homolog (E = 1e-28). In other organisms this enzyme has functions similar to T4 PNK. It is predicted to have structural similarity to Chain B of a DNA repair enzyme, polynucleotide kinase with an E value of $1.0e^{-32}$ (148). As previously suggested, Ac33 also has structural similarity to histidinol-phosphatase (an enzyme in the histidine biosynthesis pathway) (149). Orthologs are not present in BmNPV (16) or HaSNPV (17).

Ac34 (215aa:24.9kDa), (Bm25:215aa:24.8kDa), (Ha27:255aa:29.5kDa).

Orthologs of Ac34 are found in Group I and II NPV genomes. Ac34 localizes to both the nuclei and cytoplasm of infected cells but does not appear to be a structural protein. Deletion of Ac34 from an AcMNPV bacmid resulted a delay in late gene expression, a100-fold reduction the viral titer, but did not appear to affect DNA replication. This mutant was unable to establish a fatal infection in the larvae of *T. ni* via *per os* exposure (150). In another study, deletion of Ac34 resulted in no BV production, but reduction of Ac34 expression by RNAi, elevated the expression of a heterologous gene expressed from the polyhedrin promoter (151). Deletion of Bm25 also resulted in a compromised virus (15). Subsequently, Ac34 was implicated in Arp2/3 (actin nucleator actin-related protein complex) nuclear accumulation and Ac34 inhibits the CRM1 (chromosome maintenance 1) pathway that is involved in the nuclear export of proteins and RNA, resulting in nuclear retention of the Arp2/3 complex. It was also shown that Ac34 binds to P40, P34, and P20 of the Arp2/3 complex in Sf9 cells (152) and that it contains a zinc finger domain that appears to be essential for nuclear localization (153). Ac34 has also been reported to increase the transcription of late genes, inhibit the proliferation of sf9 cells, caused the abundant expression of Sf953, and activated the JNK pathway which triggers apoptosis

(154).

Ac35 (77aa:8.7kDa), (Bm26:77aa:8.7kDa), (Ha28:83aa:9.2kDa), ubiquitin-like protein.

Although it was suggested baculoviruses were the only viral lineage encoding a ubiquitin-like protein (155), they were recently identified in avipoxvirus genomes. Orthologs of ubiquitin have been found in the genomes of most alpha and beta baculoviruses, but are not present in hymenopteran or dipteran baculoviruses (156) (155). Ac35 is expressed from both early and late promoter elements (157, 158). It was observed that late in infection recombinant virus expressing GFP fusions of ubiquitin from BmNPV localized throughout the nuclei with a few concentrated foci in the cytoplasm, whereas that of HaSNPV localized mostly to the peripheral regions of nuclei (159). The phylogenetic tree indicates that, whereas the ubiquitin of most eukaryotes is almost invariant, the baculovirus tree shows a higher degree of phylogenetic diversity, particularly between GVs and NPVs, suggesting that it may have been independently incorporated into a viral genome more than once. In addition, there appear to be two different lineages of alphabaculovirus ubiquitin (155). Viral ubiquitin is BV associated (27) and appears to be present on the inner surface of viral envelopes (160). A viral mutant with a frameshift of Ac35 is viable, but a 5–10-fold reduction in BV was observed (161). It has been suggested that viral ubiquitin may inhibit steps in the host degradative pathway to stabilize what would otherwise be a short-lived viral protein (162). Ac35 interacts with Ac141(exon0) and deletion of ac141 and *vubi* limited viral infection to single cells. Nucleocapsids of BV, but not ODV are ubiquitinated by vUbi. Ac66, a BV specific nucleocapsid protein is ubiquitinated by vUbi and interacts with Ac141 and vUbi at the margins of nuclei suggesting that vUbi may be involved as a signal regulating whether nucleocapsids exit nuclei and form BV, or remain and form ODV (163). The *Spodoptera litura* NPV genome was found to contain a gene that is a fusion of *ubiquitin* and *gp37* (=Ac64). In addition, it was noted that unfused homologs of both these proteins are found in entomopox viruses (164). Although the significance of the linkage of these two proteins is not known, other such proteins have been termed 'rosetta stone' proteins because they reveal proteins that interact with one another and participate in the same molecular pathways. Consequently, when a mutation event occurs that leads to the fusion of two proteins that normally function together, the mutation is preserved because such a linkage is a normal feature of the two proteins. The presence of homologs of both these proteins in two disparate families of viruses along with the presence of a fused orf in the SlNPV genome, suggests that these orfs may participate in the same pathway, possibly as participants in a ubiquitin pathway or in ubiquitin inhibition.

Ac36 (275aa:31.3kDa), (Bm27:277aa:31.5kDa), (Ha31:311aa:35.2kDa), 39K;pp31.

Pp31 was originally identified because it contains an early promoter that is stimulated by IE-1 (165). Homologs are found in all lepidopteran NPV and GV genomes. It is phosphorylated and localized to the virogenic stroma of infected cells, and is capable of binding to DNA but is not a virion structural protein (166), although it was reported to be BV associated in a proteomic study (27). Purified PP31 was found to bind to single-stranded and double-stranded DNA with equal affinities and inhibited transcription in vitro (167). Phosphorylation of pp31 appeared to be a dynamic process (168). Several basic regions were identified that may be involved in nuclear localization or DNA binding (169). Pp31 stimulates late gene expression in a transient transcription assay (170). Deletion of the *pp31* homolog in BmNPV (Bm27) resulted in virus that, although viable, showed a reduction in late gene transcription, a 100 fold reduction in BV production, and improper formation of the virogenic stroma (81). Similar results were obtained for an AcMNPV bacmid deleted for *pp31* and it was observed that the deletion resulted in a significant decrease of the transcription of six late genes (171).

Ac 37 (112aa:13.1kDa), (Bm28:112aa:13.1kDa), (Ha32:127aa:14.6 kDa), Lef-11.

Lef-11 is present in all baculovirus genomes, except the dipteran CuniNPV. It was identified as being stimulatory for late gene expression in a transient transcription assay (51). An AcMNPV bacmid deleted for *lef-11* failed to replicate and no DNA synthesis or late gene transcription were evident, indicating that it is an essential gene. In BmNPV, oligomerization of LEF-11 is required for DNA replication (172). Although LEF-11 localizes to nuclei of infected cells, its role in DNA replication is not known (132). BmNPV LEF-11 interacts with and upregulates both a host ATPase and HSPD1 (HSP60) proteins and this appears to facilitate viral DNA replication (173). BmNPV LEF-11 has a novel nuclear localization signal (174, 175)and appears to interact with host importin α-3 (involved in the import of proteins into nuclei) and within nuclei it co-localizes with IE-1 and interacts with LEF-3(174).

Ac38 (216aa:25.3kDa), (Bm29:217aa:25.5kDa), (Ha33:238aa:28.4kDa), Nudix, ADP-ribose pyrophosphatase (ADPRase).

Homologs of Ac38 are found in all lepidopteran NPVs and GVs. It contains a conserved Nudix (nucleotide diphosphate X) motif ($GX_5EX_7REUXEEXGU$; X= any aa, U represents l, L, or V) (176) and has a homology to ADPRase, a subfamily of Nudix pyrophosphatases. Ac38 was shown to have ADPRase activity and a deletion mutant was severely compromised and produced BV at 1% the level of wt (177). Purified Bm29 also showed ADPRase activity (178). Proteins of the nudix superfamily are common in all organisms and have been reported in other viruses including T4 bacteriophage, African swine fever virus (ASFV), and poxviruses. A vaccinia virus nudix protein may negatively regulate viral gene expression by acting as a decapping enzyme (179). Deletion of the gene in vaccinia resulted in smaller plaque and low virus yield (180), similar to the *Ac38*-deleted AcMNPV. Ha33 of the *Helicoverpa armigera* NPV is a homolog Ac38 and was found to be associated with the envelope of budded virions (181).

Ac39 (363aa:43.5kDa), (Bm30:362aa:43.4kDa).

Homologs of Ac39 are found in a few Group I NPV closely related to AcMNPV and at least two Group II (AdhoNPV and ClbiNPV) genomes. Deletion showed no effects on growth curves or virus production (182).

*Ac40 (401aa:47.5kDa), (Bm31:399aa:47.3kDa), (Ha35:3590aa:39kDa), P47, a subunit of the baculovirus polymerase.

P47 homologs are found in all baculovirus genomes. P47 was originally identified as the site of a ts mutation that caused a defect in late gene expression (183, 184). P47 was found to be required for transient late gene transcription (170) and to be a component of the baculovirus late polymerase complex (185). It is likely an essential gene as a deletion/insertion mutant in the BmNPV *lef-8* homolog (Bm31) could not be isolated (15, 81).

Ac41 (181aa:21.1kDa), (Bm32:183aa:21.1kDa), (Ha36:223aa:25.8kDa), Lef-12.

Lef-12 is found in about one-half the Group I and Group II NPV genomes sequenced. Although 18 genes were originally identified as being involved in transient expression from a late promoter (170), when individually cloned, the genes failed to support late transcription. Because of its close proximity to Ac 40 (p47), Ac41 (lef-12) had not been identified in the initial screen. It was subsequently demonstrated to be required for transient late gene transcription in *S. frugiperda* cells (186, 187), but not in *T. ni* cells (186). Mutants with *lef-12* interrupted by insertional mutagenesis or by mutation of the ATG translation initiation codon were viable in both *S. frugiperda* and *T. ni* cells, although reduced yields of BV were observed (20-40% or wt) in both cell lines and the infection cycle appeared to be slowed (188). Although expressed as an (aphidicolin sensitive) late gene, initiation of *lef-12* mRNA did not appear to occur at conventional late (or early) promoter elements. It was suggested that *lef-12* may be functionally redundant in the AcMNPV genome and, therefore, it is not essential for late transcription when the rest of the virus genome is present (188). Analysis by Hhpred (77, 189)predicts that Lef-12 may be structurally related to TFIIA with a probability of about 70%. TFIIA is involved in transcriptional initiation of RNA polymerase II (190).

Ac42 (506aa:59.1kDa), (Bm33:506aa:59.2kDa), gta.

Ac42 has homology to 'global transactivator,' the DEAD-like helicase superfamily that are enzymes involved in ATP-dependent unwinding of DNA or RNA. They contain an SNF2 family N-terminal domain that is present in proteins involved in some processes, such as regulation of transcription, DNA recombination and repair, chromatin unwinding, and other functions. Homologs of this gene are found in all Group I NPV genomes. It has significant similarity to a wide variety of orfs from bacteria to marsupials, e.g., (E = 9e-61). Deletion of the Ac43 homolog from BmNPV (Bm33) did not cause any defects in BV or ODV production in BmN cells. Assays in *B. mori* larvae showed that the mutant, although similar in infectivity to the wt, took about 15 hr longer to kill when administered either by injection or per os (191).

Ac43 (77aa:8.8kDa), (Bm34:78aa:9.0kDa), (Ha37:80aa:9.5).

Homologs of Ac43 are found in all Group I and most Group II NPV genomes. It appears to be involved in late and very late gene expression as deletion of BmNPV Bm34 resulted in a reduction in occlusion body production and a lengthening of the time to death in larvae. These effects were attributed to a down regulation of *vlf-1* which is required for very late gene expression along with the reduction expression of the *fp25k* (Ac61) gene (192). A knockout of Ac43 did not appear to affect BV production, but resulted in reduced expression of polyhedrin, but those present were larger than normal. They appeared contain more singly enveloped nucleocapsids than wt (193). Analysis by Hhpred (189) predicts that Ac43 may be structurally related to several proteins including the N-terminal domain of TFIIB from *Pyrococcus furiosus* with a probability of greater than 70%.

Ac44 (131aa:15kDa), (Bm35:131aa:15.0kDa), iap related?

Homologs of Ac44 are found in most Group I and at least one Group II (SeMNPV) lepidopteran NPVs. Analysis by Hhpred (189) predicts that Ac44 is related to iap family members with a probability greater than 97% and a

Blast search indicates homology to E3 ubiquitin-protein ligase family members. Ac44 may be nonessential as a BmNPV bacmid with a Bm35 knock out appeared to be normal (15).

Ac45 (192aa:22.7kDa), (Bm36:193aa:22.5kDa).

Homologs of Ac45 are found in four close relatives of AcMNPV (PlxyNPV, BmNPV, RoMNPV, and MaviMNPV). Sequences located within Ac45 appeared to be required for Ac41 expression in a transient late transcription assay (187). Analysis by Hhpred (189)predicts that Ac45 is structurally similar to a S-phase kinase associated/F-box protein with a probability greater that 70%. F-box domains mediate protein-protein interactions. Ac45 may be nonessential as a BmNPV bacmid with a Bm36 knock out appeared to be normal (15).

Ac46 (704aa:79.1kDa). (Bm37:702aa:79.2kDa), (Ha96:672aa:76kDa), ODV-E66.

Ac46 (ODV-E66) is the only known viral chondroitinase (194) and is a component of ODV envelopes (195). Homologs of this gene are found in the genomes of most alpha- and betabaculoviruses, but not in hymenopteran or dipteran viruses. Two copies of the gene are present in some genomes (e.g., SeMNPV). When the N-terminal 23 amino acids of ODV-E66 are fused to a reporter gene, it is targeted to the nucleus (196). Chondroitinases have been shown to regulate cytokine and growth factors and can influence a variety of processes including development, inflammation, and organ morphogenesis. The crystal structure has been determined and it is most similar to bacterial chondroitin lyases suggesting it was obtained from a bacterium via horizontal gene transfer (197). ODV-E66 may be involved in the digestion of the peritrophic matrix as it contains low levels of chondroitin sulfate (194) (198). When the homolog of ODV-E66 was inactivated in BmNPV (Bm37), the mutant, although viable, took more time to kill insect larvae (199). In a study of AcMNPV, an ODV-E66 deletion was observed to kill *Plutella xylostella* larvae as efficiently as wt, however when infected per os, the LD50 was1000 fold greater for the mutant than wt virus. Therefore it was suggested that ODV-E66 is a per os infectivity factor (PIF) (200). It has also been shown that a truncated form lacking the N-terminal 66 amino acids was secreted into the medium by infected cells and had chondroitinase activity. A peptide of about 12 aa that was similar to the AcMNPV ODV-E66 sequence was observed to bind to the epithelium of guts *Heliothis virescens* and inhibited infection by AcMNPV (201). For more information on PIFs see Chapters 2 and 3.

Ac47 (88aa:10.5kDa), (Bm38:89aa:10.5kDa), TRAX-like.

Ac 47 homologs are found in several Group I lepidopteran NPVs closely related to AcMNPV. It shows 27% identity to homologs of a protein called translin-associated factor X (Trax) that binds to DNA breakpoints. Although TRAX interacts with translin, which may be involved in responses to DNA damage, transport of RNA, and control of translation, its function is not known (202). Ac47 may be nonessential as a BmNPV bacmid with a Bm38 knock out appeared to be normal (15). In AcMNPV his gene was referred to as ETS and transcriptional data for Ac47 in relation to PCNA has been described (203).

Ac48 (113aa:12.9kDa).

Ac48 homologs are found in the genomes of most Group I lepidopteran NPVs. A homolog of Ac48 is not present in the BmNPV genome (16). This gene was referred to as ETM (the mid-sized orf in the EcoRI T fragment) and transcriptional data for Ac48 in relation to PCNA has been described (203).

Ac49 (285aa:32.1kDa) (PCNA).

Ac 49 has homology to proliferating cell nuclear antigen (PCNA). PCNA homologs have been found in a few Group I and Group II alphabaculovirus genomes. The Group I PCNA homologs appear to be insect-derived and show a high degree of similarity to insect PCNAs, e.g., *S. frugiperda* (E = 6e-65). In contrast, the PCNA

homologs of two Group II viruses (TnSNPV and ChchNPV) belong to a different lineage and do not show such a close relationship to insect PCNAs, e.g., *S. frugiperda* (E = 7e-20) and are even more distantly related to the Group I baculovirus PCNAs than to those of insects. Although eukaryotic PCNA lacks an enzymatic function, it plays a role in DNA synthesis, DNA repair, and cell cycle progression. It functions as a sliding circular clamp that mediates protein interactions with DNA and is required for the coordinated synthesis of both leading and lagging strands at the replication fork during DNA replication (204). In AcMNPV it is not an essential gene (203, 205, 206) and did not appear to elevate DNA replication in transient replication assays (50). A homolog of PCNA is not present in the genome of BmNPV (16). It is not clear what role the viral PCNA plays in the infection, however over expression under the control of the p10 promotor of EGFP fusions of AcMNPV-PCNA and host cell Sf-PCNA has been examined in Sf9 cells. Both stimulated BV production and DNA replication of host and virus and Ac-PCNA elevated transcription of selected late genes and increased the larval mortality rate (207).

*Ac50 (876aa:101.8kDa), (Bm39:877aa:101.8kDa), (Ha38:901aa:105 kDa), Lef-8, baculovirus RNA polymerase subunit.

Lef-8 was originally identified as a gene required for transient late gene expression (208). Homologs are found in all baculoviruses and are also in nudiviruses. LEF-8 contains a conserved motif found in other RNA polymerases and it is thought that this is part of the catalytic site (208, 209). It is a component of the baculovirus late RNA polymerase complex (185, 210). It is likely an essential gene; in BmNPV a ts mutant located in lef-8 (A542V) was defective for BV production at the non-permissive temperature (211). In addition, a deletion mutant in the BmNPV lef-8 homolog (Bm39) was not viable (15). Also, a ts mutation L531S in Ac50 abolished very late transcription at 33 ° C (212). Inactivation of BmNPV *lef-8* prevented virus replication (213).

Ac51 (318aa:37.5kDa), (Bm40:319aa:37.8kDa), (Ha39 :194aa : 22.5kDa), DnaJ domain protein.

Homologs of Ac51 are found in all Group I and II lepidopteran NPV genomes. It is a DNA J domain protein and shows homology to a variety of bacterial proteins. In *E. coli*, DnaJ has been demonstrated to have chaperone activity and aids in folding of other proteins (214). The homolog of Ac51 in HearNPV (ha39) has an RNA recognition motif, localizes to the cytoplasm and is associated with BV (27, 215). A BmNPV bacmid with Bm40 deleted was defective for viral spread (15). Another investigation demonstrated that bm40 is a late gene that localized in nuclei and become concentrated near the nuclear membrane; deletion inactivated the virus, although there was no effect on DNA replication. EM analysis suggested the Bm40 is required for nucleocapsid egress from the nucleus, envelopment to form ODV, and embedding into OB (216). Investigations on Ac51 indicated that it is a late gene and was present in the cytoplasm and nuclei of infected cells. Upon deletion of ac51, BV production was reduced 1000 fold. However, DNA replication, virus gene expression, nucleocapsid assembly, and ODV formation were not affected. The defect in BV production appeared to be caused by a decrease in the egress of nucleocapsids from nuclei (217).

Ac52 (194aa:123.2kDa), (Bm41:194aa:23.3kDa), (Ha42:180aa: 21.3kDa).

Homologs of Ac52 are found in about one-half the Group I and II alphabaculovirus genomes. Deletion of Bm41 resulted in reduction in BV production by 1000-fold and appeared to disrupt normal nucleocapsid envelopment and polyhedron formation in infected nuclei and resulted in a 14-fold elevation of LD_{50} in larvae and an increase in time to death (218). The predicted size of Ac52 is longer (194 vs 123 aa) than previously reported (12).

*Ac53 (139aa:17kDa), (Bm42:139aa:16.9kDa), (Ha43:136aa:16.4kDa).

Homologs of Ac53 are found in all baculoviruses. Deletion of Ac53 indicated that it was an essential gene. The mutant bacmid was able to replicate DNA, but the virions were defective and appear to lack the nucleoprotein core (219). Ac53 is predicted to contain domains structurally similar to the U-box/RING-like domains found in the E3 ubiquitin ligase family (156).

Ac53a (78aa:8.6kDa), (Bm42a:78aa:8.6kDa), (Ha46:71aa:7.7kDa), Lef-10.

This orf was named Ac53a because it was not identified in the original AcMNPV genome sequence because it is a small orf encoding 78 aa and about half the 3' coding region overlaps the 5' region of Ac54. Homologs of lef-10 are found in the genomes of all Group I and most Group II NPV and GV genomes. Lef-10 was originally identified because it was required for late gene expression (13). When Bm42a was deleted from a BmNPV bacmid, the bacmid was not viable (15). It was shown that AcMNPV Lef-10 was required for viral replication and interacted with itself. A truncated form (amino acids 1-48) also supported replication and could self-aggregate. When linked to EGFP, Lef-10 formed punctate spots (220). It has been reported that LEF10 behaves as a prion (221). The full-length protein or its predicted prion-forming domain can functionally replace the prion domain of Sup35 of yeast. A high multiplicity of infection can lead to conversion of LEF10 to an aggregated state that inhibits late gene expression (220, 221).

*Ac54 (vp1054) (365aa:42.1kDa), (Bm43:365aa:42.0kDa), (Ha47:351aa:41.7kDa), Capsid protein

Homologs of Ac54 are found in all baculovirus genomes. It encodes a protein required for nucleocapsid assembly. A ts mutant failed to produce nucleocapsids at the non-permissive temperature, indicating that it is an essential gene and it was associated with both BV and ODV (222). It interacts with 38K (Ac98) (223). When the vp1054 gene was deleted from a bacmid, the bacmid did not appear to be viable and nucleocapsids appeared to be replaced with tube-like structures. It was suggested that vp1054 may be related to a cellular protein called PURa that binds to purine-rich sequences and may be involved in DNA packaging. Ac54 was shown to bind to single stranded DNA or RNA sequences that contained runs of GGN (224). Inactivation of Ac54 disrupted nucleocapsid assembly and resulted in aberrant capsid structures that were located with vp39 in the nuclear periphery. Using immunoelectron microscopy it was observed that BV/ODV-C42, PP78/83, and 38K did not associate with capsid structures when VP1054 was absent. It was found the VP1054 associates with BV/ODV-C42 and VP80 but not VP39 suggesting that VP1054 is critical for nucleocapsid assembly (225).

Ac55 (73aa:8.2kDa), (Bm44:77aa:8.6kDa), (Ha48:68aa:8.0kDa).

Homologs of Ac55 are found in the genomes of all Group I and most of the Group II NPVs. It appears to be nonessential because a BmNPV mutant deleted for this gene appeared to be normal (15).

Ac56 (84aa:9.9kDa), (Bm45:84aa:9.9kDa), (Ha49:64aa:7.4kDa).

Homologs of this orf are found in genomes of most Alphabaculoviruses. It appears to be nonessential because a BmNPV mutant deleted for this gene appeared to be normal (15).

Ac57 (161aa:19kDa), (Bm46:161aa:20.2kDa), (Ha50:171aa:20.7kDa).

Homologs of this orf are found in most Group I and II NPVs. It appears to be nonessential because a BmNPV mutant deleted for this gene appeared to be normal (15). It also appeared to be non-essential for HearSNPV (226).

Ac58, Ac58/59 (172aa:20.3kDa), (Bm47:171aa:37.8kDa), (Ha51:160aa: 19.0kDa), ChaB-like.

Ac58, Ac58/59 is a single gene, as they were found to be joined when the region was re-sequenced in the C-6 strain (12). This results in an orf predicted to encode 172 amino acids. Homologs of this orf are found in the genomes of most alphabaculoviruses. It has a ChaB domain. In *E. coli*, ChaB is thought to regulate ChaA, a cation transporter protein. It was found to localize to nuclei of infected cells (227) and was associated with AcMNPV ODV (89). It is also BV associated (27) and is hyperphosphorylated is cell extracts at 24 hpi (38). It appears to be nonessential because a BmNPV mutant deleted for this gene appeared to be normal (15).

Ac60 (87aa:10.1kDa), Bm48:83aa:9.7kDa), (Ha52:88aa:10.2kDa), (ChaB-like).

Homologs of Ac60 are found in the genomes of all Group I and II NPVs and most GVs. Similar to Ac58/59, Ac60 also has a ChaB domain. It is surprising that Ac58/59 and Ac60 are both predicted to encode ChaB domains as they do not show much sequence similarity. Alignment of the sequences resulted in an amino acid sequence identity of 15%; however, it required the insertion of several gaps, so the significance of the relatedness is not clear. In SpliNPV, two adjacent ChaB homologs were also identified. Evidence suggests that they may be DNA binding proteins (228). It appears to be nonessential because a BmNPV mutant deleted for this gene appeared to be normal (15).

Ac61 (214aa:25.2kDa), (Bm49:214aa:25.3kDa), (Ha53:217aa:25.4kDa), Few polyhedra (fp, fp-25k).

Although orthologs of Ac61 have been reported in the genomes of all alpha-, beta-, and gammabaculoviruses (156), I was unable to confirm their presence in gammabaculovirus genomes. Whereas both Ac61 and XcGV orf140 were predicted by Hhpred to be similar in structure to Line-1 orf1p (see below), the gammabaculovirus fp25K (Neab54) from (156) was not predicted to be similar. Also, I could find no relationships via PSI Blast. AC61 has been shown to be BV associated (27). Deletion is not lethal, but results in a 'few polyhedra phenotype' (fp) (229, 230). Fp-25k was more highly expressed in midgut than cultured cells suggesting it may be important in establishing the infection (39). FP mutants are defective in virion occlusion and nucleocapsid envelopment in nuclei and release two- to fivefold more infectious BV than wt in infected Sf9 cells (230, 231). The nonlethal, but readily distinguishable phenotype has facilitated investigations on this gene. FP mutations often result from the insertion of host DNA into the fp gene (229, 232). They can also be the result of errors in DNA replication (233). Mutations in the *fp* gene result in a reduction in polyhedrin gene (but not *p10*) transcription (230). Mutations also appear to affect the levels and nuclear transport of Ac46 (ODV-E66), an ODV envelope protein (234, 235). In BmNPV *fp* mutants, the few virions that were occluded appear to lack envelopes (236). A combination of reduction in the level of polyhedrin and an ODV envelope protein could contribute to the FP phenotype. The defect in occlusion and in the ODV envelope could lead to the availability of more virions for budding. A reduced level of liquefaction of larvae was also noted with an fp mutant in BmNPV (236). This was attributed to the involvement of Bm49 in the regulation of v-cathepsin expression (237). In *T. ni* cells, double *p35* (see Ac135) and *fp* mutants underwent apoptosis, whereas p35 mutants alone did not, suggesting that the *fp* gene may have pro-apoptotic properties in this cell line (238). In contrast, in BmNPV infected BmN cells, deletion of fp25k did not affect apoptosis induced by a virus with p35 deleted (239). Fp25k mutants of AcMNPV produce virions that are occluded with different efficiencies depending on the cell line or insect. When replicated in Sf cells or insects the efficiency was lower than in *T. ni* Hi F cells or larvae (240). The fp25k gene was also found to contain two hypermutable sequences of 7 adenine residues and the mutant 25k genes expressed different amounts of polyhedrin mRNA and protein depending on the cell line (241). It was suggested that fp25k may destabilize the genome thereby elevating the level of mutagenesis (242). Evidence indicates that fp25k is related to the orf1p of

the Line-1 group of retrotransposons with a probability of 99.8% according to Hhpred (189). Orf1p acts as a nucleic acid chaperone and similar to orf1p, fp25k has a coiled-coil domain and a predicted RNA binding motif (243). Although the significance the relatedness is compelling, how this gene adapted to baculovirus biology is unclear.

*Ac62 (516aa:59.3kDa), (Bm50:490aa:56.4kDa), (Ha55:519aa: 60.0kDa), Lef-9, baculovirus RNA polymerase subunit.

Lef-9 homologs are present in all baculovirus and also nudivirus genomes. It was found to be required for transient late gene expression (13) and subsequently shown to be a subunit of the baculovirus RNA polymerase (185). It contains a 7-amino acid motif (NTDCDGD or NRDCDGD except NADFDGD in the dipteran virus) similar to the Mg++ binding sequence (NADFDGD) found in the catalytic center in large RNA polymerase subunits of a few DNA-dependent RNA polymerases (13). The D residues bind Mg++ and are conserved in all these sequences. It is likely an essential gene as an insertion/deletion mutant in the BmNPV homolog (Bm50) could not be isolated (81) or did not replicate (15). Another Bm50 knockout was found to have limited effect on viral genome replication, but transcription of several early and late genes was greatly diminished (244).

Ac63 (155aa:18.5kDa), (Bm51:155aa:18.5kDa), (Ha121:154aa: 18.5kDa).

Homologs of Ac63 are found in several Group I and Group II alphabaculoviruses. A homolog in a nudivirus has been reported (245). It appears to be associated with BV envelopes (246). It appears to be nonessential because a BmNPV mutant deleted for this gene appeared to be normal (15).

Ac64 (302aa:34.8kDa), (Bm52:294aa:33.8kDa), (Ha58:279aa:32.1kDa), (GP37/P34.8, spindlin, fusolin, spheroidin-like protein).

The terminology of Ac64 has a confusing history and, in addition to GP37, has been referred to as p34.8, spindlin, fusolin, or spheroidin-like protein because of homology with an entomopox virus gene (247, 248). Evidence suggests that it is not a spheroidin-like homolog (249). Orthologs of *gp37* have been found in the genomes of most alpha and beta baculoviruses (156). In AcMNPV it is expressed as a late gene (250). In addition to entomopox, it is related to orfs in a variety of eubacteria, e.g., *Vibrio alginolyticus* (E = 5e-27). It has been suggested that the granulovirus *gp37* lineage is more closely related to the entompox lineage than to *gp37s* from NPVs (251). A homolog of Ac64 is referred to as chitinase B in the marine bacterium *Pseudoalteromonas* sp. and was found to bind to, but not digest chitin (252). The GP37 homolog in SpltNPV has been reported to contain chitin binding domains and is capable of binding to chitin (253). The GP37 of CpGV also bound chitin and was able to enhance per os infections (254). Insect proteins, such as the coagulation protein hemolectin, also have chitin-binding domains (255). GP37 was reported to be polyhedron associated in AcMNPV and to be N-glycosylated (248). It was also found to be BV associated (27). In OpMNPV infected *L. dispar* cells, GP37 was found to be an N-glycosylated protein located in cytoplasmic occlusions late in infection (256). In entomopox viruses the GP37 ortholog forms crystallized spindle-like structures. These structures have been suggested to digest the peritrophic matrix (257). Structural analysis of these spindles indicated that they contained a globular domain that is related to lytic polysaccharide monooxygenases of chitinovorous bacteria. It is thought that upon ingestion by the host, the spindles are dissolved and the monooxygenase domain is exposed and can then digest the chitin-rich peritrophic matrix (258). It has been reported that GP37 can degrade the peritrophic matrix and also facilitates the binding of ODV to midgut cells (259). The *gp37* gene is nonessential for replication in cell culture or *T. ni* larvae (247). Similar results were observed for the BmNPV homolog (Bm52) (15). The *Spodoptera litura* NPV genome was found to contain a gene that is a fusion of ubiquitin and *gp37* (for discussion, see *Ac35, ubiquitin*) and the protein was associated with the envelopes of BV and ODV (164) .

*Ac65 (984aa:114.3kDa), (Bm53:986aa:114.4kDa), (Ha67:1020aa: 119.3kDa) (DNA polymerase).

Homologs are found in all baculoviruses. The non-baculovirus homologs showing the highest level of similarity are found in herpesviruses, e.g., human herpes virus 7 (E = 1e-25), several protozoans, and archaea. A DNA polymerase homolog was originally identified in the AcMNPV genome by hybridization with degenerate primers designed based on a highly conserved domain in other DNA polymerases (260). A 3'→5' exonuclease activity specific for single-stranded DNA was shown to be associated with the DNA polymerase from *Bombyx mori* NPV (BmNPV) (261) and AcMNPV (262), suggesting that a proofreading activity was associated with this enzyme. A purified DNA polymerase from AcMNPV was characterized as being active on singly primed M13 templates (263). The polymerase is highly processive on poly (dA)-oligo dT (262). Mutations of AcMNPV DNA polymerase resistant to a variety of inhibitors have been described (264). The N-terminal 186 aa was determined to be important in the function of the protein (265), and the C-terminal ~200 aa was predicted to contain two sequences for nuclear localization and both appeared to be required (266). DNA polymerase is an essential gene because deletion is lethal in AcMNPV (267) and BmNPV (15, 81).

*Ac66 (808aa:94kDa), (Bm54:805aa:93.3kDa), (Ha66:785aa:88.9kDa).

Homologs of *Ac66* appear to be present in all baculoviruses. Many baculoviruses have two copies of Ac66, and some may have three copies (125). Ac66 is oriented in the opposite direction of DNA polymerase (Ac65) and its promoter region overlaps with the 5' region of the DNA pol orf. This orientation is conserved in many, if not all baculoviruses. Consequently, it is likely that Ac66 is conserved throughout the baculoviruses. Ac66 is transcribed as a late gene and its expression does not affect the expression of DNA pol (268). Ac66 is closely related to a variety of proteins including an actin binding protein, myosin heavy chain, and centromere protein E. Although the orf adjacent to DNA polymerase in *Neodiprion sertifer* NPV (NeseNPV) shows little homology to Ac66, it and Ac66 show homology to the same proteins, i.e., they both show almost 100% probability of being related to formins that are involved in actin nucleation, myosin, and components of a splicing complex using the HHpred program (77). Ac66 is associated with AcMNPV (89) and HearNPV (Ha66) (269) ODV and AcMNPV BV (27). Ac66 in BV but not ODV is ubiquitinated by the viral ubiquitin and appears to interact with Ac141 (predicted to be a an E3 ubiquitin ligase). It was suggested that this might be a signal for BV egress in contrast to ODV that remain in nuclei (163, 266). An AcMNPV bacmid deleted for Ac66 was severely compromised and BV titers derived from transfected cells were reduced by over 99% compared with wt. In addition, at low titers the mutant BV appeared to infect single cells and was unable to spread. Although the nucleocapsids appeared to be normal and had an electron dense core, suggesting that they contained DNA, they appeared to be trapped in the virogenic stroma, suggesting that Ac66 was required for the efficient egress of virions from nuclei. Deletion of Ac66 did not affect the levels of DNA replication or polyhedrin transcription, but the production of occlusion bodies was eliminated (270). This suggests that Ac66 is required both for egress of virions from nuclei and also may be involved in the enucleation of polyhedra. A bacmid deleted from Bm54 produced non-infectious BV and appeared to be properly assembled. Polyhedron formation also appeared to be affected (271). For additional discussion, see Chapter 5.

Ac67 (385aa:44.6kDa), (Bm55:385aa:44.9kDa), (Ha65:379aa:44.0kDa), LEF-3, (Single stranded DNA binding protein – SSB).

Lef-3 was originally found to be essential for DNA replication in transient assays (50, 51). Homologs of *lef-3* are found in the genomes of lepidopteran NPVs and GVs, but not those of hymenopteran or the dipteran NPVs. LEF-3 is a single-stranded DNA binding protein (SSB) (272) and interacts with itself as a homo-oligomer (273) (273). It also binds to helicase (274), facilitates its transport into the nucleus (275) and can drive nuclear transport into mammalian cells (276). It also may have a function in DNA replication in addition to its requirement as a helicase transport factor (277, 278). LEF-3 also interacts with alkaline nuclease and may

regulate the function of this enzyme (279, 280); it is capable of both unwinding and annealing DNA depending on its concentration or redox state (281, 282); and it can facilitate the production of structures resembling recombination intermediates via strand exchange between donor and recipient molecules in vitro (283). The lack of conservation of LEF-3 in baculoviruses might not be unexpected because, although homologs of alkaline nuclease are present in many organisms (see *Ac133*) and many have been reported to interact with an SSB (e.g., herpesvirus, ICP8 and lambda phage, red-beta), clear sequence relationships between the various SSBs are not evident (284). Insertion/deletion mutants of *lef-3* are lethal (81, 278). In another report a bacmid deleted for LEF-3 showed some evidence for limited amounts of DNA replication and late gene expression, and some infectious virus was observed although over100,000 times less than wt (285).

*Ac68 (192aa:22.3kDa), (Bm56:134aa:15.8kDa), (Ha64:133aa:15.6kDa) PIF-6.

Homologs of Ac68 are present in all baculoviruses. A frame shift in this gene did not affect transient late gene expression (187) and a deletion of Ac68 resulted in no major effects on AcMNPV production and TCID50, and no differences in the number, size, and shape of polyhedra were noted, although the lethal time was longer in T. in larvae (286). In contrast, another report suggested that Ac68 was a per os infectivity factor (PIF-6) as a deletion mutant, although producing normal appearing polyhedra, they failed to kill *T. ni* larvae (285). In addition, it is reported to be associated with the AcMNPV PIF complex (47) (287). When the homolog in BmNPV (Bm56) was deleted in a bacmid, no effects on titers in cultured cells or in BV-injected larvae were detected, although the lethal time in larvae was longer. Although enveloped ODV were present, the polyhedra produced by the mutant bacmid were abnormal and lacked virions, suggesting that Bm56 is involved in polyhedron morphogenesis (288).

Ac69 (262aa:30.4kDa), (Bm57:262aa:30.4kDa), (Ha63:274aa:31.6kDa), (MTase).

Ac69 encodes a methyltransferase and orthologs are found in the genomes of most Group I NPVs and about one-half of Group II NPVs and one hymenopteran NPV. The homolog present in the hymenopteran NPV (NeseNPV) falls within an insect, rather than a baculovirus lineage. Homologs are found in a nudivirus (Hz-1) and a variety of insects, e.g., *Anopheles gambiae* (E = 8e-18) and other invertebrates and vertebrates. Ac69 was found to stimulate late gene transcription in a transient assay (187). The gene encodes a protein with RNA Cap (Nucleoside-2′-O)-Methyltransferase activity. AcMNPV, with a null mutation of the gene, replicated normally in cell culture (289). Similar results were observed for a knockout of the homolog (Bm57) in BmNPV (15).

Ac70 (290aa:34.4kDa), host cell-specific factor-1 (hcf-1).

Homologs are present in only three other baculoviruses; two are close relatives of AcMNPV and their HCF-1 orfs are 99% (PlxyNPV) and 84% (RoMNPV) identical to that of AcMNPV, whereas the homolog in ClbiNPV is more distantly related (21% identical). HCF-1 was found to be required for transient expression of a late promoter-reporter gene by a late expression factor library in *T. ni* cells, but not SF-21 cells (290, 291). AcMNPV with null mutations in hcf-1 were found to replicate normally in both Sf-21 cells and *S. frugiperda* larvae. However, in *T. ni* cells, replication was impaired and in *T. ni* larvae the mutant showed a significantly reduced infectivity by intrahemocelic injection. Although oral infectivity was relatively normal in *T. ni* larvae, the insects died more slowly than when infected with wt (292). It was suggested that HCF-1 is a RING finger-containing protein that is dependent upon self-association and gene repression for its activity (293).

Ac71 (249aa:28.6kDa), (Bm58:249aa:28.7kDa), (Ha62:250aa:29.3kDa), iap-2.

Ac71 encodes an inhibitor of apoptosis-2 (*iap-2*) gene. Up to 6 *iap* homologs are found in baculovirus genomes (125) (126). Homologs of *iap-2* are found in the genomes of most alphabaculoviruses, and as with all *iap* genes, more distant relatives are found in many organisms. It is BV associated in AcMNPV (27). Deletion of *iap-2* had no effect on viral replication in cell culture; however, this may have been due to the presence of another apoptotic suppressor, *p35* (294). In contrast, deletion of *iap-2* (bm58) from the BmNPV genome indicated that it was required for replication in BmN cells (138). Evidence suggested that transfection of AcMNPV iap-2 into *T. ni* cells suppressed apoptosis by HearNPV infections, and although a recombinant HearNPV expressing iap-2 also suppressed apoptosis, BV production was not rescued (128). In *Epiphyas postvittana* NPV, the *iap-2* homolog was found to have anti apoptotic activity when expressed from a CMV promoter in *S. frugiperda* cells (129). However, it was observed that *iap-2* of *Lymantria dispar* MNPV induced apoptosis when transfected into Ld652Y cells. It was suggested apoptosis was suppressed by the virus because of the presence of the apoptotic repressor, *apsup* in LdMNPV (295).

Ac72 (60aa:7.1kDa), (Bm58a,60aa,7.1kDa).

Homologs of Ac72 are found in the genomes of most sequenced Group I NPVs, but not in other viruses. Bm58a localizes to the cell membrane at the late stage of infection. When Bm58a was deleted, the infected cells failed to lyse and larvae did not undergo liquefaction (296). However, in another report, deletion of this in BmNPV caused no observable differences from wt (15)

Ac73 (99aa:11.5kDa), (Bm59:99aa:11.5kDa), a BAG protein.

Homologs of Ac73 are found in the genomes of most sequenced Group I NPVs, but not in other viruses. It is BV associated in AcMNPV (27). Bm59 is an early gene and when deleted, the infection appears to progress normally (297). Analysis by Hhpred (189) indicates that it is a BAG (Bcl-2-associated athanogene) protein with greater than 99% probability. BAG proteins are regulators of molecular chaperones and share a BAG domain (BD) which binds to and regulates the Hsp70/Hsc70 family of proteins.

Ac74 (265aa:30.6kDa), (Bm60:268aa:31.0kDa), (Ha68:152aa:17.6kDa).

Homologs of Ac74 are found in the genomes of most Group I and about half Group II NPVs, but is not present in hymenopteran or dipteran NPVs or GVs. Bm60 was found to be expressed as a late gene and was localized to both the cytoplasm and nucleus of infected cells (298). It is BV associated in AcMNPV (27) and was found to be associated with AcMNPV ODV (89), but not in HearNPV ODV (269). Deletion of Bm60 from BmNPV resulted in a reduction and delay in DNA synthesis, a reduction in BV production by about 10-fold, and a lengthening of the time to kill larvae (299).

Ac75 (133aa:15.5kDa), (Bm61:133aa:15.5kDa), (Ha69:127aa:14.9kDa).

Homologs of Ac75 are present in all lepidopteran NPV, GV and hymenopteran NPV genomes, but not in the dipteran virus genome. It was found to be associated with both BV and ODV of BmNPV and localized to the ring zone of infected cells (300). In BmNPV it appears to be essential because when deleted, no BV were detected and the virions appeared to be retained in the nuclei (301). Other evidence indicates it is involved in nuclear egress of nucleocapsids and the formation of intranuclear microvesicles (302) (303).

Ac76 (84aa:9.4kDa), (Bm62:85aa:9.6kDa) (Ha70:85aa:10.0kDa).

Homologs of Ac76 are present in the genomes of all lepidopteran NPVs, GVs, and hymenopteran NPVs, but have not been reported in the dipteran virus genome. Ac76 localized to the ring zone late in infection. It is an

essential gene, as deletion of ac76 resulted in a mutant bacmid able to produce DNA to normal levels, but was deficient in intra nuclear microvesicles and was unable to produce BV (304). Ac76 appears to be present as a stable dimer that is resistant to denaturation and functions as a type II integral membrane protein in which the C-terminus is located in the ER lumen and the N-terminus interacts with the cytosol (305). Ac76 interacted with NSF and may be involved in the nuclear entry and egress of BV (302). It also interacts with components of the ESCRT-III complex and may be involved in the release of nucleocapsids at the nuclear membrane (75).

*Ac77 (379aa:44.4kDa), (Bm63:379aa:44.3.0kDa), (Ha71:412aa: 47.9kDa), Very late factor-1 (Vlf-1).

Homologs of Vlf-1 are found in all baculoviruses. It is a member of the lambda integrase (306) family of proteins. Integrases are a large group of site-specific DNA recombinases that catalyze DNA rearrangements and are involved in the integration and excision of viral genomes and decatenation of newly replicated chromosomes. A feature of these enzymes is that a conserved tyrosine forms a covalent link with DNA during the cleavage process. VLF-1 was originally identified because it influences the hyperexpression of very late genes (306). It was found to bind near the regulatory region of very late genes (307). Whereas mutations to the region that affected very late gene transcription were not lethal, other mutations, including mutation of the conserved tyrosine, appeared to be lethal to the virus (308). VLF-1 is present in both BV and ODV (308) and localizes to the ends of nucleocapsids, suggesting that it is a structural protein (309) and is required for the production of nucleocapsids. Although *vlf-1* is an essential gene, an AcMNPV bacmid with *vlf-1* knocked out (309-311) was able to synthesize viral DNA at levels similar to control bacmids. However, the mutant produces tube-like capsids that appear to lack DNA. Characterization of a bacmid with a mutation of the conserved tyrosine indicated the nucleocapsids were unable to be released from the virogenic stroma, suggesting that the protein may be involved in a final maturation step of the nucleocapsid (309). VLF-1 showed structure-dependent binding to DNA substrates with the highest binding affinity to cruciform DNA that mimics a structure common to recombination intermediates (312). See also Chapters 5 and 6.

*Ac78 (109aa:12.5kDa), (Bm64:110aa:12.7kDa), (Ha72:110aa: 12.7kDa).

Ac78 is a core gene (156) and in BmNPV it appeared to be essential (15). When deleted from AcMNPV, DNA replication was unaffected, nucleocapsids were confined to nuclei, infectious BV were not produced, and polyhedra lacked occluded virions. It is important in BV production and per os infectivity, but did not appear to be involved in DNA replication or ODV maturation (313). Ac78 was envelope associated in both BV and ODV (314) and analysis using Hhpred (189) shows over 90% probability that part of it is similar in structure to an integrin transmembrane domain. The homolog of Ac78 in HearNPV was associated with the ODV envelopes (315) and essential for production of infectious viruses and interacted with the baculovirus sulfhydryl oxidase, p33 (316). In addition, it was reported that Ac78 associates with NSF and may be involved in the nuclear entry and egress of BV (302). It also interacts with components of the ESCRT-III complex and may be involved in the egress of nucleocapsids at the nuclear membrane(75).

Ac79 (104aa:12.2kDa), (Bm65:104aa:12.2kDa).

Homologs are present in most Group I, about half the Group II NPV and GV genomes. It was found to be associated with AcMNPV ODV(89). It has a high degree of relatedness to ascovirus orfs from *T. ni*, and *S. frugiperda*, Chilo iridescent virus, and orfs from a variety of bacteria and archaea. It is predicted with over 99% probability by Hhpred (189) to be similar in structure to the GIY-YIG N-terminal endonuclease domain of UvrC involved in DNA repair (317) (318). Bacmids deleted for Ac79 resulted in reduced BV production and smaller plaque size, and showed some tube-like structures that may be aberrant capsids. Point mutations in conserved motifs shared by Ac79 and the endonuclease superfamily did not result in tube-like structures, but one of the

mutations caused a reduction in BV production (318). One study of BmNPV suggested that Bm65 is an essential gene (319), whereas another study indicated that it produced BV and could spread between cells, but with reduced efficiency (15).

*Ac80 (409aa:45.4kDa), (Bm66:403aa:44.9kDa), (Ha73:322aa: 36.6kDa), GP41, tegument protein.

GP41 is a tegument protein modified with O-linked N-acetylglucosamine, located between the virion envelope and capsid (320, 321). It was found to be associated with ODV by mass spectrometry (89, 269). Homologs are present in all baculovirus genomes. Based on the characterization of a ts mutant, Ac80 is an essential gene required for the egress of nucleocapsids from the nucleus (322). A deletion mutant of the homologous gene in BmNPV (Bm66) indicated that it produced BV and could spread between cells but with reduced efficiency (15). Deletion of AcMNPV *gp41* blocked the formation of BV and ODV. In addition, it was found that oligomerization of gp41 was required for BV production

(323). It was reported that gp4 associates with NSF and may be involved in the nuclear entry and egress of BV (302). Also, it interacts with components of the ESCRT-III complex and may be involved in the release of nucleocapsids at the nuclear membrane (75).

*Ac81 (233aa:26.9kDa), (Bm67:234aa:27.0kDa), (Ha74:241aa: 27.7kDa).

Homologs of this orf appear to be present in all baculovirus genomes and in nudiviruses (245). The BmNPV homolog (Bm67) appears to be a late expressed nonstructural gene that localizes to the cytoplasm (324). It may be essential because a deletion mutant of the homologous gene in BmNPV (Bm67) was severely compromised and did not appear to produce BV (15).

Ac82 (180aa:19.8kDa), (Bm68:181aa:20.1kDa), (Ha75:225aa:24.9kDa), Telokin-like protein (TLP).

Telokin-like protein is not like telokin! Homologs of Ac82 are found in the genomes of all lepidopteran NPVs and GVs. Telokin is the myosin binding fragment of myosin light chain kinase and is involved in muscle contraction. A polyclonal antibody prepared against smooth muscle telokin reacted with a protein from cell extracts of AcMNPV-infected Sf9 cells. This protein was called telokin-like protein. Clones that reacted with the antibody were isolated from a cDNA library of AcMNPV infected sf9 cells (325). The clones showed no sequence homology to telokin but when expressed in a pET vector, the product reacted with the telokin polyclonal antiserum. The AcMNPV sequence that produced the reactive protein contains portions of Ac82. The crystal structure of AcMNPV TLP was determined, but showed no similarity to telokin or any other characterized protein (326). Therefore, although this protein has been called telokin-like protein, its resemblance to telokin appears to be an artifact of the polyclonal antiserum. Ac82 is likely to be nonessential because when it was deleted in BmNPV (Bm68) the virus appeared to be normal, but production of BV and DNA replication was somewhat delayed. Although it showed nuclear localization and did not concentrate at the plasma cell membrane, it was found to be associated with the envelope/tegument of budded virions (327). In AcMNPV a TS mutant appeared to cause a major reduction in BV production (212). Bm68 was hyperphosphorylated during infection (38).

*Ac83, VP91, PIF-8 (847aa:96.2kDa), (Bm69:839aa:95.8kDa), (Ha76:816aa:93.5kDa)

Ac83 (PIF8) encodes a virion capsid protein called VP91 that was originally characterized in OpMNPV (328). It has also been shown to be ODV associated in AcMNPV, CuniNPV, and HaSNPV by mass spectrometry (89, 114,

329) and was found as a component of the per os infectivity factor (PIF) complex (47). Homologs are encoded by all baculovirus and are also found in nudiviruses (245) and possibly in several insect genomes. Ac83 is predicted to contain a chitin binding domain and has a high degree of predicted structural similarity by HHpred (77) to tachycitin, a 73aa antimicrobial peptide (330). However, chitin binding by Ac83 has not been detected (331) and structural predictions suggested that it lacked critical features of a chitin binding domain and may be a second zinc finger domain (332). When *ac83* was deleted from an AcMNPV bacmid, the bacmid was non-infectious. However when just the chitin binding domain region was deleted, the virus was unable to infect larvae via the midgut, but could infect via intrahaemocoelic injection, indicating that Ac83 is a per os infectivity factor and that the predicted chitin binding domain may play a major role in the ability of the virus to initiate midgut infection (331). A deletion mutant of this gene in BmNPV (Bm69) did not produce BV and results in the production of tubular structures (333). AC83 is associated with ODV nucleocapsids and envelopes and contains a cis-acting nucleotide sequence essential for nucleocapsid assembly and is called the nucleocapsid assembly-essential element (NAE) (334). In addition, three contiguous zinc finger domains were predicted that are critical for per os infectivity and it was suggested that they are involved in the localization of the PIF complex to ODV envelopes and interaction with the midgut cell membrane (332). Therefore, Ac83 has at least two functions; the gene contains a DNA sequence necessary for virion assembly and it is a PIF.

Ac84 (188aa:21.7kDa).

This orf is only found in a few other NPVs: PlxyNPV, ChchNPV, and RoMNPV, and TnSNPV. A homolog is also found in ascoviruses, e.g., *T. ni* ascovirus (E = 3e-10). It is not found in the BmNPV or the HaSNPV genomes.

Ac85 (53aa:6.4kDa).

This small orf encoding 53 aa is only found in two other NPVs that are AcMNPV variants: PlxyNPV and RoMNPV. This gene is not found in the BmNPV or HaSNPV genomes. Hhpred (189) indicates that Ac85 is structurally similar to a carbohydrate esterase with a probability of about 90%.

Ac86 (684aa:80.8kDa) (PNK/PNL).

This gene encodes a protein with RNA ligase, polynucleotide 5'-kinase, and polynucleotide 3'-phosphatase activities and may be part of an RNA repair pathway (335). Homologs are only found in a few baculovirus genomes, three are closely related to AcMNPV including AgMNPV, ApNPV, and RoMNPV, whereas the other is in a GV, SpliGV. A closely related orf is also found in a *T. ni* ascovirus (E = 2e-125). Ac86 appears to be a nonessential gene expressed early in infection (336). This gene is not found in the BmNPV or HaSNPV genomes.

Ac87 (126aa:15kDa), (Bm70:126aa:15.1kDa).

This gene appears to be present in most Group I lepidopteran NPV genomes. It was suggested that the homolog in BmNPV (Bm70) might encode a capsid protein called p15 (337). It is likely nonessential, as a deletion mutant in BmNPV (Bm70) appeared normal (15).

Ac88 (264aa:30.1kDa), (Bm71:267aa:30.7kDa), (Ha77:283aa:32.3kDa), CG30.

Homologs of Ac88 appear to be present in the genomes of most Group I and II NPVs, and also may be present in a single GV (SpliGV). An orf in *Clostridium perfringens* showed significant similarity (E = 2e-06). Ac88 contains predicted zinc finger and leucine finger domains (338). It was found to be associated with AcMNPV (89), but not in HearNPV ODV (269). Deletion of this gene from AcMNPV resulted in only subtle differences from wt (339). However, deletion of the gene from BmNPV (Bm71) resulted in a 10 to 100 fold reduction in titer and showed a longer lethal time (340). In another study of Bm71, a deletion and two RING finger mutants were

constructed. The deletion mutant produced fewer BV and fewer occlusion bodies were released into the hemolymph of infected larvae. The RING finger mutants released fewer OBs into larval hemolymph. They also noted that cg30 localized to nuclei of infected cells (341). It is predicted by Hhpred (189) to be structurally similar to several proteins involved in splicing, ubiquitin ligation, transcription, and translation with a probability of over 99%.

*Ac89 (347aa:39kDa), (Bm72:350aa:39.3kDa), (Ha78:293aa:33.4kDa), VP39.

This gene encodes the major capsid protein VP39. It is present in all baculovirus genomes. It was originally characterized in OpMNPV (342) and AcMNPV (343). It interacts with 38K (Ac98) (223). Deletion of Bm72 from BmNPV resulted in no apparent BV production (15). It has been observed that VP39 interacts with a conserved domain of kinesin 1 and it has been suggestion that this interaction is involved in the transport of nucleocapsids destined to become BV to the cell membrane after their assembly in nuclei (344). A conserved glycine at 276 is essential for infectivity and appeared to influence very late gene expression. Based on mutagenic analysis it appears to be required for proper DNA packaging and nucleocapsid assembly (345).

*Ac90 (464aa:53.9kDa), (Bm73:465aa:54.0kDa), (Ha79:3461aa: 54.0kDa), LEF-4.

LEF-4 is a component of the late baculovirus RNA polymerase (185). It is present in all baculovirus genomes and is also present in nudivirus genomes (245). This gene was originally identified as being essential for late transcription (170). LEF-4 was subsequently found to be an RNA capping enzyme (346, 347). The addition of an mRNA 5' cap structure involves the hydrolysis of the gamma phosphate of the 5'-triphosphate of the first nucleotide of pre-mRNA and the capping reaction that involves the transfer of GMP from GTP. The two reactions involve two different enzymatic activities: an RNA 5' triphosphatase to remove the terminal gamma phosphate and the addition of GMP by guanylytransferase. These two activities are present on a single protein located at the N- and C-termini, respectively, in metazoans and plants. Although having similar activity, LEF-4 is unrelated to this category of capping enzyme, but is a member of metal dependent group of capping enzymes found in fungi and protozoa (346, 348, 349). The 5' cap structure appears to serve two roles. It protects the 5' end of the mRNA from degradation by exonucleases and it interacts with translation initiation factors, thereby facilitating the initiation of translation. Capping in eukaryotes involves an enzyme that associates with the highly repetitive carboxy terminal domain (CTD) of the β' subunit of RNA polymerase II. Because the baculovirus polymerase lacks a similar domain, it is likely that it evolved to include the enzyme as part of the RNA polymerase complex. However, assuming these reactions are free from exonuclease, it is not clear why LEF-4 is required for transcription in in vitro assays. These assays monitor RNA transcripts that would not need to be capped in order to be detected. This suggests that LEF-4 may play a structural role in the organization of the polymerase subunits, or it may have some other function. LEF-4 is an essential gene and could not be deleted (350). For more information see Chapter 6.

Ac91 (224aa:24.1kDa), (Bm74:154aa:17.3kDa).

Homologs of this gene are found in genomes of all Group I lepidopteran NPV and at least two GV (CpGV and PlxyGV) genomes. It has an unusual predicted amino acid sequence: 31% proline and 18% ser/thr residues. In HearNPV the Ac91 homolog (ha80) was expressed first cytoplasmically and then in nuclei, but did not appear to be a structural protein of BV or ODV (351). Deletion of Bm74 causes few differences from wt and repair viruses in DNA synthesis or BV titers. However, the lethal time in larvae was longer by 14.7 hr (352).

*Ac92 (259aa:30.9kDa), (Bm75:259aa:30.9kDa), (Ha80:254aa: 30.8kDa), p33, sulfhydryloxidase (sox).

Ac92 is a flavin adenine dinucleotide (FAD)-linked sulfhydryl oxidase (353) (354). Proteins with sulfhydryl oxidase activity have been implicated in the protection of cells from oxidative stress caused by apoptosis (355) (356). Orthologs of Ac92 are present in all sequenced baculovirus genomes, it is associated with BV and ODV, and it is an essential gene as viable recombinants deleted for this gene have not been isolated (354) (357). Ac92 is able to form a stable complex with the human tumor suppressor gene p53 when it was expressed in a baculovirus system. When expressed by itself, p33 shows diffuse cytoplasmic staining and punctate staining of nuclei. However, when co-expressed with p53, it exclusively localizes to nuclei. Expression of human p53 in Sf cells causes apoptosis that can be blocked by co-expression of baculovirus anti-apoptotic suppressors p35 or OpIAP. However, co-expression of p53 with p33 elevated the induction of apoptosis about two-fold. By proteomic analysis, p33 appears to be an ODV-associated protein in AcMNPV (89) and HearNPV (269, 329). The crystal structure of Ac92 was described as a novel dimer composed of two pseudodimers (358). The structure of Bm75 has also been reported (359). In addition, by mutagenesis and crystallography, three domains including the active site, the dimer interface, and a salt bridge at R127-E183 were shown to be required for sulfhydryl oxidase activity (360). An ortholog of P53 has been described for *S. frugiperda* (361) and similar to human p53, Sfp53 was found to interact with Ac92 (362). It interacts with the Sfp53 DNA binding domain and a point mutation in Sfp53 that inactivated DNA binding also inactivated binding of Ac92 to Sfp53. Ac92 was also shown to oxidize Sfp53 in vitro. However, despite the ability of p33 to interact with and oxidize Sfp53 in cultured cells, no effects on Sfp53-mediated apoptosis or virus replication were observed (362). Effects on other cell types or in whole insects was not ruled out by these studies.

*Ac93 (161aa:18.4kDa), (Bm76:161aa:18.4kDa) (Ha81:162aa:19.1kDa).

This gene appears to be present in all baculovirus genomes (363). An Ac93 knockout did not produce infectious BV and may be involved in the formation of intranuclear microvesicles, (363). Ac93 interacted with NSF and may be involved in the nuclear entry and egress of BV (302). It also interacts with components of the ESCRT-III complex and may be involved in the release of nucleocapsids at the nuclear membrane (75). A BmNPV bacmid deleted for Bm76 did not produce BV (15).

*Ac94 (228aa:25.5kDa), (Bm77:228aa:25.6kDa), (Ha82:230aa: 25.9kDa), ODV-E25 (p25, 25k, e25).

Ac94 appears to be encoded by all baculovirus genomes (363). The protein encoded by this gene was originally identified in OpMNPV, and immunogold staining with a specific antibody against Ac94 was localized to ODV envelopes (364). It has also been shown to be associated with BV and ODV of AcMNPV and HearNPV (27, 89, 269, 329). The hydrophobic N-terminal 24 aa of AcMNPV ODV-E25 appears to be a nuclear targeting signal (196). Deletion of Ac94 resulted in a 100-fold reduction in infectious BV. In addition, ODV were not evident and although polyhedra were produced, they lacked virions (365). It has been reported that when ODV-E25 is expressed as an early gene under the IE-1 promoter, it accumulated on the cytoplasmic side of the nuclear membrane rather than within nuclei, and budded virus production was severely reduced. This suggests that it might play a role in the shift from BV to ODV virions. In addition, expression from the very late polyhedrin or p10 promoter reduced and delayed occlusion body formation suggesting that it may play a role in virion occlusion (366) (367). Subsequently it was found that the open reading frame of ODV-E25 encodes a microRNA that down regulates ODV-E25 expression. It was suggested that this might result in a reduction in infectious virus production and be involved in the shift to occluded virus production (368) (102). Ac94 is highly express in midgut cells (39) and associates with NSF and may be involved in the nuclear entry and egress of BV (302).

*Ac95 (1221aa:143kDa), (Bm78:1222aa:143.6kDa), (Ha84:1253aa: 146.0kDa), DNA helicase (p143).

Homologs of DNA helicase are present in all baculovirus genomes. This gene was initially identified as a ts mutant that was unable to synthesize DNA at 33° (369). The defect was localized to a homolog of DNA helicase with a predicted mass of 143 kDa (370). P143 is required for transient DNA replication (50, 51) and shows ATPase activity and is able to unwind a DNA primer annealed to a larger DNA molecule in an ATPase-dependent manner (371). Helicase is dependent on an interaction with LEF-3 for transport to the nucleus (see Ac67, LEF-3) (275). P143 been implicated in affecting viral host range (372, 373) (374) (375) and specific amino acids of the Ac-p143 protein cause rRNA degradation in BmN cells and this may be a signal for apoptosis(376) (377). Deletion is probably lethal as deletion/insertion mutants of this gene in BmNPV (Bm84) could not be isolated (81).

*Ac96 (173aa:19.8kDa), (Bm79:182aa:21.0kDa), (Ha85:173aa:19.8kDa) PIF-4.

This orf appears to be present in all baculoviruses and homologs also appear to be present in nudiviruses (245). The homolog in BmNPV (Bm79) is an ODV envelope associated protein (378) and was also found associated with the envelopes of BV (379). Deletion of Ac96 from a bacmid construct resulted in a virus that could replicate in cell lines, but not insects. Consequently it was concluded that Ac96 is a per os infectivity factor (PIF4), (379). Similar results were obtained for Bm79 (380). Pif-4 interacts with PIF-1 and PIF-3 (48) and forms part of a core complex (332) and may provide proteolytic resistance to the core structure on dissolution of polyhedral in the insect midgut (287)

Ac97 (56aa:6.5kDa).

This is a small orf (56 aa) and appears to be present only in AcMNPV. There is no homolog in BmNPV and it is positioned at the location of the apparent insertion of two bro (Ac2) homologs (see Ac2). The lack of this orf in closely related viruses may indicate that it is not a functional orf.

*Ac98 (320aa:38kDa), (Bm82:320aa:38.0kDa), (Ha86:321aa:37.9kDa), 38K.

Ac98 encodes a predicted protein of 38k and orthologs are present in all baculovirus genomes. AcMNPV Ac98 interacts with itself, VP1054 (Ac54), VP39 (Ac89), and VP80 (Ac104) and is associated with BV and ODV nucleocapsids (223). In HearNPV it interacted with itself, ODV-E56 (Ac148), GP41 (Ac80), PIF-2 (Ac22) and PIF-3 (Ac115) (381). In BmNPV, 38K interacted with itself, FP (Ac61), C41 (Ac102), EC27 (Ac144), GP64(Ac128), ODV-E25(Ac94), ODV-E18 (Ac143), and vCATH (Ac127), PKIP (Ac24), P48(Ac103), pp31 (Ac36), gp37 (Ac64) (382). An AcMNPV bacmid deletion construct, although unable to produce infectious virions, was capable of DNA synthesis, but nucleocapsid formation was disrupted. Tube-like structures that appeared to lack DNA, but stained with an anti-vp39 antibody were observed (383). It has also been suggested that Ac98 is capable of stimulating transcription in a transient transcription assay (384). It is related to a set of enzymes including CTD phosphatases and evidence indicates that it dephosphorylates the p6.9 DNA binding protein which allows it to be packaged with the viral DNA (385). Although it is required for nucleocapsid formation, it does not appear to be a structural component of ODV as determined by proteomic analysis (89, 269). However, it was detected in CuniNPV ODV (114).

*Ac99 (265aa:31kDa), (Bm83:265aa:31.1kDa), (Ha87:315aa:37.0kDa), (LEF-5).

Homologs of lef-5 are found in all baculoviruses and are also present in nudiviruses (245). LEF-5 was originally identified as being required for transient late gene expression (386). It was demonstrated to interact with itself and to contain a domain similar to that of the RNA polymerase II elongation factor TFIIS (387). Subsequent investigations indicated that LEF-5 did not enable the baculovirus polymerase to transit pause sites, and it was concluded that it functions as an initiation factor, rather than an elongation factor (388). A lef-5 knockout bacmid appeared to express early genes and replicate DNA normally, but was defective in late gene transcription, and did not yield any detectable virus when transfected in to Sf9 cells. (389).

*Ac100 (55aa:6.9kDa), (Bm84:65aa: 8.1kDa), (Ha88:109aa:11.5kDa), p6.9.

P6.9 is a small (55 aa) arginine/serine/threonine-rich DNA binding protein (390). Homologs appear to be found in all baculoviruses, but are apparently difficult to detect because of their small size and repetitive amino acid content (391). It was originally shown to be a DNA binding protein in a GV (392), and the homolog was isolated from AcMNPV (390). The high concentration of arginine and ser/thr residues is similar to protamines that are present in sperm nuclei of many higher eukaryotes and are involved in the production of highly condensed DNA. Protamines are also small molecules of 44-65 amino acids (393, 394). Arginine is positively charged, and the polyarginine tracts in protamines neutralize the phosphodiester backbone, whereas the ser and thr residues interact with other protamine molecules, thereby yielding a neutral, highly compact complex that is biochemically inert. P6.9 localizes to the nuclear matrix during infection (395). It was found to elevate virus transcription at 12-24 hpi, but did not appear to be involved in basal levels of virus transcription. It was also found to co-localize with viral DNA during this same time frame and to fractionate with RNA polymerase II at 24 hpi (396). Some localizes to the virogenic stroma but the majority was found near the inner nuclear membrane throughout the infection. It shows distinct patterns of phosphorylation with multiple forms present in association with ODV, however, only the dephosphorylated form was associated with BV (397). After synthesis, p6.9 is hyperphosphorylated, at least in part by pk-1 and this appears to be essential for high levels of expression of very late genes (398). Phosphorylation appears to occur immediately upon synthesis and p6.9 is dephosphorylated by the 38k protein (385) before being complexed with DNA (399). Using an AcMNPV bacmid deleted for p6.9, nucleocapsids were not produced although tube-like structures similar to those associated with the deletion of VLF-1 and Ac98 (see above) were observed. The mutant appeared to synthesize normal amounts of DNA, but did not produce infectious virus (400). BmNPV mir-3 appears to regulate, at least in part, the expression of BmNPV p6.9 (401).

*Ac101 (361aa:41.5kDa), (Bm85:362aa:41.6kDa), (Ha89:369aa: 42.6kDa), BV/ODV-C42.

Ac101 encodes a capsid-associated protein of both BV and ODV (89). Homologs have been identified in all sequenced baculovirus genomes (156). It was reported to interact in a yeast two-hybrid assay and by native gel electrophoresis (402) with pp78/83 (Ac8) that has been shown to localize to the basal end region of nucleocapsids (63, 64). Evidence suggests that it binds to PP78/83 and transports it into nuclei (403) and is involved in actin polymerization (404). It also interacts with FP25K (Ac61) and Ac141 (405). Deletion of Ac101 from an AcMNPV bacmid appeared to affect nucleocapsid formation but, although lethal, did not appear to affect DNA synthesis (406). Deletion/mutation of Ac101 was also reported to be lethal by others (403, 407). C42 functions to stabilize the actin nucleation factor, P78/83, by inhibiting its degradation. C42 in turn interacts with Ac102 and suppresses ubiquitination of C42 further regulating the stability of P78/83 (408-410). Micro RNA-3

(Mir-3) is encoded on the opposite strand of Ac101 and appears to be involved in its down regulation and may be involved in regulating BV and ODV production (411).

Ac102 (122aa:13.3kDa), (Bm86:123aa:13.5kDa), (Ha90:122aa: 13.8kDa), p12.

Homologs of Ac102 are found in all lepidopteran NPV, and GV genomes, but not in hymenopteran or dipteran viruses. It appears to encode an ODV-associated protein (89) in AcMNPV and HearNPV (329). It is involved in the nuclear localization of G-actin (43, 412). Deletion is lethal as insertion/deletion mutants of this gene could not be isolated in AcMNPV (43, 407) and viral spread to other cells was not observed with a BmNPV (Bm86) knockout (15). Ac102 is expressed as a late protein and is required for F-actin assembly in infected nuclei. It is a nucleocapsid protein and interacts with EC27 (Ac144), C42, and P78/83 (410). The interaction of Ac102 with C42 regulates the stability of P78/83 (see Ac101 above) (409).

*Ac103 (387aa:45.3kDa), (Bm87:387aa:45.4kDa), (Ha91:377aa: 44.0kDa), p45.

Homologs of Ac103 are present in all baculovirus genomes (156). Deletion of Ac103 was lethal, no viable BV were detected, and the constructs appeared to be deficient in the envelopment of ODV and their incorporation into occlusion bodies (413). Ac103 associates with NSF and may be involved in the nuclear entry and egress of BV (302). It was reported that Ac103 interacts with components of the ESCRT-III complex and may be involved in the release of nucleocapsids at the nuclear membrane(75).

Ac104 (691aa:79.9kDa), (Bm88:692aa:79.9kDa), (Ha92:605aa: 69.7kDa), vp80 capsid, vp87.

Homologs of Ac104 are found in all Group I and II lepidopteran NPV genomes, but not in those of GVs or hymenopteran or dipteran NPVs. It is capsid associated in both OpMNPV (414) and AcMNPV (89, 415, 416) and interacts with 38K (Ac98) (223). Deletion of Vp80 showed that it is an essential gene and resulted in nucleocapsids that were unable to move from the virogenic stroma (417). It appears to localize in nuclei near actin scaffolds that connect the virogenic stroma to the nuclear envelope. In addition, it co-immunoprecipitates with actin. It also appears to localize to one end of nucleocapsids and contains sequences similar to paramysin motifs that may be involved in the transport of virions to the periphery of nuclei (415). It forms dimers, contains a C-terminal region that was predicted to contain a basic helix-loop-helix domain, and binds to DNA (418).

Ac105 (553aa:65.6kDa), (Bm89:289aa:34.3kDa), He65, RNA editing ligase.

Homologs of Ac105 are found in the genomes of most Group I, about one-half the Group II and several GVs including Agse-, Ha-, and XecnGV. It is a member of a distinct family of ligases that includes editing ligases of trypanosomes, putative RNA ligases of many species of archaea, and also baculoviruses and an entomopoxviruses (419). It is an early-transcribed gene (420). It may be involved in the nuclear localization of G-actin (412). It appears to be a non-essential gene in AcMNPV (43) and BmNPV (15).

Ac106/107 (243aa:28.3kDa), (Bm90:249aa:28.9kDa) (Ha101:253aa: 29.0kDa).

These two orfs were found to be joined when the region was re-sequenced in the C-6 strain (12). Homologs are found in all Group I and II lepidopteran NPV, GV and hymenopteran NPV genomes, but not in that of the dipteran NPV. Deletion of Bm90 resulted in a mutant that was unable to spread between cells indicating that it is an essential gene (15).

Ac108 (105aa:11.8kDa), (Bm91:105aa:11.8kDa) (Ha95:94aa:11.0kDa) (PIF9).

Orthologs of Ac108 have been found in the genomes of all alpha, beta, and gamma baculoviruses (156). Although Ac108 was not found to be ODV-associated in AcMNPV (89) or HearNPV (269), the homolog in the *Antheraea pernyi* nucleopolyhedrovirus (p11) was found to be associated with ODV (421). In later studies it was found in the PIF complex of AcMNPV (47) and was identified as a PIF protein(422). Furthermore, the ortholog in *Spodoptera frugiperda* MNPV (sf58) appeared to be a per os infectivity factor (PIF) (423). Ac108 associates with PIF8 and is part of the complete PIF complex and when it was deleted, the virus was not orally infectious and it has been designated as PIF9 (424). In contrast, in BmNPV, Bm91 was ODV associated, but appeared to be non-essential in oral assays, although its deletion did extend the lethal time (15, 425) (425). Hhpred (189) predicted that Ac108 was similar in structure to several proteins with a probability of over 80% including Vesicle-associated membrane protein 2 of a SNARE complex and the membrane domain of E. coli histidine kinase receptor QseC.

*Ac109 (390aa:44.8kDa), (Bm92:391aa:45.0kDa), (Ha94:361aa: 41.5kDa).

Homologs of Ac109 are present in all baculovirus genomes. Evidence suggests that it is ODV-associated in AcMNPV (89) and *Helicoverpa armigera* NPV (Ha94-ODV-EC43) (269, 426) and also is BV-associated in AcMNPV (27, 427). Four studies have examined deletions of Ac109 and demonstrate that it is an essential gene and when deleted, DNA replication is not affected. One study reported that deletion of Ac109 resulted in a block in nucleocapsid and polyhedron formation (428). However, the other reports described different results. One indicated that polyhedra and virions were produced by Ac109 deletions, but the virus was not infectious (427). Another study found similar results, but also showed that the nucleocapsids had defects in envelopment and the polyhedra lacked virions (429). A fourth report also described similar findings, but indicated that the BV produced by an Ac109 knockout could enter the cytoplasm, but not nuclei, and also noted that the occlusion bodies lacked virions (430).

*Ac110 (56aa:6.8kDa), (Bm92a), (Ha93:58aa:6.9kDa), PIF-7.

Orthologs ofAc110 are found in all baculoviruses and it is a per os infectivity factor, PIF-7 (431) (332).

Ac111 (67aa:8.2kDa), (Bm93:67aa: 8.2kDa), (Ha116:71aa:8.2kDa).

Homologs of Ac111 are present in genomes of most Group I, and several Group II, e.g. Hear-, Heze-, Ld-, and LeseNPV and at least two GVs (SpliGV and XecnGV). Deletion of Bm93 had no effects on virus replication (15). Deletion of Ac111 did not affect BV production and had no effect on per os infectivity in *S. exigua* larvae, but infectivity was reduced by 5-fold in *T. ni* larvae (432) suggesting that it may be a per os infectivity factor, depending on the host insect.

Ac112/113 (258aa:30.9kDa), Apsup.

These two orfs were found to be joined when the region was re-sequenced in the C-6 strain (12). Homologs are present in several Group I and II NPV and GV genomes. It shows highly significant homology (over 50% identity) to an orf in several avian poxvirus genomes. A related orf is not present in BmNPV (16). The ortholog of this orf in LdMNPV (ld109) is an apoptosis suppressor called *apsup*. They show about 30% amino acid sequence identity, but Ac112/113 did not show any apoptotic suppressor activity (433).

Ac114 (424aa:49.3kDa), (Bm94:424aa:49.4kDa) PARG.

Homologs of Ac114 are found in most Group I NPV genomes. Hhpred analysis (189) indicates that it is a Poly(ADP-ribose) glycohydrolase (PARG) with almost 100% probability. This appears to be a baculovirus Group I PARG lineage that was not previously identified. The original baculovirus PARG is specific to Group II baculoviruses. The Group I and II PARGs show low levels of relatedness (e.g. AcMNPV and LdMNPV are less than 15% identical) and appear to represent two different lineages of this enzyme. In AcMNPV it is an ODV (89, 434) and BV associated protein (27). It is likely to be nonessential, as a BmNPV bacmid deleted for this gene (Bm94) appeared similar to wt (15).

*Ac115 (204aa:23kDa), (Bm95:204aa:23.0kDa), (Ha90:199aa:22.4kDa), pif-3.

Homologs of *pif-3* appear to be present in all baculovirus genomes. It is also present in nudivirus genomes (245). Like other *pif* genes, *pif-3* is required for oral infectivity of insect but not for infection of cultured cells (108). It forms a complex with PIF-1, -2, and -4 (381) (287) (48) and also interacts with ODV-E56 (435). For more information see Chapter 2.

Ac116 (56aa:6.4kDa), (Bm95a).

Homologs of Ac116 are found in a few Group I NPVs (Ac-, Ro-, Bm-, and PlxyNPV). Deletion of Bm95a and Bm96 showed no defects as did deletion of Bm96 alone, therefore Bm95 appears to be non-essential (15).

Ac117 (95aa:11kDa), (Bm96:95aa:10.9kDa), (Ha110:88aa:10.1kDa).

Homologs of Ac117 are found in the genomes of all Group I and some Group II NPVs. It is likely to be nonessential, as insertion/deletion mutants of this gene in BmNPV (Bm96) were similar to wt, although a slight effect on the motility of infected larvae was noted (15, 199).

Ac118 (157aa:18.7kDa).

Homologs are found in a few Group I NPVs (Ac-, Ro- and PlxyNPV) genomes. A related orf is not present in BmNPV.

*Ac119 (530aa:59.8kDa), (Bm97:527aa:59.8kDa), (Ha111:528aa: 60.3kDa), pif-1.

Homologs of *pif-1* are present in all baculovirus genomes and are also present in nudivirus genomes (245). This gene can be deleted and the mutant is still infectious for cultured cells, but is not orally infectious for insects (108). It forms a complex with PIF2 -3, and -4 (381) (287) (48). For more information see Chapter 2.

Ac120 (82aa:9.5kDa), (Bm98:82aa:9.5kDa).

Homologs of Ac120 are found in all Group I and most Group II genomes. It is likely to be nonessential, as an insertion/deletion mutation of this gene in BmNPV (Bm98) had no apparent effect on infectivity (15). Analysis using Hhpred (189) indicates with a probability of over 96% that Ac120 is related to the MIT domain (microtubule interacting and transport) of vacuolar protein sorting associated protein 4 (vps4).

Ac121 (58aa:6.7kDa), (Bm98a).

Homologs of Ac121 are only found in the genomes of Bm- and PlxyNPV. It may be a transcriptional activator of some early genes, including IE1 and pp31 (436). However, it does not appear to activate late gene expression (187). In BmNPV, it appeared to be non-essential (15).

Ac122 (62aa:7.2kDa), (Bm99:61aa:7.1kDa).

Homologs of Ac122 are present in most Group I genomes. It is likely to be nonessential, as an insertion mutation of this gene in BmNPV (Bm99) had no apparent effect on infectivity (15).

Ac123 (215aa:25kDa), (Bm100:225aa:26.0kDa), Protein kinase 2 (PK2).

Homologs of Ac123 are found in only a few NPVs including BmNPV, PlxyNPV and RoMNPV and they are all over 98% identical to AcPK2. PK2 is closely related to translation initiation factor eIF 2α kinase (e.g., B. mori (E = 2e-20)), and the homology appears to be focused on the C-terminal region of the kinase domain (437). An AcMNPV mutant deleted for *pk2* displayed no differences from wt in its infectivity to cultured cells and insect larvae (437). In contrast, PK2 (Bm100) from BmNPV was found to be required for replication in BmN cells (138). In addition, a novel eIF-2α kinase called BeK was identified from B. mori. It has a distinct N-terminal regulatory region not shared by other eIF-2α kinases. BmNPV PK2 was capable of inhibiting the enzymatic activity of BeK (438). AcMNPV PK2 inhibits yeast and human eIF2α kinases (439). Insect cells infected with wt showed reduced eIF2α phosphorylation and increased translational activity that was not observed in cells infected with the *pk2* deletion mutant. It was suggested that PK2 may be involved in a mechanism for inactivating a host stress response to virus infection (439). Sf9 cell infection by AcMNPV deleted for PK2 or by wt virus both encoding the p35 anti-apoptotic gene was found to induce the expression of BiP. BiP is a stress marker of the endoplasmic reticulum and a chaperone. It was observed, however, that the UV induction of eIF2alpha phosphorylation and the activation of caspase were mitigated more effectively by the wt virus than the mutant virus that lacks pK2, which is an eIF2α kinase inhibitor (440). The translation initiation factor eIF2α is phosphorylated by the eIF2α family of kinases. Phosphorylation of eIF2α inhibits cell mRNA translation and can lead to apoptosis. This often occurs under stress conditions such as viral infection. PK2 interferes with the function of an eIF2α kinase by binding its kinase domain thereby preventing the phosphorylation of eIF2α (441). This prevents the apoptotic signal caused by phosphorylation of eIF2α and allows viral mRNAs to be translated.

Ac124 (247aa:28.5kDa), (Bm101:244aa:28.1kDa).

Homologs of Ac124 are present in the genomes of most Group I lepidopteran NPVs. The deletion of Ac124 had few differences from wt; however, although the LD50 for larvae appeared unaltered, the time to larval death was extended (442). In BmNPV, it is associated with the envelopes of BV and in infected cells is present in the cytosol and cytoplasmic membrane (443). In AcMNPV it has been shown to be BV associated (27). A Bm101 knockout virus appear to replicate DNA normally, but did not produce infectious BV (444). In an earlier investigation it was reported that Bm101 appeared to be a non-essential gene (15). Also, a knockout of AcMNPV Ac124 had no detectable effect on the viral infection cycle and it was suggested that it may influence elevate the expression of the chitinase gene (445).

Ac125 (226aa:26.6kDa), (Bm102:227aa:26.6kDa), lef-7.

Homologs of lef-7 are present in the genomes of all Group I, and several Group II including Se-, Sf- and MacoNPV A and several GVs including Ha-, Xecn- and SfGV and can be present in two copies (446). It is a F-Box protein; the F-box is a motif of about 50 amino acids and is involved in protein-protein interaction. SfGV LEF-7 contains 3 F-Box domains (447). Lef-7 is stimulatory for transient DNA replication (51, 448). When deleted, infection was unaffected in Tn368 cells, but in Sf21 and Se1c cells DNA replication was 10% of wt (449). Deletion of BmNPV lef-7 also caused a reduction in BmNPV DNA synthesis (81). LEF-7 was found to be involved in the regulation of the DNA damage response (DDR) and it interacts with host S-phase kinase-associated protein 1 (SKP1). SKP1 is a component of a complex that interacts with and targets proteins for polyubiquitination. Deletion of *lef-7* from the AcMNPV genome resulted in the accumulation of phosphorylated H2AX and activation of the DDR that led to a major reduction in late gene expression and reduced infectious virus production by 100-fold. It was suggested that LEF-7 may interfere with the phosphorylation of H2AX

thereby diverting host DDR proteins from cellular chromatin, so that they can be exploited for viral DNA replication (450).

Ac126 (551aa:61.4kDa), (Bm103:552aa:61.8kDa), (Ha41:570aa: 65.5kDa), chitinase.

Homologs of chitinase were reported in genomes of most Alphabaculoviruses and several Betabaculoviruses(451) and is phylogenetically clustered with a number of lepidopteran chitinases, i.e., it shows 63% aa sequence identity to *B. mori* chitinase. Comparison of BmNPV and *B. mori* chitinases indicated that, although closely related, they have different properties; the viral chitinase is retained in the cell and functions under alkaline conditions, whereas the host enzyme is secreted and has reduced activity at higher pH (452). Phylogenetic studies indicate that it is more closely related to the chitinase of proteobacteria that employ the enzyme to degrade fungal chitins (453). It has a mode of action similar to *Serratia marcescens* chitinase to which it is 60.5% identical and processively hydrolyzes beta-chitin (454). In conjunction with Ac127 (cathepsin), chitinase participates in the liquefaction of insects late in infection. It is a late expressed gene and its product is localized to the cytoplasm (455) and also is BV associated (27). When it is deleted along with Ac127 (cathepsin), insects remained intact for several days after death (456). Chitinase is localized to the endoplasmic reticulum in infected cells by KEDL, an endoplasmic reticulum retention motif (457, 458). The retention in the ER may prevent the premature death and liquefaction of infected insects, allowing the virus to continue to replicate. It is thought that the presence of chitinase and cathepsin assists in the dissemination of the virus by degrading the insect upon its death. The facility with which a virus (*Anticarsia gemmatalis* NPV) can be processed for use as a biocontrol agent has been attributed to its lack of these two genes, thereby allowing collection of the virus from intact rather than disintegrated insects (459).

Ac127 (323aa:36.9kDa), (Bm104:323aa:36.9kDa), (Ha56:365aa: 42.0kDa), cathepsin, vcath, a metalloprotease.

Homologs of Ac127, cathepsin, have a similar distribution to Ac126 (chitinase) and are present in the genomes of most alphabaculoviruses and several GVs (451). The baculovirus genes are closely related to insect cathepsins, i.e. Ac127 is 39% identical to an *Apis mellifera* cathepsin. The baculovirus cathepsin appears to participate along with chitinase in the liquefaction of infected insects (see Ac126) (460). When it is deleted along with Ac126 (chitinase), insects remained intact for several days after death (456). It has been suggested that Ac127 is synthesized in an inactive form that is activated upon death of the insect by lysosomal proteinases (461). It was subsequently demonstrated that AcMNPV and CfMNPV cathepsins are expressed as pre-proenzymes that are cleaved in infected cells (462). Viral chitinase (see above) is apparently synthesized before cathepsin to facilitate the retention of cathepsin in the ER. Cathepsin is synthesized as an inactive precursor (preproV-CATH) and upon translation the N-terminal 22 amino acids encompassing the signal peptide causes the localization to the ER during which the signal peptide is cleaved. Within the ER the viral chitinase appears to interact with the proV-CATH and assists in the proper folding and causes its retention in the ER (463). Upon death of the host, proV-CATH is cleaved and activated and released from the ER along with chitinase to facilitate the degradation of the insect and release of the virus.

Ac128 (530aa:60.6kDa), (Bm105:530aa:60.6kDa), gp64, gp67.

gp64 encodes a low pH activated envelope fusion protein, and homologs are present in all Group I genomes. It is one of the major distinguishing features of these viruses. It is thought that all Group I viruses use GP64 for the entry of BV into cells, whereas all other baculoviruses lack a *gp64* homolog and use the F protein (ac23 homolog) except for hymenopteran NPVs which lack both genes. However, an ortholog of gp64 was identified in a GV (464). Orthologs of *gp64* are also found in thogotoviruses, which are members of the Orthomyxoviridae (465). GP64 (466-468) is a fatty acid acylated glycoprotein (469). Deletion of gp64 is lethal and results in viruses that

replicate in a single cell, but cannot bud out and infect surrounding cells (470, 471). The postfusion structure of GP64 has been described (472). It was found that a ubiquitin-protein ligase SINA-like 10 (SINAL10) interacted with GP64 and overexpression elevated viral production whereas inhibition caused their reduction (473). For more information see Chapter 2.

Ac129 (198aa:22.1kDa), (Bm106:195aa:21.8kDa), (Ha118:248aa: 28.4kDa), p24-capsid.

Homologs of Ac129 are present in the genomes of all Group I /II and GV genomes. Ac129 (p24) is associated with both BV and ODV of AcMNPV and OpMNPV (27, 474). Its presence in AcMNPV ODV was confirmed, however, the HearNPV homolog, He118, was not found associated with ODV (269). It is likely to be nonessential, as interruption of this gene with a transposable element in a strain of AcMNPV has been reported (475, 476). In addition, insertion/deletion mutations of this gene in BmNPV (Bm106), although viable, took slightly longer to kill insects than wt (199). Also, in LdMNPV, the original strain sequenced, lacked this gene, whereas it is present in other strains (477).

Ac130 (106aa:12.1kDa), (Bm107:106aa:12.1kDa), (Ha119:94aa: 10.7kDa), gp16.

Homologs of Ac130 are present in the genomes of most alphabaculoviruses. Ac130 localized to near the nuclear membrane and was present in a membrane fraction. Deletion caused the survival time (ST50) to increase about 6 hr (478). In OpMNPV, the homolog (Op128) is glycosylated and localized near the nuclear membrane in the cytoplasm. Although it appeared to be associated with envelopes of nucleocapsids in the cytoplasm, it was not associated with either ODV or BV (479). It appears to be a non-essential gene in BmNPV (15). Analysis by Hhpred (189), indicates that it may be related to several proteins with a probability above 80% including bacterial toxins, a heat shock binding protein, and a subunit of a filovirus fusion protein.

Ac131 (322aa:36.4kDa), (Bm108:315aa:35.4kDa), (Ha120:340aa:39.1kDa), calyx, polyhedron envelope (PE) protein, pp34.

The predicted size of Ac131 is longer (322 vs 252 aa) than previously reported (12). Orthologs of Ac131 have been found in the genomes of most alpha, beta, and gamma baculoviruses (156)(173). In addition, domains of PE may be present as fusion with segments of p10 in some GVs (see below). The calyx/PE appears to be applied in layers on the polyhedron surface (480). The calyx/PE was originally found to contain carbohydrate (481); subsequently a phosphorylated protein component was identified (482) (483). Similar results were obtained for OpMNPV and it was also found to be associated with p10 fibrillar structures (484-487). In addition, in some viral genomes, genes are present that appear to be fusions of both PE and p10 protein domains (488, 489). The Ac131 encoded protein appears to be an integral component of the calyx/PE, and when the gene is deleted, polyhedra lack an intact calyx/PE, and have a rough surface showing cavities where virions have apparently been dislodged (490). It has also been reported to be BV associated (27) although what role it may play in this phenotype is not clear. The function of the calyx/PE appears to be to encase the occlusion body in order to enhance its stability. Based on Hhpred (189) it is predicted to be similar in structure to Ac13. See Chapter 2 for additional information.

Ac132 (219aa:25.1kDa), (Bm109:220aa:25.2kDa).

Homologs of Ac132 are present in most Group I genomes. Ac132 was identified as being associated with AcMNPV ODV(89) and BV (27). Bm109 was also reported to be ODV associated (491). In BmNPV, it appear to be an essential gene (15). A knockout of Ac132 resulted in a single cell phenotype indicating that it is essential for viral propagation. However, DNA replication and the expression of some late genes appeared unaffected, but the formation of the virogenic stroma was delayed and the numbers of enveloped nucleocapsids was reduced.

OB formation was also delayed and mainly occluded singly enveloped nucleocapsids Ac132 interacted with ODV-E18 and p6.9 (492). Another report characterizing a deletion mutant indicated that BV are released from transfected cells and could enter cells but could not enter nuclei thereby preventing replication (493).

*Ac133 (419aa:48.3kDa), (Bm110:420aa:48.5kDa), (Ha114:428aa: 49.4kDa), Alkaline nuclease (AN).

Homologs of alkaline nuclease (AN) are found in all baculovirus genomes. They are also found in a variety of other viruses such as lambda phage and herpes viruses. In these viruses, the AN homolog associates with an SSB and has an exonuclease activity which generates 3' single-strand DNA ends that can participate in DNA recombination. In AcMNPV, AN interacts and co-purifies with the SSB LEF-3 and has both a 5'→3' exonuclease and an endonuclease activity (279, 280, 494). Deletion of Ac133 is lethal (495, 496). It is thought that AN is involved in DNA recombination. Homologs are also present in nudiviruses and hytrosaviruses. In *Epinotia aporema* granulovirus (EpapGV), the ortholog of Ac133 is fused with an ortholog of helicase 2 (497) (see Chapter 13) suggesting that they might act together possibly for the maturation of Okazaki intermediates. Ac133 may act as Fen nuclease in this process as its endonuclease and the single strand specific 5' to 3' exonuclease could be involved in the digestion of the primer overhangs generated by helicases. Hhpred (189) indicated the expected relationship with other exonucleases, but also showed a high degree of structural similarity to BIR-contain iap proteins near the C-terminal region.

Ac134 (Bm111:803aa:94.5kDa) (p94).

Homologs of Ac134 are present in the genomes of most Group I, a few Group II and a few GVs. Homologs are found in several polydnaviruses, e.g., *Cotesia congregata* bracovirus (E = 7e-40). The disruption of the p94 gene showed no effect on the ability of AcMNPV to infect *S. frugiperda* larvae by either the oral or intrahaemocelic route (498). Analysis by Hhpred (189) predicted relatedness of the first 131 amino acids to several proteins with a probability of over 90%. These include integrin and tumor endothelial marker 8.

Ac135 (299aa:34.8kDa), (Bm112:299aa:34.5kDa), p35.

P35 is an inhibitor of apoptosis, and homologs are limited to a few Group I NPVs closely related to AcMNPV. A homolog has also been reported in a GV of *Choristoneura occidentalis* (ChocGV) (488), and a variant (p49) is found in a Group II NPV (SpliNPV) genome (499, 500). Furthermore, a homolog most closely related to SpliNPV p49 has also been identified in an entomopox virus genome (501). P35 is able to block apoptosis in *S. frugiperda* cells caused by AcMNPV infection (502). Although deletion mutants are viable, they are severely compromised in BV production in Sf cells (502, 503). The crystal structure of p35 has been described (504) (505). For additional information, see Chapter 7.

Ac136 (240aa:27.3kDa), (Bm113:240aa:27.3kDa), (Ha22:267aa: 30.5kDa), p26.

Homologs of p26 are present in the genomes of most Group I and Group II Alphabaculoviruses, but are not present in those of GVs. Multiple copies of the gene may be present. Homologs are also found in the genomes of numerous pox viruses, e.g., Vaccinia (E = 0.15, 25% identity over 201 aa). Ac126 forms homodimers and is primarily a cytoplasmic protein (506). The examination of an AcMNPV deleted for p26 revealed no differences from wt in the cells and larvae tested (507). However, a deletion of p26 along with p10 and p74 resulted in polyhedra lacking virions (508).

Ac137 (94aa:10.3kDa), (Bm114:70aa:7.5kDa), (Ha21:87aa:9.3kDa), p10.

Homologs of p10 are found in the genomes of most Group I and II NPVs and many GVs, in some instances in multiple copies (509). They are also present in all hymenopteran NPV genomes. A p10 homolog has been characterized in an entomopox virus (510). P10 was originally identified as a very late hyper-expressed gene (511) and therefore the p10 promoter has been used in expression vectors (512). It was observed that an inhibitor of the microRNA, *bantam*, resulted in the expression level of p10 to increase 40-fold (513). P10 interacts with tubulin (514) and forms two different types of structures; microtubule-associated filaments, and tube-like structures that surround the nucleus (515). As noted above, p10 appears to be associated with the PE protein (Ac131) and in some viral genomes, genes are present that appear to be fusions of both PE and p10 protein domains (488, 489). Deletions of P10 result in polyhedra that resemble those produced by mutants lacking the calyx/polyhedron envelope protein (Ac131); they are fragile, have a rough surface showing cavities where virions have apparently been dislodged, and often show an incomplete calyx/polyhedron envelope (490, 516, 517). AcMNPV p10 is phosphorylated at serine 93 and the serine was critical for the formation of p10 associated tube-like structures (509). Hhpred (189) indicated that Ac137 was structurally related to the reovirus sigma 1 tail with a probability of about 90%. The 3 orthologs of p10 from the PxGV genome (px002, px021, and px050)] all were predicted to have a similar structure to the reovirus protein. For more information, see Chapter 2.

*Ac138 (645aa:73.9kDa), (Bm115:645aa:74.0kDa), (Ha20:688aa: 78.4kDa), p74-pif.

P74 was the first per os infectivity factor (PIF) to be identified (107, 518-521). PIFs are required for oral infection of insects, but are dispensable for infection of cultured cells. Homologs of *p74* are present in all baculovirus genomes and are also found in genomes of nudiviruses (245). Three other *pif* genes were identified in BmNPV (522) and subsequently their homologs were characterized in AcMNPV. In addition, PIF1, PIF2, and p74 mediate specific binding of occlusion derived virus to midgut cells, suggesting that they are directly involved in virus cell interaction as an initial step in infection (108). Co-infection with a wt- and a *p74*-deleted virus expressing *gfp* resulted in per os infection by the *gfp* expressing virus, suggesting the p74 did not have to be directly associated with a virus to facilitate per os infection. In addition, a 35-kDa binding partner for AcMNPV P74 was detected in extracts of brush border membrane vesicles from host larvae (*Spodoptera exigua*), but not from a non-host (*Helicoverpa armigera* larvae) (521). The identity of this host protein has not been determined. By proteomic analysis, P74 was found associated with AcMNPV, HearNPV and CuniNPV ODV (89, 269) (114); however, the other PIF proteins showed differing associations, e.g., CuniNPV (PIF-1,2,3), AcMNPV (PIF-2) and HearNPV (PIF-1). P74 appears to be cleaved into two fragments by a protease associated with occlusion bodies produced in insects. This cleavage does not occur in polyhedra produced in cell culture. The significance of the cleavage is not clear because cell culture and insect produced polyhedra appear to be equally infectious (523). P74 does not associate with the core PIF complex of (48) (287). It has been shown to be required for ODV binding (524).

Ac 139 (449aa:52.6kDa), (Bm116:451aa:52.6kDa), (Ha16:284aa: 33.6kDa), ME53.

Homologs of *ac139* are present in the genomes of all the lepidopteran NPVs and GVs, but have not been reported in hymenopteran or dipteran baculovirus genomes. It is BV and ODV associated (525). One study indicated that AcMNPV deleted for this gene is not viable and fails to replicate its DNA and does not produce nucleocapsids. However, cells transfected with DNA from the mutant showed early stages of cpe, including nuclear enlargement and the formation of granular material in the nucleus (526). This suggests that the mutant

is blocked in an early gene function. This is consistent with its original characterization as a major early (ME) gene (527). However, another study showed that deletion of Ac139 did not alter DNA replication, but results in a 1000-fold reduction in BV titer. In addition, it was found that it appears to be required both early and late in infection (525). ME53 fused to GFP localized mostly to the cytoplasm early and to nuclei late in infection. However, foci of ME53 were also noted at the cell periphery late in infection and co-localized with gp64 and VP39-capsid and was capsid associated in BV. It was suggested that it may provide a connection between the nucleocapsid and the viral envelope (528). Amino acids 109-137 contains a nuclear translocation domain and aa 101-398 are essential for BV production whereas aa 1-100 and the C-terminal 50 aa were dispensable for BV production (529).

Ac140 (60aa:7.1kDa).

This orf encodes 60 aa and is only found in AcMNPV.

Ac141 (261aa:30.1kDa), (Bm117:261aa:30.1kDa), (Ha8:285aa: 33.2kDa), exon0.

In one of few baculovirus splicing events, an internal splice site in Ac141 results in the N-terminal 38 amino acids of Ac141 also being present at the N-terminus of IE1 (Ac147) resulting in IE0, the spliced form of IE1. Ac141 is found in all lepidopteran NPVs, and orfs with low homology are also found in GV genomes. In AcMNPV it is associated with both BV and ODV nucleocapsids (27, 530) and interacts with BV/ODV-C42 (Ac101) and FP25 (Ac61) (405). Ac141 contains a predicted RING finger domain (531) that is a type of zinc finger comprising 40-60 residues that binds two zinc atoms and may be involved in protein-protein interactions. Deletion of Ac141 severely compromises BV production and results in virus that appear to be restricted to cells initially infected (530, 531). It appears to both co-localize with and co-purify with β-tubulin, and inhibitors of microtubules reduced BV production by over 85% (532). It has also been shown to interact with a conserved domain of kinesin 1, a motor protein involved in transporting cargo along microtubules to the periphery of the cell supporting a role for microtubules in the transport of virions to the cell surface (344) (533). Therefore, it has been suggested that the interaction of Ac141 with microtubules might be involved in the egress of BV. Hhpred (189) predicts with over 90% probability that the C-terminal ~90 amino acids has structural similarity to E3 protein ubiquitin ligase. Deletion of ac141 and vubi results in single cell infection and BV were not produced. The ubiquitination of Ac141 was essential for optimal production of BV. BV but not ODV nucleocapsids were ubiquitinated by vUbi. The target was Ac66 and it was shown to co-localize with vUbi and Ac141 at the nuclear periphery. It was suggested that the ubiquitination of capsid proteins may be a signal for BV egress from nuclei (163).

*Ac142 (477aa:55.4kDa), (Bm118:476aa:55.5kDa), (Ha9:468aa: 55.3kDa), p49.

Homologs of Ac142 have been identified in all sequenced baculovirus genomes. Ac142 is associated with both BV and ODV virions, and deletion of Ac142 appeared to affect nucleocapsid formation but, although lethal, did not appear to affect DNA synthesis (406). Another study describing a different bacmid construct that deleted less of the Ac142 gene showed similar results except that some nucleocapsids appeared to be fully formed, but were un-enveloped in the nucleus and were not occluded (534). It is unclear whether the difference in the two studies was due to the removal of a 3' processing signal for the upstream Ac141 gene in the former investigation, or to the presence of a significant portion of the Ac142 orf in the latter study. A BmNPV deleted for Bm118 failed to produce BV and produced polyhedra lacking virions. There appeared to be a defect in nucleocapsid formation as elongated capsid-like particles apparently devoid of DNA were observed (535). Mass spectrometry also suggests that Ac142 is ODV-associated in three different viruses (89, 114, 269). In addition, it was reported that Ac142

interacts with components of the ESCRT-III complex and may be involved in the release of nucleocapsids at the nuclear membrane (75).

*Ac143 (90aa:9.7kDa), (Bm119:101aa:10.4kDa), (Ha10:81aa:8.8kDa), ODV-E18.

Homologs of Ac143 are present in the genomes of all baculoviruses. An antibody generated against an Ac143-GST fusion reacted with a protein of 18 kDa in the ODV envelope fraction, and Ac143 was named ODV-E18 (536). Ac143 and its HearNPV homolog were found in surveys of ODV-associated proteins by mass spectrometry (89, 269). Ac143 was found to be BV associated in a proteomic analysis (27) and the predicted size of Ac143 is longer than previously reported (90 vs 62aa) (12). No BV is produced when Ac143 is deleted (537). Hhpred (189) predicts the presence of a transmembrane helix and similarity to a protein translocation complex.

*Ac144 (290aa:33.5kDa), (Bm120:290aa:33.5kDa), (Ha11:284aa:33.3kDa).

Homologs of Ac144 are present in all sequenced baculovirus genomes. Ac144 was originally named ODV-EC27 and suggested that it is a cyclin of 27kDa (538). However, another investigation using an HA-tagged Ac144 recombinant virus and anti-HA monoclonal antibodies found that Ac144 was expressed as an ~ 33.5 kDa protein which conforms to the predicted MW (406). In addition, it was found to be BV associated (27, 406). Mass spectrometry also suggests that Ac144 is ODV-associated in three different viruses (89, 114, 269). A variety of investigations have been conducted on Ac144. Initially, it was confirmed that its transcript initiates at a late promoter element (536). It was reported to interact in a yeast two-hybrid assay with Ac101 described above (also named C42) and with both Ac101 and p78/83 (Ac9) in native gel electrophoresis assays (402). Deletion of Ac144 resulted in amorphous electron dense structures that stained with vp39-capsid antibodies, but no nucleocapsids were evident. Although lethal, deletion of Ac144 did not appear to affect DNA synthesis (406).

Ac145 (97.0aa:8.9kDa), (Bm121:95aa:11.0kDa), (Ha12:92aa:10.8kDa), (pif?).

Ac145 and Ac150 encode small proteins (~9 and 11 kDa, respectively) that are related to one another (23% aa sequence identity) and are also related to a gene encoding an 11-kDa protein in an entomopox virus of *Heliothis armigera*. The predicted size of Ac145 is longer (97 vs 77 aa) than previously reported (12). Close relatives of Ac145 are found in all baculovirus genomes including lepidopteran NPVs and GVs, and hymenopteran NPVs, but not the dipteran NPV. In contrast to Ac145, close relatives of Ac150 are only found in a few NPVs closely related to AcMNPV. However, it shows significant homology ($E = \sim 10^{-3}$) to predicted proteins from several dipteran insects. Ac145 and 150 are predicted to encode a domain thought to bind to chitin (539). In one study (540), deletion of Ac145 led to a six-fold drop in infectivity in *T. ni,* but not *H. virescens* larvae. An effect of deletion of Ac150 was not detected. Deletion of both genes causes a major (39-fold) reduction of infectivity for *H. virescens*. Injection of BV of the double mutant intrahemocoelically was as infectious as wt suggesting that these genes play a role in oral infection and are pif genes. Products of *ac145* and *ac150* were found to be associated with both BV and ODV and with ODV they localized to the envelope (540). In another study (541), occluded virions deleted for Ac150 were found to be significantly less virulent when administered per os than the wt virus in *Heliothis virescens*, *S. exigua* and *T. ni* larvae. Evidence suggested that the mutant had a reduction in its ability to establish primary infections in midgut cells. The Ac145 homolog in HearSNPV was found to bind to chitin (542). Hhpred (189) predicts Ac145 is structurally related to tachycitin, an antimicrobial chitin binding protein with a probability of almost 100%.

Ac146 (201aa:22.9kDa), (Bm122:201aa:22.9kDa), (Ha13:203aa: 22.9kDa).

Homologs of Ac146 are present in the genomes of all lepidopteran NPV and GV genomes, but are not present in those of hymenopteran or dipteran. It is likely an essential gene, as infectious BV was not produced by an mutant deleted for Ac146 (543). When Bm122 was fused with gfp, nuclear localization was observed (544). Ac146 is expressed at late times pi. Deletion resulted in a defective virus that did not produce BV. A HA-tagged Ac146 bacmid construct indicated that Ac146 was associated with both BV nucleocapsids, but not envelopes of ODV suggesting that it may be a structural protein. In BV it appeared as a polypeptide of 23kDa that conforms to its predicted mass, whereas in ODV, there were two sizes, one of 23kDa and the other of 34kDa. In addition, it was reported that Ac146 interacts with components of the ESCRT-III complex and may be involved in the release of nucleocapsids at the nuclear membrane(75).

Ac147 (582aa:66.9kDa), (Bm123:584aa:66.9kDa), (Ha14:655aa: 76.0kDa), immediate early gene-1 (IE-1).

Homologs of IE-1 have been identified in all Group I and II genomes sequenced. They also appear to be present in all GV genomes, but the homology is very low, e.g., XcGVorf9 vs. Ac147 show about 10% amino acid sequence identity. However, the orientation and position of XcGV orf9 relative to more conserved orfs is similar to Ac147, suggesting that the limited homology might be real. In addition, the limited identity is located in conserved regions that are identified by other more convincing alignments, e.g., Ac-Ie1 vs. Ld-Ie1 (23% identity). Part of the IE-1 population is called IE-0 and is translated from a larger spliced mRNA, which is the only major spliced transcript described for baculoviruses (see below Ac147-0). IE-1 was originally identified because of its ability to transactivate early promoters of AcMNPV (165). The ability of IE-1 to transactivate transcription is greatly enhanced when the activated gene is linked to *hr* sequences (545). It also may participate in the negative regulation of some genes (546). IE-1 is required for transient DNA replication (50, 51). Whereas deletions of either IE-1 or IE-0 can support infectious virus production, inactivation/deletion of both these genes is lethal (547). Similar results were reported for BmNPV (81).

Ac147-0 (636aa:72kDa) (ie-0).

Part of the IE-1 population is called IE-0 and is translated from a larger spliced mRNA, which is the only major spliced transcript described for baculoviruses and in AcMNPV results in an additional 54 amino acids at the N-terminus of IE-1 for a total of 636 amino acids (548). The 5' splice site is within Ac141 and the 3' site is upstream of the Ac147 ATG. This results in 38 amino acids being identical between Ac141 and Ac147-0 with an addition 16 aa derived from the RNA upstream of the Ac147 ATG. AcMNPV IE-1 is present as a homodimer but also can form a heterodimer with IE-0, and either IE-1 or IE-0 can support infectious virus production; however, there were subtle differences in timing of events and production of BV and polyhedra, depending on which gene is being expressed, suggesting that both *ie-0* and *ie-1* are required for wt levels of infection. As described above, *ie-0* can be eliminated, as long as IE-1 is being produced (547). It was found that IE0 preferentially activates a set of viral genes at very early times in infection and it is thought that this accelerates replication and BV production (549). IE0 has a repressor function that is caused by its interaction with ie1(550). In contrast to AcMNPV, in LdMNPV only the spliced form is able to transactivate transient transcription and DNA replication (551).

*Ac148 (376aa:40.9kDa), (Bm124:375aa:41.3kDa), (Ha15:354aa: 38.9kDa), odv-e56, PIF-5.

Homologs of odv-e56 are present in the genomes of all baculovirus and are also present in nudivirus genomes (245). ODV-E56 localizes to the envelopes of occluded virions (552) in AcMNPV and other baculoviruses (553) and has also been reported to be associated with AcMNPV BV (27). An insertion mutant, in which the lacZ gene

was placed in frame at about amino acid 139 (out of 376) was viable (552). Ac148 and its homologs in HearNPV and CuniNPV were found to be ODV associated (89, 114, 269). Deletion of Ac148 from a bacmid construct resulted in a virus that could replicate in cell lines, but not insects. Consequently, it was concluded that Ac148 is a per os infectivity factor (554, 555). Similar conclusions were drawn for a BmNPV deletion of Bm124 (333).

Ac149 (107aa:12.4kDa), (Bm125:106aa:12.3kDa).

Homologs of Ac149 are present in 4 other Group I viruses closely related to AcMNPV (Bm-, Mavi-, Plxy-, and RoNPV). It is likely to be nonessential as BmNPV with insertion/deletion mutations of this gene (Bm125) appeared normal (15).

Ac150 (99aa:11.2kDa), (Bm126:115aa:13.4kDa), pif?

Ac150 is related to Ac145. In contrast to Ac145 homologs that are found in lepidopteran NPV and GV and hymenopteran NPV genomes, Ac150 is only found in a few Group I NPVs closely related to AcMNPV. in AcMNPV, deletion results in less infectivity by occluded virions for larvae (541). In BmNPV, deletion resulted in no apparent difference in BV production of mean lethal dose by occlusion bodies although the lethal time was extended somewhat (556). For more information, see Ac145 above. Hhpred (189) predicts Ac150 is structurally related to chitin binding proteins with a probability of almost 100%.

Ac151 (408aa:47kDa), (Bm127:422aa:48.8kDa), ie-2/ie-n.

Homologs of *ie-2* are limited to the genomes of most Group I lepidopteran NPVs. IE-2 contains a predicted RING finger domain and a coiled-coil domain and has ubiquitin ligase activity (557) and shows significant levels of similarity to a protein of *Trichomonas vaginalis* (E = 1e-06), an anaerobic, parasitic flagellated protozoan. IE-2 was found to augment activation by IE-1 (558-560). BmNPV IE-2 interacts with itself (561). IE-2 was required for optimal origin specific plasmid DNA replication in Sf-21 cells, but had little effect in Tn-368 cells (290). *Ie-2* deletion mutants behaved differently in Sf-21 cells in which the infection was delayed vs. Tn-5B1-4 cells, in which the infection was not delayed. In insect larvae, the mutant viruses were significantly less infectious than wt, which appeared to be due to a lack of virions in the occlusion bodies (562). IE-2 may also be involved in cell cycle regulation (563). IE2 has been shown to induce the expression of heat shock proteins and the facilitate transactivation by IE2 (564).

Ac152 (92aa:10.8kDa).

Homologs of Ac152 are present in the genomes of four Group I NPVs closely related to AcMNPV, and three Group II NPVs. It is associated with the nuclear localization of G-actin (412). Deletion resulted in reduced BV titers (43). Orthologs are not found in the BmNPV or HaSNPV genomes.

Ac153 (321aa:37.4kDa), (Bm128:309aa:36.1kDa), pe38.

Ac153 homologs have an unusual distribution being found in all Group I NPV and four GV genomes. Duplicate copies appear to be present in some of the genomes. Ac153 was originally identified because of its early transcription profile and the presence of predicted zinc finger and leucine zipper motifs (565). However, in OpMNPV it was shown to be expressed as full length (34 kda) and truncated (20 kda) forms with the larger variant functioning as a transcriptional transactivator of an early promoter (566). In addition, it appears to activate DNA replication in transient assays (50). Deletion of *pe38* results in a reduction in the expression of several genes, a delay in DNA replication, a 99% reduction in BV production, and reduced levels of DNA synthesis and was less orally infectious in larvae (567, 568). An 8-amino acid repeat in pe38 (DTVDDTVD) was shown cause insects to be resistant to the virus, whereas those lacking this sequence were sensitive to the virus (569). Hhpred (189) predicts that about 170 aa near the center of the orf is structurally related to E3 ubiquitin ligase with a probability of almost 100%. A RING finger domain is also predicted within this region.

Ac154 (81aa:9.4kDa), (Bm129:77aa:8.9kDa).

Homologs of Ac154 are present in 4 other Group I viruses closely related to AcMNPV (Bm-, Mavi-, Plxy-, and RoNPV). It is likely to be nonessential, as an insertion mutation of this gene in BmNPV (Bm129) had no apparent effect on infectivity (15).

Hrs (homologous regions).

In AcMNPV, *hrs* are comprised of repeated units of about 70-bp with an imperfect 30-bp palindrome near their center. They are repeated at eight locations in the genome with 2 to 8 repeats at each site. They are highly variable, and although they are closely related within a genome, they may show very limited homology between different viruses. For example, in the CpGV genome, tandem repeated sequences are not evident, although a 75-bp imperfect palindrome is present at 13 different locations on the genome (570). In addition, in the TnSNPV (Group II) and several other genomes, *hrs* were not found (571), reviewed in (572). *Hrs* have been implicated both as transcriptional enhancers and origins of DNA replication for several baculoviruses (545, 573-577). They bind the transcriptional activator IE-1 (Ac147) (578-580) and this binding may cause IE-1 to localize into foci which may be a prelude to replication loci (581). *Hrs* contain a high concentration of cAMP and TPA response elements (CRE and TRE) that bind cellular transcription factors and stimulate RNA polymerase II dependent transcription and enhance activation by IE-1 (582). In AcMNPV, deletion of individual *hrs* or combinations of up to five *hrs* does not significantly affect virus replication in cultured cells. The deletion of 7 hrs resulted in a 10-fold reduction in BV titers, but DNA replication appeared normal, and polyhedra were still produced. However, when all eight hrs were removed, BV production was reduced by over 1000-fold, DNA replication was severely reduced, and few polyhedral were produced (583, 584).

References

1. Vail P, Sutter G, Jay D, Gough D. Recipocal infectivity of nuclear polyhedrosis viruses of the cabbage looper and alfalfa looper. J Invertebr Pathol. 1971;17:383–388.
2. Vaughn JL, Goodwin RH, Tompkins GJ, McCawley P. The establishment of two cell lines from the insect *Spodoptera frugiperda* (Lepidoptera: Noctuidae). In Vitro. 1977;13:213–217. PubMed PMID: 68913.
3. Hink WF. Established insect cell line from the cabbage looper, *Trichoplusia ni*. Nature. 1970;226:466–467. PubMed PMID: 16057320.
4. Smith GE, Summers MD, Fraser MJ. Production of human beta interferon in insect cells infected with a baculovirus expression vector. Mol Cell Biol. 1983;3:2156–2165. PubMed PMID: 6318086.
5. Pennock GD, Shoemaker C, Miller LK. Strong and regulated expression of *Escherichia coli* B-galactosidase in insect cells with a baculovirus vector. Mol Cell Biol. 1984;4:399–406. PubMed PMID: 6325875.
6. Ayres MD, Howard SC, Kuzio J, Lopez-Ferber M, Possee RD. The complete DNA sequence of *Autographa californica* nuclear polyhedrosis virus. Virology. 1994;202:586–605. PubMed PMID: 8030224.
7. Luckow VA, Lee SC, Barry GF, Olins PO. Efficient generation of infectious recombinant baculoviruses by site-specific transposon-mediated insertion of foreign genes into a baculovirus genome propagated in Escherichia coli. J Virol. 1993;67:4566–79. PubMed PMID: 8392598.
8. Bideshi DK, Federici BA. The Trichoplusia ni granulovirus helicase is unable to support replication of Autographa californica multicapsid nucleopolyhedrovirus in cells and larvae of T. ni. J Gen Virol. 2000;81:1593–9. PubMed PMID: 10811943.
9. Datsenko KA, Wanner BL. One-step inactivation of chromosomal genes in Escherichia coli K-12 using PCR products. Proc Natl Acad Sci U S A. 2000;97:6640–5. PubMed PMID: 10829079.
10. Lung OY, Cruz-Alvarez M, Blissard GW. Ac23, an envelope fusion protein homolog in the baculovirus Autographa californica multicapsid nucleopolyhedrovirus, is a viral pathogenicity factor. J Virol. 2003;77:328–39. PubMed PMID: 12477838.

11. Maghodia AB, Jarvis DL, Geisler C. Complete Genome Sequence of the Autographa californica Multiple Nucleopolyhedrovirus Strain E2. Genome Announc. 2014.:2. PubMed PMID: 25502662.
12. Harrison RL, Bonning BC. Comparative analysis of the genomes of Rachiplusia ou and Autographa californica multiple nucleopolyhedroviruses. J Gen Virol. 2003;84:1827–42. PubMed PMID: 12810877.
13. Lu A, Miller LK. Identification of three late expression factor genes within the 33.8- to 43.4-map-unit region of *Autographa californica* nuclear polyhedrosis virus. J Virol. 1994;68:6710–6718. PubMed PMID: 8084003.
14. Harrison RL, Lynn DE. Genomic sequence analysis of a nucleopolyhedrovirus isolated from the diamondback moth, Plutella xylostella. Virus Genes. 2007;35:857–73. PubMed PMID: 17671835.
15. Ono C, Kamagata T, Taka H, Sahara K, Asano S, Bando H. Phenotypic grouping of 141 BmNPVs lacking viral gene sequences. Virus Res. 2012;165:197–206. PubMed PMID: 22421381.
16. Gomi S, Majima K, Maeda S. Sequence analysis of the genome of Bombyx mori nucleopolyhedrovirus. J Gen Virol. 1999;80:1323–37. PubMed PMID: 10355780.
17. Chen X, IJkel W, Tarchini R, Sun X, Sandbrink H, Wang H, Peters S, Zuidema D, Lankhorst R, Vlak J, Hu Z. The sequence of the *Helicoverpa armigera* single nucleocapsid nucleopolyhedrovirus genome. J Gen Virol. 2001;82:241–257. PubMed PMID: 11125177.
18. Kim D, Weaver RF. Transcriptional mapping and functional analysis of the protein tyrosine/serine phosphatase (PTPase) gene of the Autographa californica nuclear polyhedrosis virus. Virology. 1993;195:587–595. PubMed PMID: 8337833.
19. Sheng Z, Charbonneau H. The baculovirus Autographa californica encodes a protein tyrosine phosphatase. J Biol Chem. 1993;268:4728–4733. PubMed PMID: 8444848.
20. Gross CH, Shuman S. Characterization of a Baculovirus-Encoded RNA 5'-Triphosphatase. J Virol. 1998;72:7057–7063. PubMed PMID: 9696798.
21. Takagi T, Taylor GS, Kusakabe T, Charbonneau H, Buratowski S. A protein tyrosine phosphatase-like protein from baculovirus has RNA 5'-triphosphatase and diphosphatase activities. Proc Natl Acad Sci U S A. 1998;95:9808–12. PubMed PMID: 9707557.
22. Changela A, Martins A, Shuman S, Mondragón A. Crystal structure of baculovirus RNA triphosphatase complexed with phosphate. J Biol Chem. 2005;280:17848–56. PubMed PMID: 15713658.
23. Li Y, Miller LK. Properties of a baculovirus mutant defective in the protein phosphatase gene. J Virol. 1995;69:4533–4537. PubMed PMID: 7769718.
24. van Houte S, Ros VI, Mastenbroek TG, Vendrig NJ, Hoover K, Spitzen J, van Oers MM. Protein Tyrosine Phosphatase-Induced Hyperactivity Is a Conserved Strategy of a Subset of BaculoViruses to Manipulate Lepidopteran Host Behavior. PLoS One. 2012;7:e46933. PubMed PMID: 23077534.
25. Katsuma S, Koyano Y, Kang W, Kokusho R, Kamita SG, Shimada T. The baculovirus uses a captured host phosphatase to induce enhanced locomotory activity in host caterpillars. PLoS Pathog. 2012;8:e1002644. PubMed PMID: 22496662.
26. Wang F, Xue R, Li X, Hu C, Xia Q. Characterization of a protein tyrosine phosphatase as a host factor promoting baculovirus replication in silkworm, Bombyx mori. Dev Comp Immunol. 2016;57:31–7. PubMed PMID: 26684065.
27. Wang R, Deng F, Hou D, Zhao Y, Guo L, Wang H, Hu Z. Proteomics of the Autographa californica Nucleopolyhedrovirus Budded Virions. J Virol. 2010;84:7233–7242. PubMed PMID: 20444894.
28. Kamita SG, Nagasaka K, Chua JW, Shimada T, Mita K, Kobayashi M, Maeda S, Hammock BD. A baculovirus-encoded protein tyrosine phosphatase gene induces enhanced locomotory activity in a lepidopteran host. Proc Natl Acad Sci U S A. 2005;102:2584–9. PubMed PMID: 15699333.
29. Katsuma S. Phosphatase activity of Bombyx mori nucleopolyhedrovirus PTP is dispensable for enhanced locomotory activity in B. mori larvae. J Invertebr Pathol. 2015;132:228–32. PubMed PMID: 26550695.
30. Bideshi DK, Renault S, Stasiak K, Federici BA, Bigot Y. Phylogenetic analysis and possible function of bro-like genes, a multigene family widespread among large double-stranded DNA viruses of invertebrates and bacteria. J Gen Virol. 2003;84:2531–44. PubMed PMID: 12917475.

31. Asgari S, Davis J, Wood D, Wilson P, McGrath A. Sequence and organization of the Heliothis virescens ascovirus genome. J Gen Virol. 2007;88:1120–32. PubMed PMID: 17374755.
32. Kuzio J, Pearson MN, Harwood SH, Funk CJ, Evans JT, Slavicek J, Rohrmann GF. Sequence and analysis of the genome of a baculovirus pathogenic for *Lymantria dispar*. Virology. 1999;253:17–34. PubMed PMID: 9887315.
33. Lopez Ferber M, Argaud O, Croizier L, Croizier G. Diversity, distribution, and mobility of bro gene sequences in Bombyx mori nucleopolyhedrovirus. Virus Genes. 2001;22:247–54. PubMed PMID: 11450942.
34. Zhou JB, Li XQ, De-Eknamkul W, Suraporn S, Xu JP. Identification of a new Bombyx mori nucleopolyhedrovirus and analysis of its bro gene family. Virus Genes. 2012;44:539–47. PubMed PMID: 22311430.
35. Kang W, Suzuki M, Zemskov E, Okano K, Maeda S. Characterization of baculovirus repeated open reading frames (bro) in Bombyx mori nucleopolyhedrovirus. J Virol. 1999;73:10339–45. PubMed PMID: 10559352.
36. Zemskov EA, Kang W, Maeda S. Evidence for nucleic acid binding ability and nucleosome association of *Bombyx mori* nucleopolyhedrovirus BRO proteins. J Virol. 2000;74:6784–9. PubMed PMID: 10888617.
37. Kang WK, Imai N, Suzuki M, Iwanaga M, Matsumoto S, Zemskov EA. Interaction of Bombyx mori nucleopolyhedrovirus BRO-A and host cell protein laminin. Arch Virol. 2003;148:99–113. PubMed PMID: 12536298.
38. Shobahah J, Xue S, Hu D, Zhao C, Wei M, Quan Y, Yu W. Quantitative phosphoproteome on the silkworm (Bombyx mori) cells infected with baculovirus. Virol J. 2017;14:117. PubMed PMID: 28629377.
39. Shrestha A, Bao K, Chen YR, Chen W, Wang P, Fei Z, Blissard GW. Global Analysis of Baculovirus Autographa californica Multiple Nucleopolyhedrovirus Gene Expression in the Midgut of the Lepidopteran Host Trichoplusia ni. J Virol. 2018.:92. PubMed PMID: 30209166.
40. Olivera BM, Miljanich GP, Ramachandran J, Adams ME. Calcium channel diversity and neurotransmitter release: The w-conotoxins and w-agatoxins. Ann Rev Biochem. 1994;63:823–867. PubMed PMID: 7979255.
41. Eldridge R, Li Y, Miller LK. Characterization of a baculovirus gene encoding a small conotoxin-like polypeptide. J Virol. 1992;66:6563–6571. PubMed PMID: 1404603.
42. Cao Q, Zhu SY, Wu Y, Liu Y, Zhu J, Wang W. The Effect of a Small Conotoxin-Like ctx Gene from Autographa californica Nuclear Polyhedrosis Virus (AcMNPV) on Insect Hemolymph Melanization. Pol J Microbiol. 2012;61:183–189. PubMed PMID: 29334052.
43. Gandhi KM, Ohkawa T, Welch MD, Volkman LE. Nuclear localization of actin requires AC102 in Autographa californica multiple nucleopolyhedrovirus-infected cells. J Gen Virol. 2012;93:1795–803. PubMed PMID: 22592260.
44. Katsuma S, Kobayashi J, Koyano Y, Matsuda-Imai N, Kang W, Shimada T. Baculovirus-encoded protein BV/ODV-E26 determines tissue tropism and virulence in lepidopteran insects. J Virol. 2012;86:2545–55. PubMed PMID: 22190721.
45. Shen Y, Wang H, Xu W, Wu X. Bombyx mori nucleopolyhedrovirus orf133 and orf134 are involved in the embedding of occlusion-derived viruses into polyhedra. J Gen Virol. 2018;99:717–729. PubMed PMID: 29624165.
46. Wang X, Chen C, Zhang N, Li J, Deng F, Wang H, Vlak JM, Hu Z, Wang M. The group I alphabaculovirus-specific protein, AC5, is a novel component of the occlusion body but is not associated with ODVs or the PIF complex. J Gen Virol. 2018;99:585–595. PubMed PMID: 29465345.
47. Peng K, van Lent JW, Boeren S, Fang M, Theilmann DA, Erlandson MA, Vlak JM, van Oers MM. Characterization of novel components of the baculovirus per os infectivity factor complex. J Virol. 2012;86:4981–8. PubMed PMID: 22379094.
48. Zheng Q, Shen Y, Kon X, Zhang J, Feng M, Wu X. Protein-protein interactions of the baculovirus per os infectivity factors (PIFs) in the PIF complex. J Gen Virol. 2017;98:853–861. PubMed PMID: 28141488.
49. Evans JT, Leisy DJ, Rohrmann GF. Characterization of the interaction between the baculovirus replication factors, LEF-1 and LEF-2. J Virol. 1997;71:3114–3119. PubMed PMID: 9060674.

50. Kool M, Ahrens C, Goldbach RW, Rohrmann GF, Vlak JM. Identification of genes involved in DNA replication of the *Autographa californica* baculovirus. Proc Natl Acad Sci USA. 1994;91:11212–11216. PubMed PMID: 7972036.
51. Lu A, Miller LK. The roles of eighteen baculovirus late expression factor genes in transcription and DNA replication. J Virol. 1995;69:975–982. PubMed PMID: 7815565.
52. Wu CP, Huang YJ, Wang JY, Wu YL, Lo HR, Wang JC, Chao YC. Autographa californica multiple nucleopolyhedrovirus LEF-2 is a capsid protein required for amplification but not initiation of viral DNA replication. J Virol. 2010;84:5015–24. PubMed PMID: 20219928.
53. Mikhailov VS, Rohrmann GF. The Baculovirus Replication Factor LEF-1 is a DNA Primase. J Virol. 2002;76:2287–2297. PubMed PMID: 11836407.
54. Merrington CL, Kitts PA, King LA, Possee RD. An Autographa californica nucleopolyhedrovirus lef-2 mutant: consequences for DNA replication and very late gene expression. Virology. 1996;217:338–348. PubMed PMID: 8599220.
55. Sriram S, Gopinathan KP. The potential role of a late gene expression factor, lef2, from Bombyx mori nuclear polyhedrosis virus in very late gene transcription and DNA replication. Virology. 1998;251:108–22. PubMed PMID: 9813207.
56. Gearing KL, Possee RD. Functional analysis of a 603 nucleotide open reading frame upstream of the polyhedrin gene of Autographa californica nuclear polyhedrosis virus. J Gen Virol. 1990;71:251–62. PubMed PMID: 2407804.
57. Afonso CL, Tulman ER, Lu Z, Balinsky CA, Moser BA, Becnel JJ, Rock DL, Kutish GF. Genome sequence of a baculovirus pathogenic for Culex nigripalpus. J Virol. 2001;75:11157–65. PubMed PMID: 11602755.
58. Perera OP, Valles SM, Green TB, White S, Strong CA, Becnel JJ. Molecular analysis of an occlusion body protein from Culex nigripalpus nucleopolyhedrovirus (CuniNPV). J Invertebr Pathol. 2006;91:35–42. PubMed PMID: 16376931.
59. Jehle JA. The mosaic structure of the polyhedrin gene of the Autographa californica nucleopolyhedrovirus (AcMNPV). Virus Genes. 2004;29:5–8. PubMed PMID: 15215679.
60. Ji X, Sutton G, Evans G, Axford D, Owen R, Stuart DI. How baculovirus polyhedra fit square pegs into round holes to robustly package viruses. EMBO J. 2010;29:505–514. PubMed PMID: 19959989.
61. Gati C, Oberthuer D, Yefanov O, Bunker RD, Stellato F, Chiu E, Yeh SM, Aquila A, Basu S, Bean R, Beyerlein KR, Botha S, Boutet S, DePonte DP, Doak RB, Fromme R, Galli L, Grotjohann I, James DR, Kupitz C, Lomb L, Messerschmidt M, Nass K, Rendek K, Shoeman RL, Wang D, Weierstall U, White TA, Williams GJ, Zatsepin NA, Fromme P, Spence JC, Goldie KN, Jehle JA, Metcalf P, Barty A, Chapman HN. Atomic structure of granulin determined from native nanocrystalline granulovirus using an X-ray free-electron laser. Proc Natl Acad Sci U S A. 2017;114:2247–2252. PubMed PMID: 28202732.
62. Kitts PA, Possee RD. A method for producing recombinant baculovirus expression vectors at high frequency. BioTechniques. 1993;14:810–816. PubMed PMID: 8512707.
63. Vialard JE, Richardson CD. The 1,629-nucleotide open reading frame located downstream of the Autographa californica nuclear polyhedrosis virus polyhedrin gene encodes a nucleocapsid-associated phosphoprotein. J Virol. 1993;67:5859–5866. PubMed PMID: 8371345.
64. Russell RLQ, Funk CJ, Rohrmann GF. Association of a baculovirus encoded protein with the capsid basal region. Virology. 1997;227:142–152. PubMed PMID: 9007067.
65. Goley ED, Ohkawa T, Mancuso J, Woodruff JB, D'Alessio JA, Cande WZ, Volkman LE, Welch MD. Dynamic nuclear actin assembly by Arp2/3 complex and a baculovirus WASP-like protein. Science. 2006;314:464–7. PubMed PMID: 17053146.
66. Ohkawa T, Volkman LE, Welch MD. Actin-based motility drives baculovirus transit to the nucleus and cell surface. J Cell Biol. 2010;190:187–95. PubMed PMID: 20660627.
67. Reilly LM, Guarino LA. The pk-1 gene of Autographa californica multinucleocapsid nuclear polyhedrosis virus encodes a protein kinase. J Gen Virol. 1994;75:2999–3006. PubMed PMID: 7964609.

68. Liang C, Li M, Dai X, Zhao S, Hou Y, Zhang Y, Lan D, Wang Y, Chen X. Autographa californica multiple nucleopolyhedrovirus PK-1 is essential for nucleocapsid assembly. Virology. 2013. in press. PubMed PMID: 23768784.
69. Fan X, Thirunavukkarasu K, Weaver RF. Temperature-sensitive mutations in the protein kinase-1 (*pk-1*) gene of the *Autographa californica* nuclear polyhedrosis virus that block very late gene expression. Virology. 1996;224:1–9. PubMed PMID: 8862393.
70. Mishra G, Chadha P, Chaudhury I, Das RH. Inhibition of Autographa californica nucleopolyhedrovirus (AcNPV) polyhedrin gene expression by DNAzyme knockout of its serine/threonine kinase (pk1) gene. Virus Res. 2008;135:197–201. PubMed PMID: 18353480.
71. Mishra G, Chadha P, Das RH. Serine/threonine kinase (pk-1) is a component of Autographa californica multiple nucleopolyhedrovirus (AcMNPV) very late gene transcription complex and it phosphorylates a 102kDa polypeptide of the complex. Virus Res. 2008;137:147–9. PubMed PMID: 18577405.
72. Mishra G, Gautam HK, Das RH. Serine/Threonine kinase dependent transcription from the polyhedrin promoter of SpltNPV-I. Biochem Biophys Res Commun. 2007;358:942–7. PubMed PMID: 17512903.
73. Liang C, Su X, Xu G, Dai X, Zhao S. Autographa californica multiple nucleopolyhedrovirus PK1 is a factor that regulates high-level expression of very late genes in viral infection. Virology. 2017;512:56–65. PubMed PMID: 28915406.
74. Tao XY, Choi JY, Kim WJ, An SB, Liu Q, Kim SE, Lee SH, Kim JH, Woo SD, Jin BR, Je YH. Autographa californica multiple nucleopolyhedrovirus ORF11 is essential for budded-virus production and occlusion-derived-virus envelopment. J Virol. 2015;89:373–83. PubMed PMID: 25320313.
75. Yue Q, Yu Q, Yang Q, Xu Y, Guo Y, Blissard GW, Li Z. Distinct Roles of Cellular ESCRT-I and ESCRT-III Proteins in Efficient Entry and Egress of Budded Virions of Autographa californica Multiple Nucleopolyhedrovirus. J Virol. 2018.:92. PubMed PMID: 29046462.
76. Costa Navarro GS, Amalfi S, Lopez MG, Llauger G, Arneodo JD, Taboga O, Alfonso V. The Autographa californica multiple nucleopolyhedrovirus Ac12: a non-essential F box-like protein that interacts with cellular SKP1 component of the E3 ubiquitin ligase complex. Virus Res. 2019;260:67–77. PubMed PMID: 30472094.
77. Soding J. Protein homology detection by HMM-HMM comparison. Bioinformatics. 2005;21:951–60. PubMed PMID: 15531603.
78. Zhou Y, Chen K, Yao Q, Shen H, Liang G, Li X, Wang N, Li Y. Characterization of a late expression gene of Bombyx mori nucleopolyhedrovirus. Z Naturforsch C. 2010;65:508–18. PubMed PMID: 20737922.
79. Kokusho R, Koh Y, Fujimoto M, Shimada T, Katsuma S. Bombyx mori nucleopolyhedrovirus BM5 protein regulates progeny virus production and viral gene expression. Virology. 2016;498:240–249. PubMed PMID: 27614700.
80. Nagamine T, Inaba T, Sako Y. A nuclear envelop-associated baculovirus protein promotes intranuclear lipid accumulation during infection. Virology. 2019;532:108–117. PubMed PMID: 31055062.
81. Gomi S, Zhou CE, Yih W, Majima K, Maeda S. Deletion analysis of four of eighteen late gene expression factor gene homologues of the baculovirus, BmNPV. Virology. 1997;230:35–47. PubMed PMID: 9126260.
82. Wang Y, Schwedes JF, Parks D, Mann K, Tegtmeyer P. Interaction of p53 with its consensus DNA-binding site. Mol Cell Biol. 1995;15:2157–65. PubMed PMID: 7891710.
83. O'Reilly DR, Miller LK. A baculovirus blocks insect molting by producing ecdysteroid UDP-glucosyl transferase. Science. 1989.:1110–1112. PubMed PMID: 2505387.
84. O'Reilly DR, Miller LK. Regulation of expression of a baculovirus ecdysteroid UDPglucosyltransferase gene. J Virol. 1990;64:1321–1328. PubMed PMID: 2106039.
85. O’Reilly DR, Miller LK. Improvement of a baculovirus pesticide by deletion of the egt gene. Bio/ Technology. 1991;9:1086–1089.
86. Kumar S, Miller LK. Effects of serial passage of AcNPV in cell culture. Virus Res. 1987;7:335–349. PubMed PMID: 2887077.

87. Beniya H, Braunagel SC, Summers MD. Autographa californica nuclear polyhedrosis virus: subcellular localization and protein trafficking of BV/ODV-E26 to intranuclear membranes and viral envelopes. Virology. 1998;240:64–75. PubMed PMID: 9448690.
88. Burks JK, Summers MD, Braunagel SC. BV/ODV-E26: a palmitoylated, multifunctional structural protein of Autographa californica nucleopolyhedrovirus. Virology. 2007;361:194–203. PubMed PMID: 17169392.
89. Braunagel SC, Russell WK, Rosas-Acosta G, Russell DH, Summers MD. Determination of the protein composition of the occlusion-derived virus of Autographa californica nucleopolyhedrovirus. Proc Natl Acad Sci U S A. 2003;100:9797–802. PubMed PMID: 12904572.
90. Imai N, Kurihara M, Matsumoto S, Kang WK. Bombyx mori nucleopolyhedrovirus orf8 encodes a nucleic acid binding protein that colocalizes with IE1 during infection. Arch Virol. 2004;149:1581–94. PubMed PMID: 15290382.
91. Braunagel SC, Summers MD. Molecular Biology of the Baculovirus Occlusion-Derived Virus Envelope. Curr Drug Targets. 2007;8:1084–1095. PubMed PMID: 17979668.
92. Kang W, Imai N, Kawasaki Y, Nagamine T, Matsumoto S. IE1 and hr facilitate the localization of Bombyx mori nucleopolyhedrovirus ORF8 to specific nuclear sites. J Gen Virol. 2005;86:3031–8. PubMed PMID: 16227225.
93. Nie Y, Fang M, Theilmann DA. AcMNPV AC16 (DA26, BV/ODV-E26) regulates the levels of IE0 and IE1 and binds to both proteins via a domain located within the acidic transcriptional activation domain. Virology. 2009;385:484–95. PubMed PMID: 19150105.
94. Kang W, Katsuma S, Matsuda-Imai N, Kurihara M, Yoshiga T, Shimada T, Matsumoto S. Identification and characterization of host factors interacting with Bombyx mori nucleopolyhedrovirus ORF8. J Microbiol. 2012;50:469–77. PubMed PMID: 22752911.
95. O'Reilly DR, Passarelli AL, Goldman IF, Miller LK. Characterization of the DA26 gene in a hypervariable region of the Autographa californica nuclear polyhedrosis virus genome. J Gen Virol. 1990;71(Pt 5):1029–37. PubMed PMID: 2189022.
96. Hikida H, Kokusho R, Kobayashi J, Shimada T, Katsuma S. Inhibitory role of the Bm8 protein in the propagation of Bombyx mori nucleopolyhedrovirus. Virus Res. 2018;249:124–131. PubMed PMID: 29574100.
97. Nie Y, Theilmann DA. Deletion of AcMNPV AC16 and AC17 results in delayed viral gene expression in budded virus infected cells but not transfected cells. Virology. 2010;404:168–79. PubMed PMID: 20627351.
98. An SH, Xing LP, Shi WJ, Zhang CX. Characterization of Autographa californica multiple nucleopolyhedrovirus ORF17. Acta Virol. 2006;50:17–23. PubMed PMID: 16599181.
99. An SH, Wang D, Zhang-Nv Y, Guo ZJ, Xu HJ, Sun JX, Zhang CX. Characterization of a late expression gene, Open reading frame 128 of Helicoverpa armigera single nucleocapsid nucleopolyhedrovirus. Arch Virol. 2005;150:2453–66. PubMed PMID: 16052278.
100. Yang ZN, Xu HJ, Thiem SM, Xu YP, Ge JQ, Tang XD, Tian CH, Zhang CX. Bombyx mori nucleopolyhedrovirus ORF9 is a gene involved in the budded virus production and infectivity. J Gen Virol. 2009;90:162–9. PubMed PMID: 19088285.
101. Wang Y, Wu W, Li Z, Yuan M, Feng G, Yu Q, Yang K, Pang Y. ac18 is not essential for the propagation of Autographa californica multiple nucleopolyhedrovirus. Virology. 2007;367:71–81. PubMed PMID: 17573091.
102. Zhu M, Wang J, Deng R, Wang X. Functional Regulation of an Autographa californica Nucleopolyhedrovirus-Encoded MicroRNA, AcMNPV-miR-1, in Baculovirus Replication. J Virol. 2016;90:6526–6537. PubMed PMID: 27147751.
103. Wang H, Xu W, Kong X, Fan Y, Wu X. Bombyx mori nucleopolyhedrovirus protein Bm11 is involved in occlusion body production and occlusion-derived virus embedding. Virology. 2018;527:12–20. PubMed PMID: 30447410.
104. Roncarati R, Knebel-Morsdorf D. Identification of the early actin-rearrangement-inducing factor gene, arif-1, from Autographa californica multicapsid nuclear polyhedrosis virus. J Virol. 1997;71:7933–41. PubMed PMID: 9311884.

105. Dreschers S, Roncarati R, Knebel-Morsdorf D. Actin rearrangement-inducing factor of baculoviruses is tyrosine phosphorylated and colocalizes to F-actin at the plasma membrane. J Virol. 2001;75:3771–8. PubMed PMID: 11264366.
106. Kokusho R, Kawamoto M, Koyano Y, Sugano S, Suzuki Y, Shimada T, Katsuma S. Bombyx mori nucleopolyhedrovirus actin rearrangement-inducing factor 1 enhances systemic infection in B. mori larvae. J Gen Virol. 2015;96:1938–46. PubMed PMID: 25809914.
107. Pijlman GP, Dortmans JC, Vermeesch AM, Yang K, Martens DE, Goldbach RW, Vlak JM. Pivotal role of the non-hr origin of DNA replication in the genesis of defective interfering baculoviruses. J Virol. 2002;76:5605–11. PubMed PMID: 11991989.
108. Ohkawa T, Washburn JO, Sitapara R, Sid E, Volkman LE. Specific binding of Autographa californica M nucleopolyhedrovirus occlusion-derived virus to midgut cells of Heliothis virescens larvae is mediated by products of pif genes Ac119 and Ac022 but not by Ac115. J Virol. 2005;79:15258–64. PubMed PMID: 16306597.
109. Cheng C, Liu S, Chow T, Hsiao Y, Wang D, Huang J, H C. Analysis of the Complete Genome Sequence of the Hz-1 Virus Suggests that It Is Related to Members of the Baculoviridae. J Virol. 2002;76:9024–9034. PubMed PMID: 12186886.
110. Gauthier L, Cornman S, Hartmann U, Cousserans F, Evans JD, de Miranda JR, Neumann P. The Apis mellifera Filamentous Virus Genome. Viruses. 2015;7:3798–815. PubMed PMID: 26184284.
111. Pearson MN, Rohrmann GF. Transfer, incorporation, and substitution of envelope fusion proteins among members of the Baculoviridae, Orthomyxoviridae, and Metaviridae (insect retrovirus) families. J Virol. 2002;76:5301–5304. PubMed PMID: 11991958.
112. Malik HS, Henikoff S. Positive Selection of Iris, a Retroviral Envelope-Derived Host Gene in Drosophila melanogaster. PLoS Genet. 2005;1:429–43. PubMed PMID: 16244705.
113. Pearson MN, Russell R, Rohrmann GF. Characterization of a baculovirus encoded protein that is associated with infected-cell membranes and budded virions. Virology. 2001;291:22–31. PubMed PMID: 11878873.
114. Perera O, Green TB, Stevens SM Jr, White S, Becnel JJ. Proteins associated with Culex nigripalpus nucleopolyhedrovirus occluded virions. J Virol. 2007;81:4585–90. PubMed PMID: 17301145.
115. Wang M, Tan Y, Yin F, Deng F, Vlak JM, Hu Z, Wang H. The F-like protein Ac23 enhances the infectivity of the budded virus of gp64-null AcMNPV pseudotyped with baculovirus envelope fusion protein F. J Virol. 2008;82:9800–4. PubMed PMID: 18653446.
116. Wang M, Wang J, Yin F, Tan Y, Deng F, Chen X, Jehle JA, Vlak JM, Hu Z, Wang H. Unraveling the entry mechanism of baculoviruses and its evolutionary implications. J Virol. 2014;88:2301–11. PubMed PMID: 24335309.
117. Xu W, Fan Y, Wang H, Feng M, Wu X. Bombyx mori nucleopolyhedrovirus F-like protein Bm14 affects the morphogenesis and production of occlusion bodies and the embedding of ODVs. Virology. 2018;526:61–71. PubMed PMID: 30342303.
118. Fan X, McLachlin JR, Weaver RF. Identification and characterization of a protein kinase-interacting protein encoded by the Autographa californica nuclear polyhedrosis virus. Virology. 1998;240:175–182. PubMed PMID: 9454690.
119. McLachlin JR, Yang S, Miller LK. A baculovirus mutant defective in PKIP, a protein which interacts with a virus-encoded protein kinase. Virology. 1998;246:379–91. PubMed PMID: 9657956.
120. Mikhailov VS, Vanarsdall AL, Rohrmann GF. Isolation and characterization of the DNA-binding protein (DBP) of the Autographa californica multiple nucleopolyhedrovirus. Virology. 2007;370:415–29. PubMed PMID: 17935748.
121. Vanarsdall AL, Mikhailov VS, Rohrmann GF. Characterization of a baculovirus lacking the DBP (DNA-binding protein) gene. Virology. 2007;364:475–85. PubMed PMID: 17449080.
122. Zhao C, Zhang C, Chen B, Shi Y, Quan Y, Nie Z, Zhang Y, Yu W. A DNA Binding Protein Is Required for Viral Replication and Transcription in Bombyx mori Nucleopolyhedrovirus. PLoS One. 2016;11:e0159149. PubMed PMID: 27414795.

123. Shen H, Zhou Y, Zhang W, Nin B, Wang H, Wang X, Shao S, Chen H, Guo Z, Liu X, Yao Q, Chen K. Characterization of Bombyx mori nucleopolyhedrovirus with a knockout of Bm17. Cytotechnology. 2012;64:711–8. PubMed PMID: 22476564.
124. Shen H, Wang R, Han Q, Zhang W, Nin B, Zhou Y, Shao S, Yao Q, Chen K, Liu X. Characterization of Bombyx mori nucleopolyhedrovirus Bm17. J Basic Microbiol. 2013;53:808–14. PubMed PMID: 22961820.
125. Esteban DJ, Da Silva M, Upton C. New bioinformatics tools for viral genome analyses at Viral Bioinformatics - Canada. Pharmacogenomics. 2005;6:271–80. PubMed PMID: 16013958.
126. Clem RJ. Viral IAPs, then and now. Semin Cell Dev Biol. 2015;39:72–9. PubMed PMID: 25652775.
127. McLachlin JR, Escobar JC, Harrelson JA, Clem RJ, Miller LK. Deletions in the Ac-iap1 gene of the baculovirus AcMNPV occur spontaneously during serial passage and confer a cell line-specific replication advantage. Virus Res. 2001;81:77–91. PubMed PMID: 11682127.
128. Zeng X, Nan F, Liang C, Song J, Wang Q, Vlak JM, Chen X. Functional analysis of the Autographa californica nucleopolyhedrovirus IAP1 and IAP2. Sci China C Life Sci. 2009;52:761–70. PubMed PMID: 19727595.
129. Maguire T, Harrison P, Hyink O, Kalmakoff J, Ward VK. The inhibitors of apoptosis of Epiphyas postvittana nucleopolyhedrovirus. J Gen Virol. 2000;81:2803–11. PubMed PMID: 11038395.
130. Ikeda M, Yamada H, Ito H, Kobayashi M. Baculovirus IAP1 induces caspase-dependent apoptosis in insect cells. J Gen Virol. 2011;92:2654–63. PubMed PMID: 21795471.
131. Passarelli AL, Miller LK. Identification and transcriptional regulation of the baculovirus lef-6 gene. J Virol. 1994;68:4458–4467. PubMed PMID: 8207819.
132. Lin G, Blissard GW. Analysis of an Autographa californica nucleopolyhedrovirus lef-11 knockout: LEF-11 is essential for viral DNA replication. J Virol. 2002;76:2770–9. PubMed PMID: 11861844.
133. Teplova M, Wohlbold L, Khin NW, Izaurralde E, Patel DJ. Structure-function studies of nucleocytoplasmic transport of retroviral genomic RNA by mRNA export factor TAP. Nat Struct Mol Biol. 2011;18:990–8. PubMed PMID: 21822283.
134. Afonso CL, Tulman ER, Lu Z, Oma E, Kutish GF, Rock DL. The genome of Melanoplus sanguinipes entomopoxvirus. J Virol. 1999;73:533–52. PubMed PMID: 9847359.
135. Huang J, Hao B, Deng F, Sun X, Wang H, Hu Z. Open reading frame Bm21 of Bombyx mori nucleopolyhedrovirus is not essential for virus replication in vitro, but its deletion extends the median survival time of infected larvae. J Gen Virol. 2008;89:922–30. PubMed PMID: 18343833.
136. Tomalski MD, Eldridge R, Miller LK. A baculovirus homolog of a Cu/Zn superoxide dismutase gene. Virology. 1991.:149–161. PubMed PMID: 1871962.
137. Bergin D, Reeves EP, Renwick J, Wientjes FB, Kavanagh K. Superoxide production in Galleria mellonella hemocytes: identification of proteins homologous to the NADPH oxidase complex of human neutrophils. Infect Immun. 2005;73:4161–70. PubMed PMID: 15972506.
138. Katsuma S, Kawaoka S, Mita K, Shimada T. Genome-wide survey for baculoviral host homologs using the Bombyx genome sequence. Insect Biochem Mol Biol. 2008;38:1080–6. PubMed PMID: 19280699.
139. Popovici C, Roubin R, Coulier F, Birnbaum D. An evolutionary history of the FGF superfamily. Bioessays. 2005;27:849–57. PubMed PMID: 16015590.
140. Detvisitsakun C, Berretta MF, Lehiy C, Passarelli AL. Stimulation of cell motility by a viral fibroblast growth factor homolog: proposal for a role in viral pathogenesis. Virology. 2005;336:308–17. PubMed PMID: 15892971.
141. Katsuma S, Daimon T, Mita K, Shimada T. Lepidopteran ortholog of Drosophila breathless is a receptor for the baculovirus fibroblast growth factor. J Virol. 2006;80:5474–81. PubMed PMID: 16699027.
142. Katsuma S, Shimada T, Kobayashi M. Characterization of the baculovirus Bombyx mori nucleopolyhedrovirus gene homologous to the mammalian FGF gene family. Virus Genes. 2004;29:211–7. PubMed PMID: 15284481.
143. Detvisitsakun C, Hutfless EL, Berretta MF, Passarelli AL. Analysis of a baculovirus lacking a functional viral fibroblast growth factor homolog. Virology. 2006;346:258–65. PubMed PMID: 16476460.

144. Detvisitsakun C, Cain EL, Passarelli AL. The Autographa californica M nucleopolyhedrovirus fibroblast growth factor accelerates host mortality. Virology. 2007;365:70–8. PubMed PMID: 17459443.
145. Katsuma S, Horie S, Daimon T, Iwanaga M, Shimada T. In vivo and in vitro analyses of a Bombyx mori nucleopolyhedrovirus mutant lacking functional vfgf. Virology. 2006;355:62–70. PubMed PMID: 16904150.
146. Yin F, Du R, Kuang W, Yang G, Wang H, Deng F, Hu Z, Wang M. Characterization of the viral fibroblast growth factor homolog of Helicoverpa armigera single nucleopolyhedrovirus. Virol Sin. 2016;31:240–8. PubMed PMID: 27142667.
147. Means JC, Passarelli AL. Viral fibroblast growth factor, matrix metalloproteases, and caspases are associated with enhancing systemic infection by baculoviruses. Proc Natl Acad Sci U S A. 2010;107:9825–30. PubMed PMID: 20457917.
148. Wang Y, Addess KJ, Chen J, Geer LY, He J, He S, Lu S, Madej T, Marchler-Bauer A, Thiessen PA, Zhang N, Bryant SH. MMDB: annotating protein sequences with Entrez's 3D-structure database. Nucleic Acids Res. 2007;35:D298–300. PubMed PMID: 17135201.
149. Lauzon HA, Jamieson PB, Krell PJ, Arif BM. Gene organization and sequencing of the Choristoneura fumiferana defective nucleopolyhedrovirus genome. J Gen Virol. 2005;86:945–61. PubMed PMID: 15784888.
150. Cai Y, Long Z, Qiu J, Yuan M, Li G, Yang K. An ac34 Deletion Mutant of Autographa californica Nucleopolyhedrovirus Exhibits Delayed Late Gene Expression and a Lack of Virulence In Vivo. J Virol. 2012;86:10432–43. PubMed PMID: 22787232.
151. Salem TZ, Zhang F, Thiem SM. Reduced expression of Autographa californica nucleopolyhedrovirus ORF34, an essential gene, enhances heterologous gene expression. Virology. 2012;435:225–38. PubMed PMID: 23131351.
152. Mu J, Zhang Y, Hu Y, Hu X, Zhou Y, Chen X, Wang Y. The role of viral protein Ac34 in nuclear relocation of subunits of the actin-related protein 2/3 complex. Virol Sin. 2016;31:480–489. PubMed PMID: 27900558.
153. Qiu J, Tang Z, Yuan M, Wu W, Yang K. The 91-205 amino acid region of AcMNPV ORF34 (Ac34), which comprises a potential C3H zinc finger, is required for its nuclear localization and optimal virus multiplication. Virus Res. 2017;228:79–89. PubMed PMID: 27894868.
154. Zhang B, Liang A, Fu Y. Ac34 protein of AcMNPV promoted progeny virus production and induced the apoptosis in host Sf9 cells. Biotechnol Lett. 2019;41:147–158. PubMed PMID: 30421092.
155. Ma SS, Zhang Z, Xia HC, Chen L, Yang YH, Yao Q, Chen KP. Evolutionary analysis of the ubiquitin gene of baculovirus and insect hosts. Genet Mol Res. 2015;14:9963–73. PubMed PMID: 26345932.
156. Garavaglia MJ, Miele SA, Iserte JA, Belaich MN, Ghiringhelli PD. Ac53, ac78, ac101 and ac103 are newly discovered core genes in the family Baculoviridae. J Virol. 2012;86:12069–79. PubMed PMID: 22933288.
157. Guarino LA. Identification of a viral gene encoding a ubiquitin-like protein. Proc Natl Acad Sci U S A. 1990;87:409–13. PubMed PMID: 2153300.
158. Lin XA, Chen Y, Xu WH, Yi YZ, Zhang ZF. Characterization of the Autographa californica nucleopolyhedrovirus ubiquitin gene promoter. Z Naturforsch [C]. 2008;63:277–83. PubMed PMID: 18533474.
159. Guo ZJ, Zhu YM, Li GH, Chen KP, Zhang CX. Ubiquitins of Bombyx mori nucleopolyhedrovirus and Helicoverpa armigera nucleopolyhedrovirus show distinct subcellular localization in infected cells. Acta Virol. 2011;55:101–6. PubMed PMID: 21692557.
160. Guarino LA, Smith G, Dong W. Ubiquitin is attached to membranes of baculovirus particles by a novel type of phospholipid anchor. Cell. 1995;80:301–309. PubMed PMID: 7834750.
161. Reilly LM, Guarino LA. The viral ubiquitin gene of Autographa californica nuclear polyhedrosis virus is not essential for viral replication. Virology. 1996;218:243–7. PubMed PMID: 8615029.
162. Haas AL, Katzung DJ, Reback PM, Guarino LA. Functional characterization of the ubiquitin variant encoded by the baculovirus Autographa californica. Biochemistry. 1996;35:5385–94. PubMed PMID: 8611528.

163. Biswas S, Willis LG, Fang M, Nie Y, Theilmann DA. Autographa californica Nucleopolyhedrovirus AC141 (Exon0), a Potential E3 Ubiquitin Ligase, Interacts with Viral Ubiquitin and AC66 To Facilitate Nucleocapsid Egress. J Virol. 2018.:92. PubMed PMID: 29142135.
164. Li Z, Gong Y, Yin C, Wang L, Li C, Pang Y. Characterization of a novel ubiquitin-fusion gene Uba256 from Spodoptera litura nucleopolyhedrovirus. Gene. 2003;303:111–9. PubMed PMID: 12559572.
165. Guarino LA, Summers MD. Functional mapping of a trans-activating gene required for expression of a baculovirus delayed-early gene. J Virol. 1986;57:563–57l. PubMed PMID: 3944847.
166. Guarino LA, Dong W, Xu B, Broussard DR, Davis RW, Jarvis DL. The baculovirus phosphoprotein pp31 is associated with the virogenic stroma. J Virol. 1992;66:7113–7120. PubMed PMID: 1433508.
167. Guarino LA, Mistretta TA, Dong W. DNA binding activity of the baculovirus late expression factor PP31. Virus Res. 2002;90:187–95. PubMed PMID: 12457973.
168. Broussard DR, Guarino LA, Jarvis DL. Dynamic phosphorylation of Autographa californica nuclear polyhedrosis virus pp31. J Virol. 1996;70:6767–74. PubMed PMID: 8794314.
169. Broussard DR, Guarino LA, Jarvis DL. Mapping functional domains in AcMNPV pp31. Virology. 1996;222:318–31. PubMed PMID: 8806516.
170. Todd JW, Passarelli AL, Miller LK. Eighteen baculovirus genes, including *lef-11, p35, 39K*, and *p47*, support late gene expression. J Virol. 1995;69:968–974. PubMed PMID: 7815564.
171. Yamagishi J, Burnett ED, Harwood SH, Blissard GW. The AcMNPV pp31 gene is not essential for productive AcMNPV replication or late gene transcription but appears to increase levels of most viral transcripts. Virology. 2007;365:34–47. PubMed PMID: 17467768.
172. Dong ZQ, Hu N, Zhang J, Chen TT, Cao MY, Li HQ, Lei XJ, Chen P, Lu C, Pan MH. Oligomerization of Baculovirus LEF-11 Is Involved in Viral DNA Replication. PLoS One. 2015;10:e0144930. PubMed PMID: 26660313.
173. Dong ZQ, Hu N, Dong FF, Chen TT, Jiang YM, Chen P, Lu C, Pan MH. Baculovirus LEF-11 Hijack Host ATPase ATAD3A to Promote Virus Multiplication in Bombyx mori cells. Sci Rep. 2017;7:46187. PubMed PMID: 28393927.
174. Zhang J, Dong ZQ, Zhang CD, He Q, Chen XM, Cao MY, Li HQ, Xiao WF, Lu C, Pan MH. Identification of a novel nuclear localization signal of baculovirus late expression factor 11. Virus Res. 2014;184:111–9. PubMed PMID: 24607592.
175. Chen T, Dong Z, Hu N, Hu Z, Dong F, Jiang Y, Li J, Chen P, Lu C, Pan M. Baculovirus LEF-11 nuclear localization signal is important for viral DNA replication. Virus Res. 2017;238:133–140. PubMed PMID: 28648848.
176. Mildvan AS, Xia Z, Azurmendi HF, Saraswat V, Legler PM, Massiah MA, Gabelli SB, Bianchet MA, Kang LW, Amzel LM. Structures and mechanisms of Nudix hydrolases. Arch Biochem Biophys. 2005;433:129–43. PubMed PMID: 15581572.
177. Ge J, Wei Z, Huang Y, Yin J, Zhou Z, Zhong J. AcMNPV ORF38 protein has the activity of ADP-ribose pyrophosphatase and is important for virus replication. Virology. 2007;361:204–11. PubMed PMID: 17174373.
178. Chen HQ, Zhou YJ, Chen KP, Yu Q. Expression and functional validation of Bombyx mori nucleopolyhedrovirus ORF29, a conserved Nudix motif protein. Acta Virol. 2013;57:442–6. PubMed PMID: 24294958.
179. Parrish S, Resch W, Moss B. Vaccinia virus D10 protein has mRNA decapping activity, providing a mechanism for control of host and viral gene expression. Proc Natl Acad Sci U S A. 2007;104:2139–44. PubMed PMID: 17283339.
180. Parrish S, Moss B. Characterization of a vaccinia virus mutant with a deletion of the D10R gene encoding a putative negative regulator of gene expression. J Virol. 2006;80:553–61. PubMed PMID: 16378957.
181. Wang D, An SH, Guo ZJ, Xu HJ, Zhang CX. Characterization of Helicoverpa armigera nucleopolyhedrovirus orf33 that encodes a novel budded virion derived protein, BV-e31. Arch Virol. 2005;150:1505–15. PubMed PMID: 15834653.

182. Yu M, Carstens EB. Characterization of an Autographa californica multiple nucleopolyhedrovirus mutant lacking the ac39(p43) gene. Virus Res. 2011;155:300–6. PubMed PMID: 20974197.
183. Partington S, Yu H, Lu A, Carstens EB. Isolation of temperature sensitive mutants of Autographa californica nuclear polyhedrosis virus: phenotype characterization of baculovirus mutants defective in very late gene expression. Virology. 1990;175:91–102. PubMed PMID: 2408231.
184. Carstens EB, Lu AL, Chan HLB. Sequence, transcriptional mapping, and overexpression of p47, a baculovirus gene regulating late gene expression. J Virol. 1993;67:2513–2520. PubMed PMID: 8474157.
185. Guarino LA, Xu B, Jin J, Dong W. A virus-encoded RNA polymerase purified from baculovirus-infected cells. J Virol. 1998;72:7985–7991. PubMed PMID: 9733837.
186. Rapp JC, Wilson JA, Miller LK. Nineteen baculovirus open reading frames, including LEF-12, support late gene expression. J Virol. 1998;72:10197–206. PubMed PMID: 9811761.
187. Li L, Harwood SH, Rohrmann GF. Identification of additional genes that influence baculovirus late gene expression. Virology. 1999;255:9–19. PubMed PMID: 10049816.
188. Guarino LA, Mistretta TA, Dong W. Baculovirus lef-12 is not required for viral replication. J Virol. 2002;76:12032–43. PubMed PMID: 12414945.
189. Zimmermann L, Stephens A, Nam SZ, Rau D, Kubler J, Lozajic M, Gabler F, Soding J, Lupas AN, Alva V. A Completely Reimplemented MPI Bioinformatics Toolkit with a New HHpred Server at its Core. J Mol Biol. 2018;430:2237–2243. PubMed PMID: 29258817.
190. Louder RK, He Y, Lopez-Blanco JR, Fang J, Chacon P, Nogales E. Structure of promoter-bound TFIID and model of human pre-initiation complex assembly. Nature. 2016;531:604–9. PubMed PMID: 27007846.
191. Katsuma S, Fujii T, Kawaoka S, Shimada T. Bombyx mori nucleopolyhedrovirus SNF2 global transactivator homologue (Bm33) enhances viral pathogenicity in B. mori larvae. J Gen Virol. 2008;89:3039–46. PubMed PMID: 19008391.
192. Katsuma S, Shimada T. Bombyx mori nucleopolyhedrovirus ORF34 is required for efficient transcription of late and very late genes. Virology. 2009;392:230–7. PubMed PMID: 19651423.
193. Tao XY, Choi JY, Wang Y, Roh JY, Lee JH, Liu Q, Park JB, Kim JS, Kim W, Je YH. Functional characterization of Autographa californica multiple nucleopolyhedrovirus ORF43 and phenotypic changes of ORF43-knockout mutant. J Microbiol. 2013;51:515–21. PubMed PMID: 23990304.
194. Sugiura N, Setoyama Y, Chiba M, Kimata K, Watanabe H. Baculovirus envelope protein ODV-E66 is a novel chondroitinase with distinct substrate specificity. J Biol Chem. 2011;286:29026–34. PubMed PMID: 21715327.
195. Hong T, Braunagel SC, Summers MD. Transcription, translation, and cellular localization of PDV-E66: A structural protein of the PDV envelope of Autographa californica nuclear polyhedrosis virus. Virology. 1994;204:210–224. PubMed PMID: 8091653.
196. Hong T, Summers M, Braunagel S. N-terminal sequences from Autographa californica nuclear polyhedrosis virus envelope proteins ODV-E66 and ODV-E25 are sufficient to direct reporter proteins to the nuclear envelope, intranuclear microvesicles and the envelope of occlusion derived virus. Proc Natl Acad Sci U S A. 1997;8:4050–4055. PubMed PMID: 9108103.
197. Kawaguchi Y, Sugiura N, Onishi M, Kimata K, Kimura M, Kakuta Y. Crystallization and X-ray diffraction analysis of chondroitin lyase from baculovirus: envelope protein ODV-E66. Acta Crystallogr Sect F Struct Biol Cryst Commun. 2012;68:190–2. PubMed PMID: 22297996.
198. Sugiura N, Ikeda M, Shioiri T, Yoshimura M, Kobayashi M, Watanabe H. Chondroitinase from baculovirus Bombyx mori nucleopolyhedrovirus and chondroitin sulfate from silkworm Bombyx mori. Glycobiology. 2013;23:1520–30. PubMed PMID: 24052236.
199. Gomi S, Kamita SG, Maeda S. Deletion analysis of all genes of Bombyx mori nucleopolyhedrovirus (BmNPV). RIKEN Review. 1999;22:39–41.
200. Xiang X, Chen L, Hu X, Yu S, Yang R, Wu X. Autographa californica multiple nucleopolyhedrovirus odv-e66 is an essential gene required for oral infectivity. Virus Res. 2011;158:72–8. PubMed PMID: 21440017.

201. Sparks WO, Rohlfing A, Bonning BC. A peptide with similarity to baculovirus ODV-E66 binds the gut epithelium of Heliothis virescens and impedes infection with Autographa californica multiple nucleopolyhedrovirus. J Gen Virol. 2011;92:1051–60. PubMed PMID: 21228132.
202. Claussen M, Koch R, Jin ZY, Suter B. Functional characterization of Drosophila Translin and Trax. Genetics. 2006;174:1337–47. PubMed PMID: 17028328.
203. Crawford AM, Miller LK. Characterization of an early gene accelerating expression of late genes of the baculovirus Autographa californica nuclear polyhedrosis virus. J Virol. 1988;62:2773–2781. PubMed PMID: 3292791.
204. Johnson A, O'Donnell M. CELLULAR DNA REPLICASES: Components and Dynamics at the Replication Fork. Ann Rev Biochem. 2005;74:283–315. PubMed PMID: 15952889.
205. Iwahori S, Ikeda M, Kobayashi M. Generation and characterization of *Autographa californica* nucleopolyhedrovirus mutants defective in *pcna* gene homologoue. J Insect Biotechnol Sericology. 2002;71:129–139.
206. Iwahori S, Ikeda M, Kobayashi M. Association of Sf9 cell proliferating cell nuclear antigen with the DNA replication site of Autographa californica multicapsid nucleopolyhedrovirus. J Gen Virol. 2004;85:2857–62. PubMed PMID: 15448347.
207. Fu Y, Wang R, Liang A. Function analysis of Ac-PCNA and Sf-PCNA during the Autographa californica multiple nucleopolyhedrovirus infection process. Mol Cell Biochem. 2018;443:57–68. PubMed PMID: 29075988.
208. Passarelli AL, Todd JW, Miller LK. A baculovirus gene involved in late gene expression predicts a large polypeptide with a conserved motif of RNA polymerases. J Virol. 1994;68:4673–4678. PubMed PMID: 8207843.
209. Titterington JS, Nun TK, Passarelli AL. Functional dissection of the baculovirus late expression factor-8 gene: sequence requirements for late gene promoter activation. J Gen Virol. 2003;84:1817–26. PubMed PMID: 12810876.
210. Crouch EA, Cox LT, Morales KG, Passarelli AL. Inter-subunit interactions of the Autographa californica M nucleopolyhedrovirus RNA polymerase. Virology. 2007;367:265–74. PubMed PMID: 17604071.
211. Shikata M, Sano Y, Hashimoto Y, Matsumoto T. Isolation and characterization of a temperature-sensitive mutant of Bombyx mori nucleopolyhedrovirus for a putative RNA polymerase gene. J Gen Virol. 1998;79(Pt 8):2071–8. PubMed PMID: 9714259.
212. Gauthier D, Thirunavukkarasu K, Faris BL, Russell DL, Weaver RF. Characterization of an Autographa californica multiple nucleopolyhedrovirus dual mutant: ORF82 is required for budded virus production, and a point mutation in LEF-8 alters late and abolishes very late transcription. J Gen Virol. 2012;93:364–73. PubMed PMID: 22031528.
213. Ioannidis K, Swevers L, Iatrou K. Bombyx mori nucleopolyhedrovirus lef8 gene: effects of deletion and implications for gene transduction applications. J Gen Virol. 2016;97:786–96. PubMed PMID: 26701681.
214. Langer T, Lu C, Echols H, Flanagan J, Hayer MK, Hartl FU. Successive action of DnaK, DnaJ and GroEL along the pathway of chaperone-mediated protein folding. Nature. 1992;356:683–9. PubMed PMID: 1349157.
215. Xu HJ, Liu YH, Yang ZN, Zhang CX. Characterization of ORF39 from Helicoverpa armigera single-nucleocapsid nucleopolyhedrovirus, the gene containing RNA recognition motif. J Biochem Mol Biol. 2006;39:263–9. PubMed PMID: 16756754.
216. Shen Y, Feng M, Wu X. Bombyx mori nucleopolyhedrovirus ORF40 is essential for budded virus production and occlusion-derived virus envelopment. J Gen Virol. 2018;99:837–850. PubMed PMID: 29676725.
217. Qiu J, Tang Z, Cai Y, Wu W, Yuan M, Yang K. The Autographa californica multiple nucleopolyhedrovirus ac51 gene is required for efficient nuclear egress of nucleocapsids and is essential for in vivo virulence. J Virol. 2019.:93. PubMed PMID: 30429334.

218. Tian CH, Zhao JF, Xu YP, Xue J, Zhang BQ, Cui YJ, Zhang MJ, Bao YY, Zhang CX. Involvement of Bombyx mori nucleopolyhedrovirus ORF41 (Bm41) in BV production and ODV envelopment. Virology. 2009;387:184–92. PubMed PMID: 19249804.
219. Liu C, Li Z, Wu W, Li L, Yuan M, Yang K, Pang Y. Autographa californica multiple nucleopolyhedrovirus ac53 plays a role in nucleocapsid assembly. Virology. 2008;382:59–68. PubMed PMID: 18851866.
220. Xu X, Zhou X, Nan H, Zhao Y, Bai Y, Ou Y, Chen H. Aggregation of AcMNPV LEF-10 and Its Impact on Viral Late Gene Expression. PLoS One. 2016;11:e0154835. PubMed PMID: 27152613.
221. Nan H, Chen H, Tuite MF, Xu X. A viral expression factor behaves as a prion. Nat Commun. 2019;10:359. PubMed PMID: 30664652.
222. Olszewski J, Miller LK. Identification and characterization of a baculovirus structural protein, VP1054, required for nucleocapsid formation. J Virol. 1997;71:5040–5050. PubMed PMID: 9188569.
223. Wu W, Liang H, Kan J, Liu C, Yuan M, Liang C, Yang K, Pang Y. Autographa californica Multiple Nucleopolyhedrovirus 38K Is a Novel Nucleocapsid Protein That Interacts with VP1054, VP39, VP80 and Itself. J Virol. 2008;82:12356–64. PubMed PMID: 18922869.
224. Marek M, Romier C, Galibert L, Merten O, van Oers MM. Baculovirus VP1054 is an acquired cellular PURα, a nucleic-acid6n binding protein specific for GGN repeats. J Virol. 2013;87:8465–80. PubMed PMID: 23720732.
225. Guan Z, Zhong L, Li C, Wu W, Yuan M, Yang K. The Autographa californica Multiple Nucleopolyhedrovirus ac54 Gene Is Crucial for Localization of the Major Capsid Protein VP39 at the Site of Nucleocapsid Assembly. J Virol. 2016;90:4115–4126. PubMed PMID: 26865720.
226. Chen Y, Zheng F, Tao L, Zheng Z, Liu Y, Wang H. Helicoverpa armaigera nucleopolyhedrovirus ORF50 is an early gene not essential for virus propagation in vitro and in vivo. Virus Genes. 2012;45:149–60. PubMed PMID: 22581445.
227. Guo ZJ, Wang DX, Yao Q, Chen KP, Zhang CX. Identification of a novel functional nuclear localization signal in the protein encoded by open reading frame 47 of Bombyx mori nucleopolyhedrovirus. Arch Virol. 2010;155:1943–50. PubMed PMID: 20706853.
228. Li Z, Li L, Yu H, Li S, Pang Y. Characterization of two homologues of ChaB in Spodoptera litura multicapsid nucleopolyhedrovirus. Gene. 2006;372:33–43. PubMed PMID: 16488560.
229. Beames B, Summers MD. Location and nucleotide sequence of the 25k protein missing from baculovirus few polyhedra (FP) mutants. Virology. 1989;168:344–353. PubMed PMID: 2644735.
230. Harrison RL, Jarvis DL, Summers MD. The role of the AcMNPV 25K gene, "FP25," in baculovirus polh and p10 expression. Virology. 1996;226:34–46. PubMed PMID: 8941320.
231. Fraser MJ, Brusca JS, Smith GE, Summers MD. Transposon mediated mutagenesis of a baculovirus. Virology. 1985;145:356–361. PubMed PMID: 2992159.
232. Beames B, Summers MD. Sequence comparison of cellular and viral copies of host cell DNA insertions found in Autographa californica nuclear polyhedrosis virus. Virology. 1990;174:354–63. PubMed PMID: 2154879.
233. Bischoff DS, Slavicek JM. Phenotypic and genetic analysis of Lymantria dispar nucleopolyhedrovirus few polyhedra mutants: mutations in the 25K FP gene may be caused by DNA replication errors. J Virol. 1997;71:1097–1106. PubMed PMID: 8995630.
234. Braunagel SC, Burks JK, Rosas-Acosta G, Harrison RL, Ma H, Summers MD. Mutations within the Autographa californica nucleopolyhedrovirus FP25K gene decrease the accumulation of ODV-E66 and alter its intranuclear transport. J Virol. 1999;73:8559–70. PubMed PMID: 10482609.
235. Rosas-Acosta G, Braunagel SC, Summers MD. Effects of deletion and overexpression of the Autographa californica nuclear polyhedrosis virus FP25K gene on synthesis of two occlusion-derived virus envelope proteins and their transport into virus-induced intranuclear membranes. J Virol. 2001;75:10829–42. PubMed PMID: 11602724.
236. Katsuma S, Noguchi Y, Zhou CL, Kobayashi M, Maeda S. Characterization of the 25K FP gene of the baculovirus Bombyx mori nucleopolyhedrovirus: implications for post-mortem host degradation. J Gen Virol. 1999;60:783–91. PubMed PMID: 10092020.

237. Katsuma S, Nakanishi T, Shimada T. Bombyx mori nucleopolyhedrovirus FP25K is essential for maintaining a steady-state level of v-cath expression throughout the infection. Virus Res. 2009;140:155–60. PubMed PMID: 19100790.
238. Kelly BJ, King LA, Possee RD, Chapple SD. Dual mutations in the Autographa californica nucleopolyhedrovirus FP-25 and p35 genes result in plasma-membrane blebbing in Trichoplusia ni cells. J Gen Virol. 2006;87:531–6. PubMed PMID: 16476974.
239. Nakanishi T, Shimada T, Katsuma S. Characterization of a Bombyx mori nucleopolyhedrovirus mutant lacking both fp25K and p35. Virus Genes.41:144–8. PubMed PMID: 20508980.
240. Cheng XH, Kumar S, Arif BM, Krell PJ, Zhang CX, Cheng XW. Cell-dependent polyhedra production and virion occlusion of AcMNPV fp25k mutants in vitro and in vivo. J Gen Virol. 2012;94:177–86. PubMed PMID: 22993192.
241. Cheng XH, Hillman CC, Zhang CX, Cheng XW. Reduction of polyhedrin mRNA and protein expression levels in Sf9 and High Five cell lines but not in Sf21 infected with AcMNPV fp25k mutants. J Gen Virol. 2012;94:166–76. PubMed PMID: 23015742.
242. Li S, Wang M, Shen S, Hu Z, Wang H, Deng F. The FP25K Acts as a Negative Factor for the Infectivity of AcMNPV Budded Virus. PLoS One. 2015;10:e0128471. PubMed PMID: 26020780.
243. Garretson TA, McCoy JC, Cheng XW. Baculovirus FP25K Localization: Role of the Coiled-Coil Domain. J Virol. 2016;90:9582–9597. PubMed PMID: 27512078.
244. Zhang Y, Shi Y, Yu H, Li J, Quan Y, Shu T, Nie Z, Zhang Y, Yu W. Functional characterization of Bombyx mori nucleopolyhedrovirus mutant lacking late expression factor 9. Acta Virol. 2016;60:281–9. PubMed PMID: 27640438.
245. Wang Y, Kleespies RG, Huger AM, Jehle JA. The genome of Gryllus bimaculatus nudivirus indicates an ancient diversification of baculovirus-related nonoccluded nudiviruses of insects. J Virol. 2007;81:5395–406. PubMed PMID: 17360757.
246. Tian CH, Tang XD, Xu HJ, Ge JQ, Miao YG, Zhang CX. Bombyx mori nucleopolyhedrovirus ORF51 encodes a budded virus envelope associated protein. Virus Genes. 2008. PubMed PMID: 19085095.
247. Cheng X, Krell P, Arif B. P34.8 (GP37) is not essential for baculovirus replication. J Gen Virol. 2001;82:299–305. PubMed PMID: 11161266.
248. Vialard JE, Yuen L, Richardson CD. Identification and characterization of a baculovirus occlusion body glycoprotein which resembles spheroidin, an entomopoxvirus protein. Journal of Virology. 1990;64:5804–5811. PubMed PMID: 2243377.
249. Hall RL, Moyer RW. Identification of an *Amsacta* spheroidin-like protein within occlusion bodies of *Choristoneura* entomopoxviruses. Virology. 1993;192:179–187. PubMed PMID: 8517016.
250. Wu J, Miller LK. Sequence, transcription, and translation of a late gene of the Autographa californica nuclear polyhedrosis virus encoding a 34.8 K polypeptide. Journal of General Virology. 1989;70:2449–2459. PubMed PMID: 2674327.
251. Salvador R, Ferrelli ML, Berretta MF, Mitsuhashi W, Biedma ME, Romanowski V, Sciocco-Cap A. Analysis of EpapGV gp37 gene reveals a close relationship between granulovirus and entomopoxvirus. Virus Genes. 2012;45:610–3. PubMed PMID: 22899338.
252. Techkarnjanaruk S, Goodman AE. Multiple genes involved in chitin degradation from the marine bacterium Pseudoalteromonas sp. strain S91. Microbiology. 1999;145:925–934. PubMed PMID: 10220172.
253. Li Z, Li C, Yang K, Wang L, Yin C, Gong Y, Pang Y. Characterization of a chitin-binding protein GP37 of Spodoptera litura multicapsid nucleopolyhedrovirus. Virus Res. 2003;96:113–22. PubMed PMID: 12951271.
254. Liu X, Ma X, Lei C, Xiao Y, Zhang Z, Sun X. Synergistic effects of Cydia pomonella granulovirus GP37 on the infectivity of nucleopolyhedroviruses and the lethality of Bacillus thuringiensis. Arch Virol. 2011;156:1707–15. PubMed PMID: 21643992.
255. Lemaitre B, Hoffmann J. The host defense of Drosophila melanogaster. Annu Rev Immunol. 2007;25:697–743. PubMed PMID: 17201680.

256. Gross CH, Wolgamot GM, Russell RLQ, Pearson MN, Rohrmann GF. A 37 kda glycoprotein from a baculovirus of *Orgyia pseudotsugata* is localized to cytoplasmic inclusion bodies. Journal of Virology. 1993;67:469–475. PubMed PMID: 8380088.
257. Mitsuhashi W, Miyamoto K. Disintegration of the peritrophic membrane of silkworm larvae due to spindles of an entomopoxvirus. J Invertebr Pathol. 2003;82:34–40. PubMed PMID: 12581717.
258. Chiu E, Hijnen M, Bunker RD, Boudes M, Rajendran C, Aizel K, Olieric V, Schulze-Briese C, Mitsuhashi W, Young V, Ward VK, Bergoin M, Metcalf P, Coulibaly F. Structural basis for the enhancement of virulence by viral spindles and their in vivo crystallization. Proc Natl Acad Sci U S A. 2015;112:3973–8. PubMed PMID: 25787255.
259. Liu X, Fang W, Fan R, Zhang L, Lei C, Zhang J, Nian W, Dou T, An S, Zhou L, Sun X. Granulovirus GP37 Facilitated ODVs Cross Insect Peritrophic Membranes and Fuse with Epithelia. Toxins. 2019.:11. PubMed PMID: 30836616.
260. Tomalski MD, Wu J, Miller LK. The location, sequence, transcription, and regulation of a baculovirus DNA polymerase gene. Virology. 1988;167:591–600. PubMed PMID: 3059678.
261. Mikhailov V, Marlyev K, Ataeva J, Kullyev P, Atrzhev A. Characterization of 3' -> 5' exonuclease associated with DNA polymerase of silkworm nuclear polyhedrosis ivrus. Nucleic Acids Research. 1986;14:3841–3857. PubMed PMID: 3012482.
262. McDougal VV, Guarino LA. Autographa californica nuclear polyhedrosis virus DNA polymerase: measurements of processivity and strand displacement. J Virol. 1999;73:4908–18. PubMed PMID: 10233952.
263. Hang X, Guarino LA. Purification of Autographa californica nucleopolyhedrovirus DNA polymerase from infected insect cells. J Gen Virol. 1999;80:2519–26. PubMed PMID: 10501509.
264. Feng G, Thumbi DK, de Jong J, Hodgson JJ, Arif BM, Doucet D, Krell PJ. Selection and Characterization of Autographa californica Multiple Nucleopolyhedrovirus DNA Polymerase Mutations. J Virol. 2012;86:13576–88. PubMed PMID: 23035236.
265. Chen G, Yan Q, Fang Y, Wu L, Krell PJ, Feng G. The N Terminus of Autographa californica Multiple Nucleopolyhedrovirus DNA Polymerase Is Required for Efficient Viral DNA Replication and Virus and Occlusion Body Production. J Virol. 2018.:92. PubMed PMID: 29563284.
266. Feng G, Krell PJ. Autographa californica multiple nucleopolyhedrovirus DNA polymerase C terminus is required for nuclear localization and viral DNA replication. J Virol. 2014;88:10918–33. PubMed PMID: 25008932.
267. Vanarsdall AL, Okano K, Rohrmann GF. Characterization of the replication of a baculovirus mutant lacking the DNA polymerase gene. Virology. 2005;331:175–180. PubMed PMID: 15582664.
268. Ohresser M, Morin N, Cerutti M, Delsert C. Temporal regulation of a complex and unconventional promoter by viral products. J Virol. 1994;68:2589–2597. PubMed PMID: 8139038.
269. Deng F, Wang R, Fang M, Jiang Y, Xu X, Wang H, Chen X, Arif BM, Guo L, Wang H, Hu Z. Proteomics analysis of Helicoverpa armigera single nucleocapsid nucleopolyhedrovirus identified two new occlusion-derived virus-associated proteins, HA44 and HA100. J Virol. 2007;81:9377–85. PubMed PMID: 17581982.
270. Ke J, Wang J, Deng R, Wang X. Autographa californica multiple nucleopolyhedrovirus ac66 is required for the efficient egress of nucleocapsids from the nucleus, general synthesis of preoccluded virions and occlusion body formation. Virology. 2008;374:421–31. PubMed PMID: 18241908.
271. Zhang MJ, Tian CH, Fan XY, Lou YH, Cheng RL, Zhang CX. Bombyx mori nucleopolyhedrovirus ORF54, a viral desmoplakin gene, is associated with the infectivity of budded virions. Arch Virol. 2012;157:1241–51. PubMed PMID: 22446883.
272. Hang X, Dong W, Guarino LA. The *lef-3* gene of *Autographa californica* nuclear polyhedrosis virus encodes a single-stranded DNA-binding protein. J Virol. 1995;69:3924–3928. PubMed PMID: 7745748.
273. Downie K, Adetola G, Carstens EB. Characterization of protein-protein interaction domains within the baculovirus Autographa californica multiple nucleopolyhedrovirus late expression factor LEF-3. J Gen Virol. 2013;94:2530–5. PubMed PMID: 23997180.

274. Evans JT, Rosenblatt GS, Leisy DJ, Rohrmann GF. Characterization of the interaction between the baculovirus ssDNA- binding protein (LEF-3) and putative helicase (P143). J Gen Virol. 1999;80:493–500. PubMed PMID: 10073712.
275. Wu Y, Carstens EB. A baculovirus single-stranded DNA binding protein, LEF-3, mediates the nuclear localization of the putative helicase P143. Virology. 1998;247:32–40. PubMed PMID: 9683569.
276. Au V, Yu M, Carstens EB. Characterization of a baculovirus nuclear localization signal domain in the late expression factor 3 protein. Virology. 2009;385:209–17. PubMed PMID: 19073335.
277. Chen Z, Carstens EB. Identification of domains in Autographa californica multiple nucleopolyhedrovirus late expression factor 3 required for nuclear transport of P143. J Virol. 2005;79:10915–22. PubMed PMID: 16103143.
278. Yu M, Carstens EB. Identification of a domain of the baculovirus Autographa californica multiple nucleopolyhedrovirus single-strand DNA-binding protein LEF-3 essential for viral DNA replication. J Virol. 2010;84:6153–62. PubMed PMID: 20357098.
279. Mikhailov V, Okano K, Rohrmann G. Baculovirus Alkaline Nuclease Possesses a 5'->3' Exonuclease Activity and Associates with the DNA-Binding Protein LEF-3. J Virol. 2003;77:2436–2444. PubMed PMID: 12551981.
280. Mikhailov V, Okano K, Rohrmann G. Specificity of the Endonuclease Activity of the Baculovirus Alkaline Nuclease for Single-stranded DNA. J Biol Chem. 2004;279:14734–14745. PubMed PMID: 14736888.
281. Mikhailov VS, Okano K, Rohrmann GF. The Redox State of the Baculovirus Single-stranded DNA-binding Protein LEF-3 Regulates Its DNA Binding, Unwinding, and Annealing Activities. J Biol Chem. 2005;280:29444–53. PubMed PMID: 15944160.
282. Mikhailov V. Helix-destabilizing properties of the baculovirus single-stranded DNA-binding protein (LEF-3). Virology. 2000;270:180–9. PubMed PMID: 10772990.
283. Mikhailov VS, Okano K, Rohrmann GF. Structural and functional analysis of the baculovirus single-stranded DNA-binding protein LEF-3. Virology. 2006;346:469–478. PubMed PMID: 16375940.
284. Iyer LM, Koonin EV, Aravind L. Classification and evolutionary history of the single-strand annealing proteins, RecT, Redbeta, ERF and RAD52. BMC Genomics. 2002;3:8. PubMed PMID: 11914131.
285. Nie Y, Fang M, Erlandson MA, Theilmann DA. Analysis of the autographa californica multiple nucleopolyhedrovirus overlapping gene pair lef3 and ac68 reveals that AC68 is a per os infectivity factor and that LEF3 is critical, but not essential, for virus replication. J Virol. 2012;86:3985–94. PubMed PMID: 22278232.
286. Li G, Wang J, Deng R, Wang X. Characterization of AcMNPV with a deletion of ac68 gene. Virus Genes. 2008;37:119–27. PubMed PMID: 18483845.
287. Boogaard B, van Oers MM, van Lent JWM. An Advanced View on Baculovirus per Os Infectivity Factors. Insects. 2018.:9. PubMed PMID: 30018247.
288. Xu H, Yang Z, Zhao J, Tian C, Ge J, Tang X, Bao Y, Zhang C. Bombyx mori nucleopolyhedrovirus ORF56 encodes an occlusion-derived virus protein and is not essential for budded virus production. J Gen Virol. 2008;89:1212–1219. PubMed PMID: 18420799.
289. Wu X, Guarino LA. Autographa californica nucleopolyhedrovirus orf69 encodes an RNA cap (nucleoside-2'-O)-methyltransferase. J Virol. 2003;77:3430–40. PubMed PMID: 12610118.
290. Lu A, Miller LK. Differential requirements for baculovirus late expression factor genes in two cell lines. J Virol. 1995;69:6265–6272. PubMed PMID: 7666527.
291. Tachibana A, Hamajima R, Tomizaki M, Kondo T, Nanba Y, Kobayashi M, Yamada H, Ikeda M. HCF-1 encoded by baculovirus AcMNPV is required for productive nucleopolyhedrovirus infection of non-permissive Tn368 cells. Sci Rep. 2017;7:3807. PubMed PMID: 28630398.
292. Lu A, Miller LK. Species-specific effects of the hcf-1 gene on baculovirus virulence. J Virol. 1996;70:5123–30. PubMed PMID: 8764020.
293. Wilson JA, Forney SD, Ricci AM, Allen EG, Hefferon KL, Miller LK. Expression and mutational analysis of Autographa californica nucleopolyhedrovirus HCF-1: functional requirements for cysteine residues. J Virol. 2005;79:13900–14. PubMed PMID: 16254326.

294. Griffiths CM, Barnett AL, Ayres MD, Windass J, King LA, Possee RD. In vitro host range of Autographa californica nucleopolyhedrovirus recombinants lacking functional p35, iap1 or iap2. J Gen Virol. 1999;80:1055–1066. PubMed PMID: 10211976.
295. Yamada H, Shibuya M, Kobayashi M, Ikeda M. Baculovirus Lymantria dispar multiple nucleopolyhedrovirus IAP2 and IAP3 do not suppress apoptosis, but trigger apoptosis of insect cells in a transient expression assay. Virus Genes. 2012;45:370–9. PubMed PMID: 22798056.
296. Yang R, Zhang J, Feng M, Wu X. Identification of Bombyx mori nucleopolyhedrovirus bm58a as an auxiliary gene and its requirement for cell lysis and larval liquefaction. J Gen Virol. 2016;97:3039–3050. PubMed PMID: 27667819.
297. Hu X, Shen Y, Zheng Q, Wang G, Wu X, Gong C. Bm59 is an early gene, but is unessential for the propagation and assembly of Bombyx mori nucleopolyhedrovirus. Mol Genet Genomics. 2016;291:145–54. PubMed PMID: 26210473.
298. Du MF, Yin XM, Guo ZJ, Zhu LJ. Characterization of a late gene, ORF60 from Bombyx mori nucleopolyhedrovirus. J Biochem Mol Biol. 2006;39:737–42. PubMed PMID: 17129410.
299. Guo ZJ, Qiu LH, An SH, Yao Q, Park EY, Chen KP, Zhang CX. Open reading frame 60 of the Bombyx mori nucleopolyhedrovirus plays a role in budded virus production. Virus Res. 2010;151:185–91. PubMed PMID: 20576538.
300. Shen H, Chen K, Yao Q, Zhou Y. Characterization of the Bm61 of the Bombyx mori nucleopolyhedrovirus. Curr Microbiol. 2009;59:65–70. PubMed PMID: 19319594.
301. Shen H, Chen K. BM61 of Bombyx mori nucleopolyhedrovirus: its involvement in the egress of nucleocapsids from the nucleus. FEBS Lett. 2012;586:990–5. PubMed PMID: 22569252.
302. Guo YJ, Fu SH, Li LL. Autographa californica multiple nucleopolyhedrovirus ac75 is required for egress of nucleocapsids from the nucleus and formation of de novo intranuclear membrane microvesicles. PLoS One. 2017;12:e0185630. PubMed PMID: 28968422.
303. Shi A, Hu Z, Zuo Y, Wang Y, Wu W, Yuan M, Yang K. Autographa californica Multiple Nucleopolyhedrovirus ac75 Is Required for the Nuclear Egress of Nucleocapsids and Intranuclear Microvesicle Formation. J Virol. 2018.:92. PubMed PMID: 29212928.
304. Hu Z, Yuan M, Wu W, Liu C, Yang K, Pang Y. Autographa californica multiple nucleopolyhedrovirus ac76 is involved in intranuclear microvesicle formation. J Virol. 2010;84:7437–47. PubMed PMID: 20484514.
305. Wei D, Wang Y, Zhang X, Hu Z, Yuan M, Yang K. Autographa californica nucleopolyhedrovirus Ac76: a dimeric type II integral membrane protein that contains an inner nuclear membrane-sorting motif. J Virol. 2014;88:1090–103. PubMed PMID: 24198428.
306. McLachlin JR, Miller LK. Identification and characterization of vlf-1, a baculovirus gene involved in very late gene expression. J Virol. 1994;68:7746–7756. PubMed PMID: 7966564.
307. Yang S, Miller LK. Activation of baculovirus very late promoters by interaction with very late factor 1. J Virol. 1999;73:3404–9. PubMed PMID: 10074194.
308. Yang S, Miller LK. Expression and mutational analysis of the baculovirus very late factor 1 (vlf-1) gene. Virology. 1998;245:99–109. PubMed PMID: 9614871.
309. Vanarsdall AL, Okano K, Rohrmann GF. Characterization of the role of VLF-1 in baculovirus capsid structure and DNA processing. J Virol. 2006;80:1724–1733. PubMed PMID: 16439529.
310. Vanarsdall AL, Okano K, Rohrmann GF. Characterization of a baculovirus with a deletion of vlf-1. Virology. 2004;326:191–201. PubMed PMID: 15262507.
311. Li Y, Wang J, Deng R, Zhang Q, Yang K, Wang X. vlf-1 deletion brought AcMNPV to defect in nucleocapsid formation. Virus Genes. 2005;31:275–84. PubMed PMID: 16175333.
312. Mikhailov V, Rohrmann G. Binding of the baculovirus very late expression factor 1 (VLF-1) to different DNA structures. BMC Mol Biol. 2002;3:14. PubMed PMID: 12350233.
313. Chen L, Shen Y, Yang R, Wu X, Hu W, Shen G. Bombyx mori nucleopolyhedrovirus (BmNPV) Bm64 is required for BV production and per os infection. Virol J. 2015;12:173. PubMed PMID: 26497116.

314. Tao XY, Choi JY, Kim WJ, Lee JH, Liu Q, Kim SE, An SB, Lee SD, Jin BR, Je YH. The Autographa californica multiple nucleopolyhedrovirus ORF78 is essential for BV production and general occlusion body formation. J Virol. 2013;87:8441–50. PubMed PMID: 23698311.
315. Hou D, Zhang L, Deng F, Fang W, Wang R, Liu X, Guo L, Rayner S, Chen X, Wang H, Hu Z. Comparative Proteomics Reveal Fundamental Structural and Functional Differences between the Two Progeny Phenotypes of a Baculovirus. J Virol. 2013;87:829–39. PubMed PMID: 23115289.
316. Huang H, Wang M, Deng F, Hou D, Arif BM, Wang H, Hu Z. The ha72 core gene of baculovirus is essential for budded virus production and occlusion-derived virus embedding, and amino acid K22 plays an important role in its function. J Virol. 2014;88:705–709. PubMed PMID: 24089571.
317. Aravind L, Walker DR, Koonin EV. Conserved domains in DNA repair proteins and evolution of repair systems. Nucleic Acids Res. 1999;27:1223–42. PubMed PMID: 9973609.
318. Wu W, Passarelli AL. The Autographa californica M nucleopolyhedrovirus ac79 gene encodes an early gene product with structural similarities to UvrC and intron-encoded endonucleases that is required for efficient budded virus production. J Virol. 2012;86:5614–25. PubMed PMID: 22419804.
319. Tang Q, Li G, Yao Q, Chen L, Feng F, Yuan Y, Chen K. Bm65 is Essential for the Propagation of Bombyx mori Nucleopolyhedrovirus. Curr Microbiol. 2013;66:22–9. PubMed PMID: 23053485.
320. Whitford M, Faulkner P. A structural polypeptide of the baculovirus Autographa californica nuclear polyhedrosis virus contains 0-linked N-acetylglucosamine. J Virol. 1992;66:3324–3329. PubMed PMID: 1583718.
321. Whitford M, Faulkner P. Nucleotide sequence and transcriptional analysis of a gene encoding gp41, a structural glycoprotein of the baculovirus Autographa californica nuclear polyhedrosis virus. J Virol. 1992;66:4763–4768. PubMed PMID: 1629955.
322. Olszewski J, Miller LK. A role for baculovirus GP41 in budded virus production. Virology. 1997;233:292–301. PubMed PMID: 9217053.
323. Li Y, Shen S, Hu L, Deng F, Vlak JM, Hu Z, Wang H, Wang M. The Functional Oligomeric State of Tegument Protein GP41 Is Essential for Baculovirus Budded Virion and Occlusion-Derived Virion Assembly. J Virol. 2018.:92. PubMed PMID: 29643237.
324. Chen HQ, Chen KP, Yao Q, Guo ZJ, Wang LL. Characterization of a late gene, ORF67 from Bombyx mori nucleopolyhedrovirus. FEBS Lett. 2007;581:5836–5842. PubMed PMID: 18053810.
325. Raynes DA, Hartshorne DJ, Guerriero VJ. Sequence and expression of a baculovirus protein with antigenic similarity to telokin. J Gen Virol. 1994.:1807–1809. PubMed PMID: 7517434.
326. Holden HM, Wesenberg G, Raynes DA, Hartshorne DJ, Guerriero VJ, Rayment I. Molecular structure of a proteolytic fragment of TLP20. Acta Crystallogr D Biol Crystallogr. 1996;52:1153–60. PubMed PMID: 15299576.
327. Iwanaga M, Kurihara M, Kobayashi M, Kang W. Characterization of Bombyx mori nucleopolyhedrovirus orf68 gene that encodes a novel structural protein of budded virus. Virology. 2002;297:39–47. PubMed PMID: 12083834.
328. Russell RL, Rohrmann GF. Characterization of P91, a protein associated with virions of an Orgyia pseudotsugata baculovirus. Virology. 1997;233:210–23. PubMed PMID: 9201231.
329. Hou D, Zhang L, Deng F, Fang W, Wang R, Liu X, Guo L, Rayner S, Chen X, Wang H, Hu Z. 2012. Comparative Proteomics Reveal Fundamental Structural and Functional Differences between the Two Progeny Phenotypes of a Baculovirus. J Virol doi:JVI.02329-12 [pii] doi: 10.1128/JVI.02329-12.
330. Suetake T, Tsuda S, Kawabata S, Miura K, Iwanaga S, Hikichi K, Nitta K, Kawano K. Chitin-binding proteins in invertebrates and plants comprise a common chitin-binding structural motif. J Biol Chem. 2000;275:17929–32. PubMed PMID: 10770921.
331. Zhu S, Wang W, Wang Y, Yuan M, Yang K. The baculovirus core gene ac83 is required for nucleocapsid assembly and per os infectivity of Autographa californica nucleopolyhedrovirus. J Virol. 2013;87:10573–86. PubMed PMID: 23864639.
332. Javed MA, Biswas S, Willis LG, Harris S, Pritchard C, van Oers MM, Donly BC, Erlandson MA, Hegedus DD, Theilmann DA. Autographa californica Multiple Nucleopolyhedrovirus AC83 is a Per Os Infectivity

Factor (PIF) Protein Required for Occlusion-Derived Virus (ODV) and Budded Virus Nucleocapsid Assembly as well as Assembly of the PIF Complex in ODV Envelopes. J Virol. 2017;91:02115–16. PubMed PMID: 28031365.
333. Xiang X, Chen L, Guo A, Yu S, Yang R, Wu X. The Bombyx mori nucleopolyhedrovirus (BmNPV) ODV-E56 envelope protein is also a per os infectivity factor. Virus Res. 2011;155:69–75. PubMed PMID: 20817055.
334. Huang Z, Pan M, Zhu S, Zhang H, Wu W, Yuan M, Yang K. The Autographa californica Multiple Nucleopolyhedrovirus ac83 Gene Contains a cis-Acting Element That Is Essential for Nucleocapsid Assembly. J Virol. 2017.:91. PubMed PMID: 28031366.
335. Martins A, Shuman S. Characterization of a baculovirus enzyme with RNA ligase, polynucleotide 5'-kinase, and polynucleotide 3'-phosphatase activities. J Biol Chem. 2004;279:18220–31. PubMed PMID: 14747466.
336. Durantel D, Croizier L, Ayres MD, Croizier G, Possee RD, Lopez-Ferber M. The pnk/pnl gene (ORF 86) of Autographa californica nucleopolyhedrovirus is a non-essential, immediate early gene. J Gen Virol. 1998;79(Pt 3):629–37. PubMed PMID: 9519844.
337. Lu M, Iatrou K. Characterization of a domain of the genome of BmNPV containing a functional gene for a small capsid protein and harboring deletions eliminating three open reading frames that are present in AcNPV. Gene. 1997;185:69–75. PubMed PMID: 9034315.
338. Thiem SM, Miller LK. A baculovirus gene with a novel transcription pattern encodes a polypeptide with a zinc finger and a leucine zipper. Journal of Virology. 1989;63:4489–4497. PubMed PMID: 2507791.
339. Passarelli AL, Miller LK. In vivo and in vitro analyses of recombinant baculoviruses lacking a functional cg30 gene. J Virol. 1994;68:1186–90. PubMed PMID: 8289348.
340. Zhang MJ, Cheng RL, Lou YH, Ye WL, Zhang T, Fan XY, Fan HW, Zhang CX. Disruption of Bombyx mori nucleopolyhedrovirus ORF71 (Bm71) results in inefficient budded virus production and decreased virulence in host larvae. Virus Genes. 2012;45:161–8. PubMed PMID: 22585339.
341. Ishihara G, Shimada T, Katsuma S. Functional characterization of Bombyx mori nucleopolyhedrovirus CG30 protein. Virus Res. 2013;174:52–9. PubMed PMID: 23507307.
342. Pearson MN, Russell RLQ, Rohrmann GF, Beaudreau GS. P39, a major baculovirus structural protein: Immunocytochemical characterization and genetic location. Virology. 1988;167:407–413. PubMed PMID: 3059676.
343. Thiem SM, Miller LK. Identification, sequence, and transcriptional mapping of the major capsid protein gene of the baculovirus *Autographa californica* nuclear polyhedrosis virus. J Virol. 1989;63:2008–2018. PubMed PMID: 2649691.
344. Danquah JO, Botchway S, Jeshtadi A, King LA. Direct interaction of baculovirus capsid proteins VP39 and EXON0 with kinesin-1 in insect cells determined by fluorescence resonance energy transfer-fluorescence lifetime imaging microscopy. J Virol. 2012;86:844–53. PubMed PMID: 22072745.
345. Katsuma S, Kokusho R. A Conserved Glycine Residue Is Required for Proper Functioning of a Baculovirus VP39 Protein. J Virol. 2017.:91. PubMed PMID: 28077638.
346. Gross CH, Shuman S. RNA 5'-triphosphatase, nucleoside triphosphatase, and guanylyltransferase activities of baculovirus LEF-4 protein. J Virol. 1998;72:10020–8. PubMed PMID: 9811740.
347. Jin J, Dong W, Guarino LA. The LEF-4 subunit of baculovirus RNA polymerase has RNA 5'- triphosphatase and ATPase activities. J Virol. 1998;72:10011–9. PubMed PMID: 9811739.
348. Martins A, Shuman S. Mutational analysis of baculovirus capping enzyme Lef4 delineates an autonomous triphosphatase domain and structural determinants of divalent cation specificity. J Biol Chem. 2001;276:45522–9. PubMed PMID: 11553638.
349. Martins A, Shuman S. The domain order of mammalian capping enzyme can be inverted and baculovirus phosphatase can function in cap formation in vivo. Virology. 2002;304:167–75. PubMed PMID: 12504559.
350. Knebel-Morsdorf D, Quadt I, Li Y, Montier L, Guarino LA. Expression of baculovirus late and very late genes depends on LEF-4, a component of the viral RNA polymerase whose guanyltransferase function is essential. J Virol. 2006;80:4168–73. PubMed PMID: 16571832.

351. Wang D, Zhang CX. Helicoverpa armigera nucleopolyhedrovirus ORF80 encodes a late, nonstructural protein. J Biochem Mol Biol. 2007;40:65–71. PubMed PMID: 17244484.
352. Shen H, Chen K, Yao Q, Yu W, Pan Y, Huo J, Xia H, Huang G. Characterization of Bombyx mori nucleopolyhedrovirus orf74, a novel gene involved in virulence of virus. Virus Genes. 2009;38:487–94. PubMed PMID: 19340569.
353. Long CM, Rohrmann GF, Merrill GF. The conserved baculovirus protein p33 (Ac92) is a flavin adenine dinucleotide-linked sulfhydryl oxidase. Virology. 2009;388:231–5. PubMed PMID: 19409596.
354. Wu W, Passarelli AL. Autographa californica M nucleopolyhedrovirus Ac92 (ORF92, P33) is required for budded virus production and multiply-enveloped occlusion-derived virus formation. J Virol. 2010;84:12351–61. PubMed PMID: 20861245.
355. Morel C, Adami P, Musard JF, Duval D, Radom J, Jouvenot M. Involvement of sulfhydryl oxidase QSOX1 in the protection of cells against oxidative stress-induced apoptosis. Exp Cell Res. 2007;313:3971–82. PubMed PMID: 17927979.
356. Thirunavukkarasu C, Wang LF, Harvey SA, Watkins SC, Chaillet JR, Prelich J, Starzl TE, Gandhi CR. Augmenter of liver regeneration: an important intracellular survival factor for hepatocytes. J Hepatol. 2008;48:578–88. PubMed PMID: 18272248.
357. Nie Y, Fang M, Theilmann DA. Autographa californica multiple nucleopolyhedrovirus core gene ac92 (p33) is required for the efficient budded virus production. Virology. 2011;409:38–45. PubMed PMID: 20965540.
358. Hakim M, Mandelbaum A, Fass D. Structure of a baculovirus sulfhydryl oxidase, a highly divergent member of the erv flavoenzyme family. J Virol. 2011;85:9406–13. PubMed PMID: 21752922.
359. Hou Y, Xia Q, Yuan YA. Crystal structure of Bombyx mori nucleopolyhedrovirus ORF75 reveals a pseudo-dimer of thiol oxidase domains with a putative substrate-binding pocket. J Gen Virol. 2012;93:2142–51. PubMed PMID: 22764321.
360. Kuang W, Zhang H, Wang M, Zhou NY, Deng F, Wang H, Gong P, Hu Z. Three Conserved Regions in Baculovirus Sulfhydryl Oxidase P33 Are Critical for Enzymatic Activity and Function. J Virol. 2017.:91. PubMed PMID: 28904203.
361. Huang N, Clem RJ, Rohrmann GF. Characterization of cDNAs encoding p53 of Bombyx mori and Spodoptera frugiperda. Insect Biochem Mol Biol. 2011;41:613–9. PubMed PMID: 21497653.
362. Wu W, Clem RJ, Rohrmann GF, Passarelli AL. 2013. The baculovirus sulfhydryl oxidase Ac92 (P33) interacts with the Spodoptera frugiperda P53 protein and oxidizes it in vitro. 447:197-207.
363. Yuan M, Huang Z, Wei D, Hu Z, Yang K, Pang Y. Identification of Autographa californica nucleopolyhedrovirus ac93 as a core gene and its requirement for intranuclear microvesicle formation and nuclear egress of nucleocapsids. J Virol. 2011;85:11664–74. PubMed PMID: 21880748.
364. Russell RLQ, Rohrmann GF. A 25 kilodalton protein is associated with the envelopes of occluded baculovirus virions. Virology. 1993;195:532–540. PubMed PMID: 8337828.
365. Chen L, Hu X, Xiang X, Yu S, Yang R, Wu X. Autographa californica multiple nucleopolyhedrovirus odv-e25 (Ac94) is required for budded virus infectivity and occlusion-derived virus formation. Arch Virol. 2012;157:617–25. PubMed PMID: 22218963.
366. Luo XC, Wang SS, Zhang J, Qian DD, Wang SM, Li LL. Effects of Early or Overexpression of the Multiple Nucleopolyhedrovirus (ODV-E25) on Virus Replication. PLoS One. 2013;8:e65635. PubMed PMID: 23825525.
367. Chen L, Yang R, Hu X, Xiang X, Yu S, Wu X. The formation of occlusion-derived virus is affected by the expression level of ODV-E25. Virus Res. 2013;173:404–14. PubMed PMID: 23298549.
368. Zhu M, Wang J, Deng R, Xiong P, Liang H, Wang X. A MicroRNA Encoded by Autographa californica Nucleopolyhedrovirus Regulates Expression of Viral Gene ODV-E25. J Virol. 2013;87:13029–34. PubMed PMID: 24027316.
369. Gordon JD, Carstens E. Phenotypic characterization and physical mapping of a terperature-sensitive mutant of AcMNPV defective in DNA synthesis. Virology. 1984;138:69–81. PubMed PMID: 6093362.
370. Lu A, Carstens EB. Nucleotide sequence of a gene essential for viral DNA replication in the baculovirus *Autographa californica* nuclear polyhedrosis virus. Virology. 1991;181:336–347. PubMed PMID: 1994581.

371. McDougal VV, Guarino LA. The autographa californica nuclear polyhedrosis virus p143 gene encodes a DNA helicase. J Virol. 2000;74:5273–9. PubMed PMID: 10799604.
372. Maeda S, Kamita SG, Kondo A. Host range expansion of *Autographa californica* nuclear polyhedrosis virus (NPV) following recombination of a 0.6-kilobase-pair DNA fragment originating from *Bombyx mori* NPV. J Virol. 1993;67:6234–6238. PubMed PMID: 8396678.
373. Croizier G, Croizier L, Argaud O, Poudevigne D. Extension of *Autographa californica* nuclear polyhedrosis virus host range by interspecific replacement of a short DNA sequence in the p143 helicase gene. Proc Natl Acad Sc USA. 1994;91:48–52. PubMed PMID: 8278405.
374. Hill T, Unckless RL. Baculovirus Molecular Evolution via Gene Turnover and Recurrent Positive Selection of Key Genes. J Virol. 2017.:91. PubMed PMID: 28814516.
375. Nagamine T, Sako Y. A Role for the Anti-Viral Host Defense Mechanism in the Phylogenetic Divergence in Baculovirus Evolution. PLoS One. 2016;11:e0156394. PubMed PMID: 27244571.
376. Hamajima R, Kobayashi M, Ikeda M. Identification of amino acid residues of AcMNPV P143 protein involved in rRNA degradation and restricted viral replication in BM-N cells from the silkworm Bombyx mori. Virology. 2015;485:244–51. PubMed PMID: 26313611.
377. Hamajima R, Kobayashi M, Ikeda M. P143 proteins from heterologous nucleopolyhedroviruses induce apoptosis in BM-N cells derived from the silkworm Bombyx mori. Virus Res. 2017;233:70–76. PubMed PMID: 28315706.
378. Xu HJ, Yang ZN, Wang F, Zhang CX. Bombyx mori nucleopolyhedrovirus ORF79 encodes a 28-kDa structural protein of the ODV envelope. Arch Virol. 2006;151:681–95. PubMed PMID: 16328137.
379. Fang M, Nie Y, Harris S, Erlandson MA, Theilmann DA. Autographa californica multiple nucleopolyhedrovirus core gene ac96 encodes a per Os infectivity factor (PIF-4). J Virol. 2009;83:12569–78. PubMed PMID: 19759145.
380. Dong ZQ, Zhang J, Chen XM, He Q, Cao MY, Wang L, Li HQ, Xiao WF, Pan CX, Lu C, Pan MH. Bombyx mori nucleopolyhedrovirus ORF79 is a per os infectivity factor associated with the PIF complex. Virus Res. 2014;184:62–70. PubMed PMID: 24583368.
381. Peng K, van Oers MM, Hu Z, van Lent JW, Vlak JM. Baculovirus per os infectivity factors form a complex on the surface of occlusion-derived virus. J Virol. 2010;84:9497–504. PubMed PMID: 20610731.
382. Zhang J, Feng M, Fan Y, Xu W, Zheng Q, Wu X. Networks of protein-protein interactions among structural proteins of budded virus of Bombyx mori nucleopolyhedrovirus. Virology. 2018;518:163–171. PubMed PMID: 29510333.
383. Wu W, Lin T, Pan L, Yu M, Li Z, Pang Y, Yang K. Autographa californica multiple nucleopolyhedrovirus nucleocapsid assembly is interrupted upon deletion of the 38K gene. J Virol. 2006;80:11475–85. PubMed PMID: 16987976.
384. Hefferon KL. ORF98 of Autographa californica nucleopolyhedrosisvirus is an auxiliary factor in late gene expression. Can J Microbiol. 2003;49:157–63. PubMed PMID: 12795401.
385. Lai Q, Wu W, Li A, Wang W, Yuan M, Yang K. The 38K-Mediated Specific Dephosphorylation of the Viral Core Protein P6.9 Plays an Important Role in the Nucleocapsid Assembly of Autographa californica Multiple Nucleopolyhedrovirus. J Virol. 2018.:92. PubMed PMID: 29444944.
386. Passarelli AL, Miller LK. Identification of genes encoding late expression factors located between 56.0 and 65.4 map units of the Autographa californica nuclear polyhedrosis virus genome. Virology. 1993;197:704–714. PubMed PMID: 8249293.
387. Harwood SH, Li L, Ho PS, Preston AK, Rohrmann GF. AcMNPV late expression factor-5 interacts with itself and contains a zinc ribbon domain that is required for maximal late transcription activity and is homologous to elongation factor TFIIS. Virology. 1998;250:118–134. PubMed PMID: 9770426.
388. Guarino LA, Dong W, Jin J. In vitro activity of the baculovirus late expression factor LEF-5. J Virol. 2002;76:12663–75. PubMed PMID: 12438592.
389. Su J, Lung O, Blissard GW. The Autographa californica multiple nucleopolyhedrovirus lef-5 gene is required for productive infection. Virology. 2011;416:54–64. PubMed PMID: 21601232.

390. Wilson ME, Mainprize TH, Friesen PD, Miller LK. l987. Location, transcription, and sequence of a baculovirus gene encoding a small arginine-rich polypeptide. J Virol.61:66l–666. PubMed PMID: 3023708.
391. Garcia-Maruniak A, Maruniak JE, Zanotto PM, Doumbouya AE, Liu JC, Merritt TM, Lanoie JS. Sequence analysis of the genome of the Neodiprion sertifer nucleopolyhedrovirus. J Virol. 2004;78:7036–51. PubMed PMID: 15194780.
392. Tweeten KA, Bulla LA, Consigli RA. Characterization of an extremely basic protein derived from granulosis virus nucleocapsid. J Virol. 1980;33:866–876. PubMed PMID: 16789190.
393. Balhorn R. A model for the structure of chromatin in mammalian sperm. J Cell Biol. 1982;93:298–305. PubMed PMID: 7096440.
394. Nakano M, Kasai K, Yoshida K, Tanimoto T, Tamaki Y, Tobita T. Conformation of the fowl protamine, galline, and its binding properties to DNA. J Biochem. 1989;105:133–137. PubMed PMID: 2738040.
395. Wilson ME, Price KH. Association of Autographa californica nuclear polyhedrosis virus (AcMNPV) with the nuclear matrix. Virology. 1988;167:233–241. PubMed PMID: 3055664.
396. Peng Y, Li K, Pei RJ, Wu CC, Liang CY, Wang Y, Chen XW. The protamine-like DNA-binding protein P6.9 epigenetically up-regulates Autographa californica multiple nucleopolyhedrovirus gene transcription in the late infection phase. Virol Sin. 2012;27:57–68. PubMed PMID: 22270807.
397. Liu X, Zhao H, Fang Z, Yuan M, Yang K, Pang Y. Distribution and phosphorylation of the basic protein P6.9 of Autographa californica nucleopolyhedrovirus. J Virol. 2012;86:12217–27. PubMed PMID: 22951830.
398. Li A, Zhao H, Lai Q, Huang Z, Yuan M, Yang K. Posttranslational Modifications of Baculovirus Protamine-Like Protein P6.9 and the Significance of Its Hyperphosphorylation for Viral Very Late Gene Hyperexpression. J Virol. 2015;89:7646–59. PubMed PMID: 25972542.
399. Oppenheimer DI, Volkman LE. Proteolysis of p6.9 induced by cytochalasin D in Autographa californica M nuclear polyhedrosis virus-infected cells. Virology. 1995;207:1–11. PubMed PMID: 7871717.
400. Wang M, Tuladhar E, Shen S, Wang H, van Oers MM, Vlak JM, Westenberg M. Specificity of baculovirus P6.9 basic DNA-binding proteins and critical role of the C terminus in virion formation. J Virol. 2010;84:8821–8. PubMed PMID: 20519380.
401. Singh CP, Singh J, Nagaraju J. bmnpv-miR-3 facilitates BmNPV infection by modulating the expression of viral P6.9 and other late genes in Bombyx mori. Insect Biochem Mol Biol. 2014;49:59–69. PubMed PMID: 24698834.
402. Braunagel SC, Guidry PA, Rosas-Acosta G, Engelking L, Summers MD. Identification of BV/ODV-C42, an Autographa californica nucleopolyhedrovirus orf101-encoded structural protein detected in infected-cell complexes with ODV-EC27 and p78/83. J Virol. 2001;75:12331–8. PubMed PMID: 11711623.
403. Wang Y, Wang Q, Liang C, Song J, Li N, Shi H, Chen X. Autographa californica multiple nucleopolyhedrovirus nucleocapsid protein BV/ODV-C42 mediates the nuclear entry of P78/83. J Virol. 2008;82:4554–61. PubMed PMID: 18287235.
404. Li K, Wang Y, Bai H, Wang Q, Song J, Zhou Y, Wu C, Chen X. The putative pocket protein binding site of Autographa californica nucleopolyhedrovirus BV/ODV-C42 is required for virus-induced nuclear actin polymerization. J Virol. 2010;84:7857–68. PubMed PMID: 20484515.
405. Fang M, Nie Y, Dai X, Theilmann DA. Identification of AcMNPV EXON0 (ac141) domains required for efficient production of budded virus, dimerization and association with BV/ODV-C42 and FP25. Virology. 2008;375:265–76. PubMed PMID: 18313716.
406. Vanarsdall AL, Pearson MN, Rohrmann GF. Characterization of baculovirus constructs lacking either the Ac 101, Ac 142, or the Ac 144 open reading frame. Virology. 2007;367:187–95. PubMed PMID: 17585983.
407. Lu A, Craig A, Casselman R, Carstens EB. Nucleotide sequence, insertional mutagenesis, and transcriptional mapping of a conserved region of the baculovirus Autographa californica nuclear polyhedrosis virus (map unit 64.8-66.9). Can J Microbiol. 1996;42:1267–73. PubMed PMID: 8989865.
408. Wang Y, Zhang Y, Han S, Hu X, Zhou Y, Mu J, Pei R, Wu C, Chen X. Identification of a novel regulatory sequence of actin nucleation promoting factor encoded by Autographa californica multiple nucleopolyhedrovirus. J Biol Chem. 2015;290:9533–41. PubMed PMID: 25691574.

409. Zhang Y, Hu X, Mu J, Hu Y, Zhou Y, Zhao H, Wu C, Pei R, Chen J, Chen X, Wang Y. Ac102 Participates in Nuclear Actin Polymerization by Modulating BV/ODV-C42 Ubiquitination during Autographa californica Multiple Nucleopolyhedrovirus Infection. J Virol. 2018.:92. PubMed PMID: 29618641.
410. Hepp SE, Borgo GM, Ticau S, Ohkawa T, Welch MD. Baculovirus AC102 Is a Nucleocapsid Protein That Is Crucial for Nuclear Actin Polymerization and Nucleocapsid Morphogenesis. J Virol. 2018.:92. PubMed PMID: 29540600.
411. Jiao Y, Wang J, Deng R, Yu X, Wang X. AcMNPV-miR-3 is a miRNA encoded by Autographa californica nucleopolyhedrovirus and regulates the viral infection by targeting ac101. Virus Res. 2019. doi: 10.1016/j.virusres.2019.05.004. PubMed PMID: 31077766.
412. Ohkawa T, Rowe AR, Volkman LE. Identification of six Autographa californica multicapsid nucleopolyhedrovirus early genes that mediate nuclear localization of G-actin. J Virol. 2002;76:12281–9. PubMed PMID: 12414968.
413. Yuan M, Wu W, Liu C, Wang Y, Hu Z, Yang K, Pang Y. A highly conserved baculovirus gene p48 (ac103) is essential for BV production and ODV envelopment. Virology. 2008;379:87–96. PubMed PMID: 18656219.
414. Müller R, Pearson MN, Russell RLQ, Rohrmann GF. A capsid-associated protein of the multicapsid nuclear polyhedrosis virus of *Orgyia pseudotsugata*: Genetic location, sequence, transcriptional mapping, and immunocytochemical characterization. Virology. 1990;176:133–144. PubMed PMID: 2184573.
415. Marek M, Merten OW, Galibert L, Vlak JM, van Oers MM. Baculovirus VP80 protein and the F-actin cytoskeleton interact and connect the viral replication factory with the nuclear periphery. J Virol. 2011;85:5350–62. PubMed PMID: 21450830.
416. Lu A, Carstens EB. Nucleotide sequence and transcriptional analysis of the p80 gene of Autographa californica nuclear polyhedrosis virus: a homologue of the Orgyia pseudotsugata nuclear polyhedrosis virus capsid-associated gene. Virology. 1992;190:201–209. PubMed PMID: 1529529.
417. Marek M, van Oers MM, Devaraj FF, Vlak JM, Merten OW. Engineering of baculovirus vectors for the manufacture of virion-free biopharmaceuticals. Biotechnol Bioeng. 2011;108:1056–67. PubMed PMID: 21449023.
418. Marek M, Merten OW, Francis-Devaraj F, Oers MM. Essential C-terminal region of the baculovirus minor capsid protein VP80 binds DNA. J Virol. 2012;86:1728–38. PubMed PMID: 22090126.
419. Ho CK, Shuman S. Bacteriophage T4 RNA ligase 2 (gp24.1) exemplifies a family of RNA ligases found in all phylogenetic domains. Proc Natl Acad Sci U S A. 2002;99:12709–14. PubMed PMID: 12228725.
420. Becker D, Knebel-Morsdorf D. Sequence and temporal appearance of the early transcribed baculovirus gene HE65. J Virol. 1993;67:5867–72. PubMed PMID: 8371346.
421. Shi SL, Pan MH, Lu C. Characterization of Antheraea pernyi nucleopolyhedrovirus p11 gene, a homologue of Autographa californica nucleopolyhedrovirus orf108. Virus Genes. 2007;35:97–101. PubMed PMID: 17072759.
422. Boogaard B, Evers F, van Lent JWM, van Oers MM. The baculovirus Ac108 protein is a per os infectivity factor and a component of the ODV entry complex. J Gen Virol. 2019. doi: 10.1099/jgv.0.001200. PubMed PMID: 30694169.
423. Simon O, Palma L, Williams T, Lopez-Ferber M, Caballero P. Analysis of a naturally-occurring deletion mutant of Spodoptera frugiperda multiple nucleopolyhedrovirus reveals sf58 as a new per os infectivity factor of lepidopteran-infecting baculoviruses. J Invertebr Pathol. 2012;109:117–26. PubMed PMID: 22041202.
424. Wang X, Shang Y, Chen C, Liu S, Chang M, Zhang N, Hu H, Zhang F, Zhang T, Wang Z, Liu X, Lin Z, Deng F, Wang H, Zou Z, Vlak JM, Wang M, Hu Z. Baculovirus per os Infectivity Factor Complex: Components and Assembly. J Virol. 2019. doi: 10.1128/JVI.02053-18. PubMed PMID: 30602603.
425. Tang Q, Li G, Yao Q, Chen L, Lv P, Lian C, Chen K. Bm91 is an envelope component of ODV but is dispensable for the propagation of Bombyx mori nucleopolyhedrovirus. J Invertebr Pathol. 2013;113:70–7. PubMed PMID: 23391406.

426. Fang M, Wang H, Wang H, Yuan L, Chen X, Vlak JM, Hu Z. Open reading frame 94 of Helicoverpa armigera single nucleocapsid nucleopolyhedrovirus encodes a novel conserved occlusion-derived virion protein, ODV-EC43. J Gen Virol. 2003;84:3021–7. PubMed PMID: 14573807.
427. Fang M, Nie Y, Theilmann DA. Deletion of the AcMNPV core gene ac109 results in budded virions that are non-infectious. Virology. 2009;389:66–74. PubMed PMID: 19411088.
428. Lin L, Wang J, Deng R, Ke J, Wu H, Wang X. ac109 is required for the nucleocapsid assembly of Autographa californica multiple nucleopolyhedrovirus. Virus Res. 2009;144:130–5. PubMed PMID: 19393701.
429. Lehiy CJ, Wu W, Berretta MF, Passarelli AL. Autographa californica M nucleopolyhedrovirus open reading frame 109 affects infectious budded virus production and nucleocapsid envelopment in the nucleus of cells. Virology. 2013;435:442–52. PubMed PMID: 23149091.
430. Alfonso V, Maroniche GA, Reca SR, Lopez MG, Del Vas M, Taboga O. AcMNPV Core Gene ac109 Is Required for Budded Virion Transport to the Nucleus and for Occlusion of Viral Progeny. PLoS One. 2012;7:e46146. PubMed PMID: 23049963.
431. Jiantao L, Zhu L, Zhang S, Deng Z, Huang Z, Yuan M, Wu W, Yang K. The Autographa californica multiple nucleopolyhedrovirus ac110 gene encodes a new per os infectivity factor. Virus Res. 2016;221:30–7. PubMed PMID: 27212681.
432. Li S, Li L, Zhao H, Liu W. Disruption of Autographa Californica Multiple Nucleopolyhedrovirus ac111 Results in Reduced per os Infectivity in a Host-Dependent Manner. Viruses. 2018.:10. PubMed PMID: 30262719.
433. Yamada H, Shibuya M, Kobayashi M, Ikeda M. Identification of a novel apoptosis suppressor gene from the baculovirus Lymantria dispar multicapsid nucleopolyhedrovirus. J Virol. 2011;85:5237–42. PubMed PMID: 21411519.
434. Liang G, Li G, Chen K, Yao Q, Chen H, Zhou Y. Bombyx mori nucleopolyhedrovirus ORF94, a novel late protein is identified to be a component of ODV structural protein. Curr Microbiol. 2010;61:190–6. PubMed PMID: 20135318.
435. Peng K, Wu M, Deng F, Song J, Dong C, Wang H, Hu Z. Identification of protein-protein interactions of the occlusion-derived virus-associated proteins of Helicoverpa armigera nucleopolyhedrovirus. J Gen Virol. 2010;91:659–70. PubMed PMID: 19906939.
436. Gong M, Jin J, Guarino LA. Mapping of ORF121, a factor that activates baculovirus early gene expression. Virology. 1998;244:495–503. PubMed PMID: 9601517.
437. Li Y, Miller LK. Expression and functional analysis of a baculovirus gene encoding a truncated protein kinase homolog. Virology. 1995;206:314–323. PubMed PMID: 7831787.
438. Prasad MD, Han SJ, Nagaraju J, Lee WJ, Brey PT. Cloning and characterization of an eukaryotic initiation factor-2alpha kinase from the silkworm, Bombyx mori. Biochim Biophys Acta. 2003;1628:56–63. PubMed PMID: 12850273.
439. Dever TE, Sripriya R, McLachlin JR, Lu J, Fabian JR, Kimball SR, Miller LK. Disruption of cellular translational control by a viral truncated eukaryotic translation initiation factor 2alpha kinase homolog. Proc Natl Acad Sci U S A. 1998.:4164–9. PubMed PMID: 9539707.
440. Aarti I, Rajesh K, Ramaiah KV. Phosphorylation of eIF2 alpha in Sf9 cells: a stress, survival and suicidal signal. Apoptosis. 2010;15:679–92. PubMed PMID: 20162453.
441. Li JJ, Cao C, Fixsen SM, Young JM, Ono C, Bando H, Elde NC, Katsuma S, Dever TE, Sicheri F. Baculovirus protein PK2 subverts eIF2alpha kinase function by mimicry of its kinase domain C-lobe. Proc Natl Acad Sci U S A. 2015;112:E4364–73. PubMed PMID: 26216977.
442. Liang C, Lan D, Zhao S, Liu L, Xue Y, Zhang Y, Wang Y, Chen X. The Ac124 protein is not essential for the propagation of Autographa californica multiple nucleopolyhedrovirus, but it is a viral pathogenicity factor. Arch Virol. 2015;160:275–84. PubMed PMID: 25380680.
443. Chen H, Li M, Huang G, Mai W, Chen K, Zhou Y. Bombyx mori nucleopolyhedrovirus ORF101 encodes a budded virus envelope associated protein. Curr Microbiol. 2014;69:158–63. PubMed PMID: 24677040.

444. Chen H, Li M, Mai W, Tang Q, Li G, Chen K, Zhou Y. Analysis of BmNPV orf101 disruption: orf101 is essential for mediating budded virus production. Cytotechnology. 2014;66:1021–9. PubMed PMID: 25300342.
445. Fang Z, Que Y, Li J, Zhang Z. The deletion of the AcMNPV ac124 gene resulted in a decrease in chitinase transcription. Virus Res. 2019;263:151–158. PubMed PMID: 30711578.
446. Harrison RL, Mowery JD, Rowley DL, Bauchan GR, Theilmann DA, Rohrmann GF, Erlandson MA. The complete genome sequence of a third distinct baculovirus isolated from the true armyworm, Mythimna unipuncta, contains two copies of the lef-7 gene. Virus Genes. 2018;54:297–310. PubMed PMID: 29204787.
447. Ferrelli ML, Pidre ML, Ghiringhelli PD, Torres S, Fabre ML, Masson T, Cedola MT, Sciocco-Cap A, Romanowski V. Genomic analysis of an Argentinean isolate of Spodoptera frugiperda granulovirus reveals that various baculoviruses code for Lef-7 proteins with three F-box domains. PLoS One. 2018;13:e0202598. PubMed PMID: 30133523.
448. Morris TD, Todd JW, Fisher B, Miller LK. Identification of *lef-7*: A baculovirus gene affecting late gene expression. Virology. 1994;200:360–369. PubMed PMID: 8178427.
449. Chen CJ, Thiem SM. Differential infectivity of two Autographa californica nucleopolyhedrovirus mutants on three permissive cell lines is the result of lef-7 deletion. Virology. 1997;227:88–95. PubMed PMID: 9007061.
450. Mitchell JK, Byers NM, Friesen PD. Baculovirus F-Box Protein LEF-7 Modifies the Host DNA Damage Response To Enhance Virus Multiplication. J Virol. 2013;87:12592–9. PubMed PMID: 24027328.
451. Ishimwe E, Hodgson JJ, Clem RJ, Passarelli AL. Reaching the melting point: Degradative enzymes and protease inhibitors involved in baculovirus infection and dissemination. Virology. 2015;479-480:637–49. PubMed PMID: 25724418.
452. Daimon T, Katsuma S, Kang W, Shimada T. Comparative studies of Bombyx mori nucleopolyhedrovirus chitinase and its host ortholog, BmChi-h. Biochem Biophys Res Commun. 2006;345:825–33. PubMed PMID: 16701557.
453. Hughes AL, Friedman R. Genome-Wide Survey for Genes Horizontally Transferred from Cellular Organisms to Baculoviruses. Mol Biol Evol. 2003;20:979–8. PubMed PMID: 12716988.
454. Fukamizo T, Sato H, Mizuhara M, Ohnuma T, Gotoh T, Hiwatashi K, Takahashi S. Chitinase from Autographa californica Multiple Nucleopolyhedrovirus: Rapid Purification from Sf-9 Medium and Mode of Action. Biosci Biotechnol Biochem. 2011;75:1763–9. PubMed PMID: 21897030.
455. Hawtin R, Arnold LH, Chappell MD, Ayres MD, Kitts PA, Gooday GW, Possee RD. Identification of a chitinase gene in the *Autographa californica* nuclear polyhedrosis virus, p 41. *In* (ed),
456. Hawtin RE, Zarkowska T, Arnold K, Thomas CJ, Gooday GW, King LA, Kuzio JA, Possee RD. Liquefaction of Autographa californica nucleopolyhedrovirus-infected insects is dependent on the integrity of virus-encoded chitinase and cathepsin genes. Virology. 1997;238:243–253. PubMed PMID: 9400597.
457. Thomas CJ, Brown HL, Hawes CR, Lee BY, Min MK, King LA, Possee RD. Localization of a baculovirus-induced chitinase in the insect cell endoplasmic reticulum. J Virol. 1998;72:10207–12. PubMed PMID: 9811762.
458. Saville GP, Patmanidi AL, Possee RD, King LA. Deletion of the Autographa californica nucleopolyhedrovirus chitinase KDEL motif and in vitro and in vivo analysis of the modified virus. J Gen Virol. 2004;85:821–31. PubMed PMID: 15039525.
459. Oliveira JV, Wolff JL, Garcia-Maruniak A, Ribeiro BM, de Castro ME, de Souza ML, Moscardi F, Maruniak JE, Zanotto PM. Genome of the most widely used viral biopesticide: Anticarsia gemmatalis multiple nucleopolyhedrovirus. J Gen Virol. 2006;87:3233–50. PubMed PMID: 17030857.
460. Slack JM, Kuzio J, Faulkner P. Characterization of *v-cath*, a cathepsin L-like proteinase expressed by the baculovirus *Autographa californica* multiple nuclear polyhedrosis virus. J Gen Virol. 1995;76:1091–1098. PubMed PMID: 7730794.
461. Hom LG, Ohkawa T, Trudeau D, Volkman LE. Autographa californica M nucleopolyhedrovirus ProV-CATH is activated during infected cell death. Virology. 2002;296:212–8. PubMed PMID: 12069520.

462. Hodgson JJ, Arif BM, Krell PJ. Autographa californica multiple nucleopolyhedrovirus and Choristoneura fumiferana multiple nucleopolyhedrovirus v-cath genes are expressed as pre-proenzymes. J Gen Virol. 2009;90:995–1000. PubMed PMID: 19264635.
463. Hodgson JJ, Arif BM, Krell PJ. Interaction of Autographa californica multiple nucleopolyhedrovirus cathepsin protease progenitor (proV-CATH) with insect baculovirus chitinase as a mechanism for proV-CATH cellular retention. J Virol. 2011;85:3918–29. PubMed PMID: 21289117.
464. Ardisson-Araujo DM, Melo FL, Clem RJ, Wolff JL, Ribeiro BM. A Betabaculovirus-Encoded gp64 Homolog Codes for a Functional Envelope Fusion Protein. J Virol. 2016;90:1668–72. PubMed PMID: 26537678.
465. Morse MA, Marriott AC, Nuttall PA. The glycoprotein of Thogoto virus (a tick-borne orthomyxo-like virus) is related to the baculovirus glycoprotein gp64. Virology. 1992;186:640–646. PubMed PMID: 1733105.
466. Hohmann AW, Faulkner P. Monoclonal antibodies to baculovirus structural proteins: determination of specificities by western blot analysis. Virology. 1983;125:432–444. PubMed PMID: 6340331.
467. Whitford M, Stewart S, Kuzio J, Faulkner P. Identification and sequence analysis of a gene encoding gp67 an abundant envelope glycoprotein of the baculovirus, *Autographa californica* nuclear polyhedrosis virus. J Virol. 1989;63:1393–1399. PubMed PMID: 2644449.
468. Volkman LE. l986. The 64K envelope protein of budded *Autographa californica* nuclear polyhedrosis virus. Curr Top Microbiol Immunol.131:103–118. PubMed PMID: 3545692.
469. Roberts TE, Faulkner P. Fatty acid acylation of the 67K envelope glycoprotein of a baculovirus: *Autographa californica* nuclear polyhedrosis virus. Virology. 1989;172:377–381. PubMed PMID: 2672565.
470. Monsma SA, Oomens AGP, Blissard GW. The gp64 envelope fusion protein is an essential baculovirus protein required for cell-to-cell transmission of infection. J Virol. 1996;70:4607–4616. PubMed PMID: 8676487.
471. Oomens AG, Blissard GW. Requirement for GP64 to drive efficient budding of *Autographa californica* multicapsid nucleopolyhedrovirus. Virology. 1999;254:297–314. PubMed PMID: 9986796.
472. Kadlec J, Loureiro S, Abrescia NG, Stuart DI, Jones IM. The postfusion structure of baculovirus gp64 supports a unified view of viral fusion machines. Nat Struct Mol Biol. 2008;10:1024–30. PubMed PMID: 18776902.
473. Feng M, Kong X, Zhang J, Xu W, Wu X. Identification of a novel host protein SINAL10 interacting with GP64 and its role in Bombyx mori nucleopolyhedrovirus infection. Virus Res. 2018;247:102–110. PubMed PMID: 29447976.
474. Wolgamot GM, Gross CH, Russell RLQ, Rohrmann GF. Immunocytochemical characterization of p24, a baculovirus capsid-associated protein. J Gen Virol. 1993;74:103–107. PubMed PMID: 8423444.
475. Gombart AF, Blissard GW, Rohrmann GF. Characterization of the genetic organization of the HindIII-M region of the multicapsid nuclear polyhedrosis virus of Orgyia pseudotsugata reveals major differences among baculoviruses. J Gen Virol. 1989;70:1815–1828. PubMed PMID: 2661722.
476. Schetter C, Oellig C, Doerfler W. An insertion of insect cell DNA in the 81-map-unit segment of *Autographa californica* nuclear polyhedrosis virus DNA. J Virol. 1990;64:1844–1850. PubMed PMID: 2157067.
477. Slavicek JM, Hayes-Plazolles N. The Lymantria dispar nucleopolyhedrovirus contains the capsid-associated p24 protein gene. Virus Genes. 2003;26:15–8. PubMed PMID: 12680688.
478. Yang M, Huang C, Qian DD, Li LL. Functional characterization of Autographa californica multiple nucleopolyhedrovirus gp16 (ac130). Virology. 2014;464-465:341–352. PubMed PMID: 25113905.
479. Gross CH, Wolgamot GM, Russell RLQ, Pearson MN, Rohrmann GF. A baculovirus encoded 16 kDa glycoprotein localizes near the nuclear membrane of infected cells. Virology. 1993;192:386–390. PubMed PMID: 8517029.
480. Sajjan DB, Hinchigeri SB. Structural Organization of Baculovirus Occlusion Bodies and Protective Role of Multilayered Polyhedron Envelope Protein. Food Environ Virol. 2016;8:86–100. PubMed PMID: 26787118.

481. Minion FC, Coons LB, Broome JR. Characterization of the polyhedral envelope of the nuclear polyhedrosis virus of *Heliothis virescens*. J Invertebr Pathol. 1979;34:303–307.
482. Whitt MA, Manning JS. A phosphorylated 34-kDa protein and a subpopulation of polyhedrin are thiol-linked to the carbohydrate layer surrounding a baculovirus occlusion body. Virology. 1988;163:33–42. PubMed PMID: 3279702.
483. van Lent JWM, Groenen JTM, Klinge-Roode EC, Rohrmann GF, Zuidema D, Vlak JM. Localization of the 34kDa polyhedron envelope protein in *Spodoptera frugiperda* cells infected with *Autographa californica* nuclear polyhedrosis virus. Archives of Virology. 1990;111:103–114. PubMed PMID: 2109589.
484. Gombart AF, Pearson MN, Rohrmann GF, Beaudreau GS. A baculovirus polyhedral envelope-associated protein: genetic location, nucleotide sequence, and immunocytochemical characterization. Virology. 1989;169:182–193. PubMed PMID: 2646825.
485. Russell RLQ, Rohrmann GF. A baculovirus polyhedron envelope protein: Immunogold localization in infected cells and mature polyhedra. Virology. 1990;174:177–184. PubMed PMID: 2403704.
486. Russell RLQ, Pearson MN, Rohrmann GF. Immunoelectron microscopic examination of *Orgyia pseudotsugata* multicapsid nuclear polyhedrosis virus-infected *Lymantria dispar* cells: time course and localization of major polyhedron-associated proteins. J Gen Virol. 1991;72:275–283. PubMed PMID: 1993872.
487. Lee SY, Poloumienko A, Belfry S, Qu X, Chen W, MacAfee N, Morin B, Lucarotti C, Krause M. A common pathway for p10 and calyx proteins in progressive stages of polyhedron envelope assembly in AcMNPV-infected Spodoptera frugiperda larvae. Arch Virol. 1996;141:1247–58. PubMed PMID: 8774685.
488. Escasa SR, Lauzon HA, Mathur AC, Krell PJ, Arif BM. Sequence analysis of the Choristoneura occidentalis granulovirus genome. J Gen Virol. 2006;87:1917–33. PubMed PMID: 16760394.
489. Lange M, Jehle JA. The genome of the Cryptophlebia leucotreta granulovirus. Virology. 2003;317:220–36. PubMed PMID: 14698662.
490. Gross CH, Russell RLQ, Rohrmann GF. The Orgyia pseudotsugata baculovirus p10 and polyhedron envelope protein genes: analysis of their relative expression levels and role in polyhedron structure. J Gen Virol. 1994;75:1115–1123. PubMed PMID: 8176372.
491. Zhou Y, Yao Q, Shen H, Xia H, Lin F, Chen K. Characterization of Bombyx mori Nucleopolyhedrovirus ORF109 that Encodes a 25-kDa Structural Protein of the Occlusion-Derived Virion. Curr Microbiol. 2010;61:451–7. PubMed PMID: 20372907.
492. Yang M, Wang S, Yue XL, Li LL. Autographa californica multiple nucleopolyhedrovirus orf132 encodes a nucleocapsid-associated protein required for budded-virus and multiply enveloped occlusion-derived virus production. J Virol. 2014;88:12586–98. PubMed PMID: 25142609.
493. Fang Z, Li C, Wu W, Yuan M, Yang K. The Autographa californica multiple nucleopolyhedrovirus Ac132 plays a role in nuclear entry. J Gen Virol. 2016;97:3030–3038. PubMed PMID: 27608627.
494. Li L. Characterization of a baculovirus alkaline nuclease. J Virol. 2000;74:6401–6407. Rohrmann. PubMed PMID: 10864651.
495. Okano K, Vanarsdall AL, Rohrmann GF. Characterization of a baculovirus lacking the Alkaline Nuclease Gene. J Virol. 2004;78:10650–10656. PubMed PMID: 15367632.
496. Okano K, Vanarsdall AL, Rohrmann GF. A Baculovirus alkaline nuclease knock out construct produces fragmented DNA and aberrant capsids. Virology. 2007;359:46–54. PubMed PMID: 17046043.
497. Ferrelli ML, Salvador R, Biedma ME, Berretta MF, Haase S, Sciocco-Cap A, Ghiringhelli PD, Romanowski V. Genome of Epinotia aporema granulovirus (EpapGV), a polyorganotropic fast killing betabaculovirus with a novel thymidylate kinase gene. BMC Genomics. 2012;13:548. PubMed PMID: 23051685.
498. Clem RJ, Robson M, Miller LK. Influence of infection route on the infectivity of baculovirus mutants lacking the apoptosis-inhibiting gene *p35* and the adjacent gene *p94*. J Virol. 1994;68:6759–6762. PubMed PMID: 8084009.
499. Du Q, Lehavi D, Faktor O, Qi Y, Chejanovsky N. Isolation of an apoptosis suppressor gene of the Spodoptera littoralis nucleopolyhedrovirus. J Virol. 1999;73:1278–85. PubMed PMID: 9882332.

500. Zoog SJ, Schiller JJ, Wetter JA, Chejanovsky N, Friesen PD. Baculovirus apoptotic suppressor P49 is a substrate inhibitor of initiator caspases resistant to P35 in vivo. Embo J. 2002;21:5130–40. PubMed PMID: 12356729.
501. Means JC, Penabaz T, Clem RJ. Identification and functional characterization of AMVp33, a novel homolog of the baculovirus caspase inhibitor p35 found in Amsacta moorei entomopoxvirus. Virology. 2007;358:436–47. PubMed PMID: 17010407.
502. Clem RJ, Fechheimer M, Miller LK. Prevention of apoptosis by a baculovirus gene during infection of insect cells. Science. 1991;254:1388–1390. PubMed PMID: 1962198.
503. Herschberger PA, Dickson JA, Friesen PD. Site-specific mutagenesis of the 35-kilodalton protein gene encoded by Autographa californica nuclear polyhedrosis virus: cell line-specific effects on virus replication. J Virol. 1992;66:5525–5533. PubMed PMID: 1501287.
504. dela Cruz WP, Friesen PD, Fisher AJ. Crystal structure of baculovirus P35 reveals a novel conformational change in the reactive site loop after caspase cleavage. J Biol Chem. 2001;276:32933–9. PubMed PMID: 11402050.
505. Fisher AJ, Cruz W, Zoog SJ, Schneider CL, Friesen PD. Crystal structure of baculovirus P35: role of a novel reactive site loop in apoptotic caspase inhibition. Embo J. 1999;18:2031–9. PubMed PMID: 10205157.
506. Goenka S, Weaver RF. The p26 gene of the Autographa californica nucleopolyhedrovirus: Timing of transcription, and cellular localization and dimerization of product. Virus Res. 2008;31:136–44. PubMed PMID: 17935816.
507. Simon O, Williams T, Caballero P, Possee RD. Effects of Acp26 on in vitro and in vivo productivity, pathogenesis and virulence of Autographa californica multiple nucleopolyhedrovirus. Virus Res. 2008;136:202–5. PubMed PMID: 18538883.
508. Wang L, Salem TZ, Campbell DJ, Turney CM, Kumar CM, Cheng XW. Characterization of a virion occlusion-defective Autographa californica multiple nucleopolyhedrovirus mutant lacking the p26, p10 and p74 genes. J Gen Virol. 2009;90:1641–8. PubMed PMID: 19264658.
509. Raza F, McGouran JF, Kessler BM, Possee RD, King LA. Phosphorylation Induces Structural Changes in the Autographa californica Nucleopolyhedrovirus P10 Protein. J Virol. 2017.:91. PubMed PMID: 28424279.
510. Alaoui-Ismaili MH, Richardson CD. Insect virus proteins (FALPE and p10) self-associate to form filaments in infected cells. J Virol. 1998;72:2213–23. PubMed PMID: 9499079.
511. Kuzio JD, Rohel Z, Curry CJ, Krebs A, Carstens EB, Faulkner P. Nucleotide sequence of the p10 polypeptide gene of *Autographa californica* nuclear polyhedrosis virus. Virology. 1984;139:414–418. PubMed PMID: 18639833.
512. Weyer U, Possee RD. A baculovirus dual expression vector derived from the Autographa californica nuclear polyhedrosis virus polyhedrin and p10 promoters: co-expression of two influenza virus genes in insect cells. J Gen Virol. 1991;72(Pt 12):2967–74. PubMed PMID: 1765769.
513. Shi X, Ran Z, Li S, Yin J, Zhong J. The Effect of MicroRNA bantam on Baculovirus AcMNPV Infection in Vitro and in Vivo. Viruses. 2016.:8. PubMed PMID: 27196923.
514. Patmanidi AL, Possee RD, King LA. Formation of P10 tubular structures during AcMNPV infection depends on the integrity of host-cell microtubules. Virology. 2003;317:308–20. PubMed PMID: 14698669.
515. Carpentier DC, Griffiths CM, King LA. The baculovirus P10 protein of Autographa californica nucleopolyhedrovirus forms two distinct cytoskeletal-like structures and associates with polyhedral occlusion bodies during infection. Virology. 2008;371:278–91. PubMed PMID: 17991504.
516. Vlak JM, Klinkenberg FA, Zaal KJM, Usmany M, Klinge-roode EC, Geervliet JBF, Roosien J, Lent JWV. Functional studies on the p10 gene of *Autographa californica* nuclear polyhedrosis virus using a recombinant expressing a p10-b-galactosidase fusion gene. J Gen Virol. 1988;69:765–776. PubMed PMID: 3128641.
517. Williams GV, Rohel DZ, Kuzio J, Faulkner P. A cytopathological investigation of *Autographa californica* nuclear polyhedrosis virus p10 gene function using insertion/deletion mutants. J Gen Virol. 1989;70:187–202. PubMed PMID: 2659726.

518. Faulkner P, Kuzio J, Williams GV, Wilson JA. Analysis of p74, a PDV envelope protein of Autographa californica nucleopolyhedrovirus required for occlusion body infectivity in vivo. J Gen Virol. 1997;78:3091–3100. PubMed PMID: 9400957.
519. Haas-Stapleton EJ, Washburn JO, Volkman LE. P74 mediates specific binding of Autographa californica M nucleopolyhedrovirus occlusion-derived virus to primary cellular targets in the midgut epithelia of Heliothis virescens larvae. J Virol. 2004;78:6786–6789. PubMed PMID: 15194753.
520. Kuzio J, Jaques R, Faulkner P. Identification of p74, a gene essential for virulence of baculovirus occlusion bodies. Virology. 1989;173:759–63. PubMed PMID: 2688302.
521. Zhou W, Yao L, Xu H, Yan F, Qi Y. The function of envelope protein p74 from Autographa californica M nucleopolyhedrovirus in primary infection to host. Virus Genes. 2005;30:139–150. PubMed PMID: 15744572.
522. Ohkawa T. 1997. Identification and characterization of genes of the baculovirus Bombyx mori nucleopolyhedrovirus (BmNPV) involved in viral pathogenesis. . PhD thesis University of California, Davis, Calif.
523. Peng K, van Lent JW, Vlak JM, Hu Z, van Oers MM. In situ cleavage of baculovirus occlusion-derived virus receptor binding protein P74 in the peroral infectivity complex. J Virol. 2011;85:10710–8. PubMed PMID: 21849453.
524. Mu J, van Lent JW, Smagghe G, Wang Y, Chen X, Vlak JM, van Oers MM. Live imaging of baculovirus infection of midgut epithelium cells: a functional assay of per os infectivity factors. J Gen Virol. 2014;95:2531–9. PubMed PMID: 25006078.
525. de Jong J, Arif BM, Theilmann DA, Krell PJ. Autographa californica multiple nucleopolyhedrovirus me53 (ac140) is a nonessential gene required for efficient budded-virus production. J Virol. 2009;83:7440–8. PubMed PMID: 19457997.
526. Xi Q, Wang J, Deng R, Wang X. Characterization of AcMNPV with a deletion of me53 gene. Virus Genes. 2007;34:223–32. PubMed PMID: 17096186.
527. Knebel-Mörsdorf D, Kremer A, Jahnel F. Baculovirus gene ME53, which contains a putative zinc finger motif, is one of the major early-transcribed genes. J Virol. 1993;67:753–8. PubMed PMID: 8093490.
528. de Jong J, Theilmann DA, Arif BM, Krell PJ. Immediate-early protein ME53 forms foci and colocalizes with GP64 and the major capsid protein VP39 at the cell membranes of Autographa californica multiple nucleopolyhedrovirus-infected cells. J Virol. 2011;85:9696–707. PubMed PMID: 21775466.
529. Liu Y, de Jong J, Nagy E, Theilmann DA, Krell PJ. Nuclear Translocation Sequence and Region in Autographa californica Multiple Nucleopolyhedrovirus ME53 That Are Important for Optimal Baculovirus Production. J Virol. 2016;90:3953–3965. PubMed PMID: 26842471.
530. Fang M, Dai X, Theilmann DA. Autographa californica multiple nucleopolyhedrovirus EXON0 (ORF141) is required for efficient egress of nucleocapsids from the nucleus. J Virol. 2007;81:9859–69. PubMed PMID: 17626083.
531. Dai X, Stewart TM, Pathakamuri JA, Li Q, Theilmann DA. Autographa californica multiple nucleopolyhedrovirus exon0 (orf141), which encodes a RING finger protein, is required for efficient production of budded virus. J Virol. 2004;78:9633–44. PubMed PMID: 15331696.
532. Fang M, Nie Y, Theilmann DA. AcMNPV EXON0 (AC141) which is required for the efficient egress of budded virus nucleocapsids interacts with beta-tubulin. Virology. 2009;385:496–504. PubMed PMID: 19155039.
533. Biswas S, Blissard GW, Theilmann DA. Trichoplusia ni Kinesin-1 Associates with Autographa californica Multiple Nucleopolyhedrovirus Nucleocapsid Proteins and Is Required for Production of Budded Virus. J Virol. 2016;90:3480–95. PubMed PMID: 26763996.
534. McCarthy CB, Dai X, Donly C, Theilmann DA. Autographa californica multiple nucleopolyhedrovirus ac142, a core gene that is essential for BV production and ODV envelopment. Virology. 2008;372:325–39. PubMed PMID: 18045640.
535. Yang ZN, Xu HJ, Park EY, Zhang CX. 2008. Characterization of Bombyx mori nucleopolyhedrovirus with a deletion of bm118. Virus Res.

536. Braunagel SC, He H, Ramamurthy P, Summers MD. Transcription, translation, and cellular localization of three Autographa californica nuclear polyhedrosis virus structural proteins: ODV-E18, ODV-E35 and ODV-EC27. Virology. 1996;222:100–114. PubMed PMID: 8806491.
537. McCarthy CB, Theilmann DA. AcMNPV ac143(odv-e18) is essential for mediating budded virus production and is the 30th baculovirus core gene. Virology. 2008;375:277–91. PubMed PMID: 18328526.
538. Belyavskyi M, Braunagel SC, Summers MD. The structural protein ODV-EC27 of Autographa californica nucleopolyhedrovirus is a multifunctional viral cyclin. Proc Natl Acad Sci U S A. 1998;95:11205–10. PubMed PMID: 9736714.
539. Dall D, Luque T, O'Reilly DR. Insect-virus relationships: sifting by informatics. Bioessays. 2001;23:184–193. PubMed PMID: 11169592.
540. Lapointe R, Popham HJ, Straschil U, Goulding D, O'Reilly DR, Olszewski JA. Characterization of two Autographa californica nucleopolyhedrovirus proteins, Ac145 and Ac150, which affect oral infectivity in a host-dependent manner. J Virol. 2004;78:6439–48. PubMed PMID: 15163737.
541. Zhang JH, Ohkawa T, Washburn JO, Volkman LE. Effects of Ac150 on virulence and pathogenesis of Autographa californica multiple nucleopolyhedrovirus in noctuid hosts. J Gen Virol. 2005;86:1619–27. PubMed PMID: 15914839.
542. Wang D, Zhang CX. HearSNPV orf83 encodes a late, nonstructural protein with an active chitin-binding domain. Virus Res. 2006;117:237–43. PubMed PMID: 16313991.
543. Dickison VL, Willis LG, Sokal NR, Theilmann DA. Deletion of AcMNPV ac146 eliminates the production of budded virus. Virology. 2012;431:29–39. PubMed PMID: 22682215.
544. Ge JQ, Zhao JF, Shao YM, Tian CH, Zhang CX. Characterization of an early gene orf122 from Bombyx mori nucleopolyhedrovirus. Mol Biol Rep. 2009;36:543–8. PubMed PMID: 18246445.
545. Guarino LA, Summers MD. Interspersed homologous DNA of *Autographa californica* nuclear polyhedrosis virus enhances delayed-early gene expression. J Virol. 1986;60:215–223. PubMed PMID: 16789258.
546. Leisy DJ, Rasmussen C, Owusu O, Rohrmann GF. A mechanism for negative gene regulation in *Autographa californica* multicapsid nuclear polyhedrosis virus. J Virol. 1997;71:5088–5094. PubMed PMID: 9188574.
547. Stewart TM, Huijskens I, Willis LG, Theilmann DA. The Autographa californica multiple nucleopolyhedrovirus ie0-ie1 gene complex is essential for wild-type virus replication, but either IE0 or IE1 can support virus growth. J Virol. 2005;79:4619–29. PubMed PMID: 15795248.
548. Chisholm GE, Henner DJ. Multiple early transcripts and splicing of the *Autographa californica* nuclear polyhedrosis virus IE-1 gene. J Virol. 1988;62:3193–3200. PubMed PMID: 3043024.
549. Sokal N, Nie Y, Willis LG, Yamagishi J, Blissard GW, Rheault MR, Theilmann DA. Defining the roles of the baculovirus regulatory proteins IE0 and IE1 in genome replication and early gene transactivation. Virology. 2014;468-470:160–171. PubMed PMID: 25173193.
550. Ono C, Sato M, Taka H, Asano S, Matsuura Y, Bando H. Tightly regulated expression of Autographa californica multicapsid nucleopolyhedrovirus immediate early genes emerges from their interactions and possible collective behaviors. PLoS One. 2015;10:e0119580. PubMed PMID: 25816136.
551. Pearson MN, Rohrmann GF. Splicing is required for transactivation by the immediate early gene 1 of the Lymantria dispar multicapsid nuclear polyhedrosis virus. Virology. 1997;235:153–165. PubMed PMID: 9300047.
552. Braunagel SC, Elton DM, Ma H, Summers MD. Identification and analysis of an *Autographa californica* nuclear polyhedrosis virus structural protein of the occlusion-derived virus envelope: ODV-E56. Virology. 1996;217:97–110. PubMed PMID: 8599240.
553. Theilmann DA, Chantler JK, Stewart S, Flipsen HTM, Vlak JM, Crook NE. Characterization of a highly conserved baculovirus structural protein that is specific for occlusion-derived virions. Virology. 1996;218:148–158. PubMed PMID: 8615018.
554. Harrison RL, Sparks WO, Bonning BC. Autographa californica multiple nucleopolyhedrovirus ODV-E56 envelope protein is required for oral infectivity and can be substituted functionally by Rachiplusia ou multiple nucleopolyhedrovirus ODV-E56. J Gen Virol. 2010;91:1173–82. PubMed PMID: 20032203.

555. Sparks WO, Harrison RL, Bonning BC. Autographa californica multiple nucleopolyhedrovirus ODV-E56 is a per os infectivity factor, but is not essential for binding and fusion of occlusion-derived virus to the host midgut. Virology. 2011. PubMed PMID: 20970820.
556. Hao B, Huang J, Sun X, Deng F, Zhang Y, Wang H, Chen H, Hu Z. Variants of open reading frame Bm126 in wild-type Bombyx mori nucleopolyhedrovirus isolates exhibit functional differences. J Gen Virol. 2009;90:153–61. PubMed PMID: 19088284.
557. Imai N, Matsumoto S, Kang W. Formation of Bombyx mori nucleopolyhedrovirus IE2 nuclear foci is regulated by the functional domains for oligomerization and ubiquitin ligase activity. J Gen Virol. 2005;86:637–44. PubMed PMID: 15722524.
558. Carson DD, Guarino LA, Summers MD. Functional mapping of an AcNPV immediate early gene which augments expression of the IE-1 trans-activated 39K gene. Virology. 1988;162:444–451. PubMed PMID: 3277328.
559. Carson DD, Summers MD, Guarino LA. Molecular analysis of a baculovirus regulatory gene. Virology. 1991;182:279–286. PubMed PMID: 2024466.
560. Yoo S, Guarino LA. The *Autographa californica* nuclear polyhedrosis virus *ie2* gene encodes a transcriptional regulator. Virology. 1994;202:746–753. PubMed PMID: 8030237.
561. Imai N, Kang W, Iwabuchi K, Sato K, Maeda S. Analysis of interaction between molecules of Bombyx mori nucleopolyhedrovirus IE-2 using a yeast two-hybrid system. Acta Virol. 2000;44:199–202. PubMed PMID: 11155366.
562. Prikhod'ko EA, Lu A, Wilson JA, Miller LK. In vivo and in vitro analysis of baculovirus ie-2 mutants. J Virol. 1999;73:2460–8. PubMed PMID: 9971831.
563. Prikhod'ko EA, Miller LK. Role of baculovirus IE2 and its RING finger in cell cycle arrest. J Virol. 1998;72:684–92. PubMed PMID: 9420274.
564. Tung H, Wei SC, Lo HR, Chao YC. Baculovirus IE2 Stimulates the Expression of Heat Shock Proteins in Insect and Mammalian Cells to Facilitate Its Proper Functioning. PLoS One. 2016;11:e0148578. PubMed PMID: 26863132.
565. Krappa R, Knebel-Mörsdorf D. Identification of the very early transcribed baculovirus gene PE-38. J Virol. 1991;65:805–812. PubMed PMID: 1987375.
566. Wu X, Stewart S, Theilmann DA. Alternative transcriptional initiation as a novel mechanism for regulating expression of a baculovirus *trans* activator. J Virol. 1993;67:5833–5842. PubMed PMID: 8371344.
567. Milks ML, Washburn JO, Willis LG, Volkman LE, Theilmann DA. Deletion of pe38 attenuates AcMNPV genome replication, budded virus production, and virulence in Heliothis virescens. Virology. 2003;310:224–34. PubMed PMID: 12781710.
568. Jiang SS, Chang IS, Huang LW, Chen PC, Wen CC, Liu SC, Chien LC, Lin CY, Hsiung CA, Juang JL. Temporal transcription program of recombinant Autographa californica multiple nucleopolyhedrosis virus. J Virol. 2006;80:8989–99. PubMed PMID: 16940511.
569. Gebhardt MM, Eberle KE, Radtke P, Jehle JA. Baculovirus resistance in codling moth is virus isolate-dependent and the consequence of a mutation in viral gene pe38. Proc Natl Acad Sci U S A. 2014;111:15711–6. PubMed PMID: 25331863.
570. Luque T, Finch R, Crook N, O'Reilly DR, Winstanley D. The complete sequence of the Cydia pomonella granulovirus genome. J Gen Virol. 2001;82:2531–47. PubMed PMID: 11562546.
571. Willis LG, Siepp R, Stewart TM, Erlandson MA, Theilmann DA. Sequence analysis of the complete genome of Trichoplusia ni single nucleopolyhedrovirus and the identification of a baculoviral photolyase gene. Virology. 2005;338:209–26. PubMed PMID: 15951000.
572. Thumbi DK, Eveleigh RJ, Lucarotti CJ, Lapointe R, Graham RI, Pavlik L, Lauzon HA, Arif BM. Complete sequence, analysis and organization of the Orgyia leucostigma nucleopolyhedrovirus genome. Viruses. 2011;3:2301–27. PubMed PMID: 22163346.
573. Guarino LA, Gonzalez MA, Summers MD. Complete sequence and enhancer function of the homologous DNA regions of *Autographa californica* nuclear polyhedrosis virus. J Virol. 1986;60:224–229. PubMed PMID: 16789259.

574. Leisy DJ, Rohrmann GF. Characterization of the replication of plasmids containing *hr* sequences in baculovirus-infected *Spodoptera frugiperda* cells. Virology. 1993;196:722–730. PubMed PMID: 8372444.
575. Pearson MN, Bjornson RM, Ahrens C, Rohrmann GF. Identification and characterization of a putative origin of DNA replication in the genome of a baculovirus pathogenic for *Orgyia pseudotsugata*. Virology. 1993;197:715–725. PubMed PMID: 8249294.
576. Pearson MN, Bjornson RM, Pearson GD, Rohrmann GF. The *Autographa californica* baculovirus genome: Evidence for multiple replication origins. Science. 1992;257:1382–1384. PubMed PMID: 1529337.
577. Pearson MN, Rohrmann GF. *Lymantria dispar* nuclear polyhedrosis virus homologous regions: characterization of their ability to function as replication origins. J Virol. 1995;69:213–221. PubMed PMID: 7983712.
578. Choi J, Guarino LA. The baculovirus transactivator IE1 binds to viral enhancer elements in the absence of insect cell factors. J Virol. 1995;69:4548–4551. PubMed PMID: 7769721.
579. Leisy DJ, Rasmussen C, Kim H-T, Rohrmann GF. The *Autographa californica* nuclear polyhedrosis virus homologous region 1a: Identical sequences are essential for DNA replication activity and transcriptional enhancer function. Virology. 1995;208:742–752. PubMed PMID: 7747446.
580. Rodems SM, Friesen PD. The hr5 transcriptional enhancer stimulates early expression from the *Autographa californica* nuclear polyhedrosis virus genome but is not required for virus replication. J Virol. 1993;67:5776–5785. PubMed PMID: 8371342.
581. Nagamine T, Kawasaki Y, Iizuka T, Matsumoto S. Focal Distribution of Baculovirus IE1 Triggered by Its Binding to the hr DNA Elements. JVirol. 2005;79:39–46. PubMed PMID: 15596799.
582. Landais I, Vincent R, Bouton M, Devauchelle G, Duonor-Cerutti M, Ogliastro M. Functional analysis of evolutionary conserved clustering of bZIP binding sites in the baculovirus homologous regions (hrs) suggests a cooperativity between host and viral transcription factors. Virology. 2006;344:421–31. PubMed PMID: 16198391.
583. Carstens EB, Wu Y. No single homologous repeat region is essential for DNA replication of the baculovirus Autographa californica multiple nucleopolyhedrovirus. J Gen Virol. 2007;88:114–22. PubMed PMID: 17170443.
584. Bossert M, Carstens EB. Sequential deletion of AcMNPV homologous regions leads to reductions in budded virus production and late protein expression. Virus Res. 2018;256:125–133. PubMed PMID: 30121325.

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