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Encyclopedia of *Autographa californica* Nucleopolyhedrovirus Genes*

David P. A. Cohen[1], Martin Marek[1,2], Bryn G. Davies[3], Just M. Vlak[1] and Monique M. van Oers[1**]

(1.Wageningen University, Laboratory of Virolo, Box 629, 6700AP wageningen, The Netherlands; 2. Généthon, Department of Bioprocess Development, Evry, France; 3. University of York, YCR Cancer Research, Dept. of Biology, Heslington, York, United Kingdom)

Abstract: The *Autographa californica* multiple capsid nucleopolyhedrovirus (AcMNPV) was the first baculovirus for which the complete nucleotide sequence became known. Since then 15 years lapsed and much research has been performed to elucidate putative functions of the annotated open reading frames of this virus and this endeavour is still ongoing. AcMNPV is the most well-known and well-studied baculovirus species, not in the least for its application as a vector for the high-level expression of foreign genes in insect cells. This article is the first monograph of a single baculovirus and gives a current overview of what is known about the 151 AcMNPV ORFs, including (putative) function and temporal and spatial presence of transcripts and protein. To date 60 ORFs have a proven function, another 19 ORFs have homologs for which functions are known in other baculoviruses and 72 ORFs are still enigmatic. This paper should assist the reader in quickly finding the essentials of AcMNPV.

Key words: Baculovirus; *Autographa californica* multiple capsid nucleopolyhedrovirus(AcMNPV); Functional genomics; Review

Baculoviruses are viruses of invertebrates that are widely used as biopesticides for the protection of agricultural crops and forests against insect pests (59). This practice has already occurred for over 70 years and these viruses have a perfect safety record to date. More recently these baculoviruses have been used as vectors for the high-level expression of foreign genes (254) and for the transfer of foreign genes into vertebrate systems (40). A most notable characteristic of baculoviruses is the rod-shaped morphology of the virions, hence, the family name *Baculoviridae* (23). These rod-shaped virions are found occluded in large polyhedral shaped, proteinaceous capsules (polyhedra, 0.1-15 μm in diameter) or in smaller granular capsules (granula) 0.3 till 0.5 μm in length and 0.1 to 0.3 μm in diameter (43). These capsules are often collectively called occlusion bodies (OBs). Baculoviruses share this occlusion phenotype with the genetically unrelated cypoviruses (CPV) and entomopoxviruses (EPV).

The family *Baculoviridae* comprises four genera, *Alphabaculovirus*, *Betabaculovirus*, *Gammabaculovirus*

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** Corresponding author.
Phone: +31-317-485082, Fax: +31-317-484820
E-mail: monique.vanoers@wur.nl

and *Deltabaculovirus* (118). The *Alphabaculovirus* genus contains the nucleopolyhedroviruses (NPVs) of lepidopteran insects and the *Betabaculovirus* genus encompasses the granuloviruses (GVs) of lepidopteran hosts. The NPVs from hymenopterans form the genus *Gammabaculovirus* and the *Deltabaculovirus* genus encompasses the NPVs from dipteran hosts. The Alphabaculoviruses are further divided in group I and group II NPVs on the basis of phylogenetic analysis (99) and the type of envelope fusion protein (GP64 or F, respectively). The virions of NPVs as found in the occlusion bodies may contain single (S) or multiple (M) nucleopcapsids, but this is not a taxonomical denominator. Collectively about 700 baculoviruses have been described genetically, but only a minority have been characterised to the extent that they can be called a species. Baculoviruses occur in a very wide range of insect hosts, but each virus by itself in general has a narrow host range. The most notable example of a baculovirus with multiple hosts is *Autographa californica* MNPV, the type species of the Alphabaculoviruses, belonging to the group I NPVs.

Baculoviruses have a complex 'life' cycle. They infect their larval host orally and the virions, upon release from the proteinaceous capsules (hence their name occlusion derived virions = ODVs), replicate in the epithelial cells of the larval midgut. Infectious virions (budded virions = BVs) are produced in these cells and released into the hemolymph and tracheal system to invade and infect other organs and tissues of the insect larva. Replication of the Gammabaculoviruses is restricted to the midgut (144). At the end of the infection virions are occluded into OBs, which are released into the environment from the insect body upon death. In the OB form baculoviruses can persist in the environment for many years. For some baculoviruses, notably AcMNPV, the replication cycle can also be completed in cell culture using BVs as inoculum and this has greatly enhanced our current understanding of the cell biology and genetics of baculovirus infections (for more details (279)).

Baculoviruses contain a double-stranded, circular and superhelical DNA molecule, which replicates in the cell nucleus. After synthesis the DNA is packaged in a number of proteins to form nucleocapsids. One or more nucleocapsids are wrapped in an envelope, which is *de novo* formed in the nucleus of infected cells. Single or multiple virion packages are occluded in GVs and NPVs, respectively. The size of baculovirus genomes depends on the species and ranges from 80 to 180 kilobasepairs (kbp), hence encompassing a variable numbers of ORFs (266). Gene homology, gene content and gene location can be used to construct reliable phylogenetic trees to show the relatedness among baculoviruses (99).

The transcription of baculoviruses occurs in a cascaded fashion and four classes of transcripts are discriminated. The immediate early (IE) transcripts are made by host RNA polymerases, a process independent of *de novo* protein synthesis. Delayed early (DE) transcripts require translation of IE viral transcripts for their synthesis. Late (L) transcripts are expressed after the onset of DNA replication and very late (VL) transcripts are those that are still expressed very late after infection, sometimes at very high levels (polyhedrin, p10). Baculovirus late and very late transcription occurs via a virus-encoded RNA polymerase, which is α-amanitin insensitive. Baculovirus genes are hence categorized as immediate-early, delayed-early, late and very late genes. Baculovirus transcripts may

have 5'and 3' co-terminal ends and hence may overlap in sequence and time of expression. A canonical baculovirus transcription initiation motif (TAAG) is present in the promoter region of L and VL genes, whereas a more common motif (CAGT) is often associated with early baculovirus gene expression (recent review (213)).

The fact that for replication in cell culture only BVs are required and the ODV phenotype is dispensable allowed the development of the baculovirus expression system for production of recombinant protein in insect cells (254). Baculovirus VL genes are highly expressed but not required for virus pro- pagation in cell culture, enabling their replacement with foreign genes. The promoters of the polyhedrin and p10 genes are extensively used as cassettes to drive the expression of single or multiple foreign genes in a baculovirus background. The development of an AcMNPV bacmid greatly facilitated the functional analysis of baculovirus genes, since it not only simplified the engineering of baculovirus expression vectors (172), but also made the construction of (knock-out) mutants much easier. The deletion of the *cathepsin* and the *chitinase* genes for instance, has improved the integrity of secreted recombinant proteins (120). The insertion of genes for the modification of glycoproteins in the Golgi system, has allowed the production of complex, mammalian-like glycoproteins in insect cells (115). AcMNPV can also be used as a delivery vector for mammalian cells and as gene therapy vector, either as a gene carrier or as a production system for other gene therapy vectors such as adeno-associated viruses (108, 174, 244). The baculovirus insect cell expression system is still being tailored and optimised to meet the demands of both the scientist as well as the commerce.

AcMNPV was isolated in 1969 by the late Dr. Patrick V. Vail and colleagues from a single virosed insect larva near Riverside (264). The insect was assigned as alfalfa looper or *A. californica*, but could also have been *Trichoplusia ni* as liquefied larvae are difficult to determine taxonomically. Later the late Dr. Lois K. Miller isolated an AcMNPV variant from *A. californica* on sunflower. The virus has an extremely wide host range, infecting insect species across several lepidopteran subfamilies (225). AcMNPV also replicates efficiently in cultured insect cells, such as Sf9, Sf21, Tn368, Tni High Five, and Se-UCR. Various clonal isolates of AcMNPV have been described (E2, L1, C6, HR). The genome of the AcMNPV C6 isolate was the first baculovirus genome that was sequenced completely in 1994 (GenBank: NC_001623) (9). The circular double stranded DNA genome is 133,894 bp in size with a GC-content of 40.7 %. Partial resequencing of the AcMNPV genome ((92) led to a few modifications to the original sequence, which are not yet incorporated in the GenBank entry, resulting now in a total of 151 assigned open reading frames (ORFs). The encoded proteins range in size between 50 aa (normally set as the under limit for a baculovirus ORF) to 1221 aa (DNA helicase). All genes, except one (IE-0/IE-1), produce non-spliced transcripts. Over the years through collective effort of many laboratories around the world, functions have been assigned to many of the encoded gene products. However, the function of many ORFs - even some with orthologs in (many) other baculovirus species - remains enigmatic. At this moment in time nearly 50 baculovirus genomes have been completely sequenced and the genetic relatedness among the baculoviruses became

apparent when further baculoviruses were being sequenced (266).

Eight regions with homologous repeats (*hr*s), each with a set of 28-mer imperfect palindromes, are present dispersed throughout the AcMNPV genome (9, 141). These *hr*s can act as origins of DNA replication in cell culture (135) and as enhancers of gene expression (33, 234, 271). Within the gene *ac134 (p94)*, a sequence of direct and inverted repeats, palindromes and AT-rich regions different from the *hrs* is found and called the *non-hr*, which can also serve as an origin of DNA replication (134, 138). The *non-hr* region is also associated with the formation of "defective interfering particles" (DIs), which are generated as an artifact in cell culture and which interfere with the replication and production of infectious BVs (145, 222). These DI particles are baculoviruses with reduced size and genome content and a higher frequency of *non-hr* sequences. DIs are unable to propagate autonomously.

The purpose of this review is to provide an overview of the current knowledge on the function of AcMNPV ORFs and to serve as a starting point for researchers and students to gather further detailed information on particular ORFs. The overview will also assist researchers working with other baculoviruses, which carry homologous genes. In this review, all ORFs are listed in their order of appearance in the AcMNPV genome beginning wit the *ptp* gene (5'-3') and named according to the GenBank file (NC_ 001623). We choose for an encyclopaedic layout in which a short description of each ORF is presented, together with a small number of selected literature references referring to key publications, and/or review papers through which further relevant literature may be found. In the current paper the description of each ORF starts with the ORF number, e.g. *ac1,* where *ac* stands for AcMNPV and "1" for the number of the ORF as indicated in the database. This ORF number is followed by the name of the gene and by the name of the gene product. A genomic map of AcMNPV is given in Fig. 1, which serves to visualize the direction of transcription for individual ORFs and their genetic environment. The indicated sizes are the predicted molecular masses and the length in amino acids (aa) for the primary translation products. Post translational modifications can of course affect the actual size of the protein. A summary of the data is presented in Table 1. In this table the ORFs are also functionally categorized into four groups: genes for virion structure, DNA replication, transcription and auxiliary functions. Auxiliary genes are those that are not necessary for virus replication but give replication advantages for the virus at the level of the cell, the organism or the ecosystem (197).

In Table 2 and Table 3, AcMNPV gene orthologs are indicated for the 48 baculoviruses that have been completely sequenced (December 2008). The numbers correspond to their respective ORF number in the particular virus. Homologous genes have been found using Basic Local Alignment Tool (6) for proteins available through the website http://blast.ncbi.nlm.nih.gov/ with the following search set: non-redundant protein sequence database; organism: dsDNA viruses, no RNA stage; blast-p algorithm. Baculoviruses have a common set of 30 genes and these genes are designated as the baculovirus core genes (178, 179). Two AcMNPV genes have homologs in all baculoviruses except for the Deltabaculoviruses (*ac25* and *ac145*), one AcMNPV gene has a homolog in all, except Gammabaculoviruses (*ac23*), twenty in all Alpha- and

Betabaculoviruses and sixteen additional genes have homologs in all sequenced Alphabaculoviruses (Table 2 and Table 3).

ORF DESCRIPTIONS

Ac1: *ptp*/*bvp*, protein tyrosine phosphatase or baculovirus phosphatase

This ORF encodes a protein (19.3 kDa; 168 aa) with a chimerical character as it has the characteristics of a protein tyrosine phosphatase (PTP), but it also has RNA-tri/diphosphatase activity (255). The preferred substrate for PTP is RNA and it crystallizes in a metazoan RNA capping enzyme fashion (27). Later it was renamed to baculovirus phosphatase (BVP), which is a protein only produced by group I NPVs. The AcMNPV *ptp/bvp* gene appears to be associated

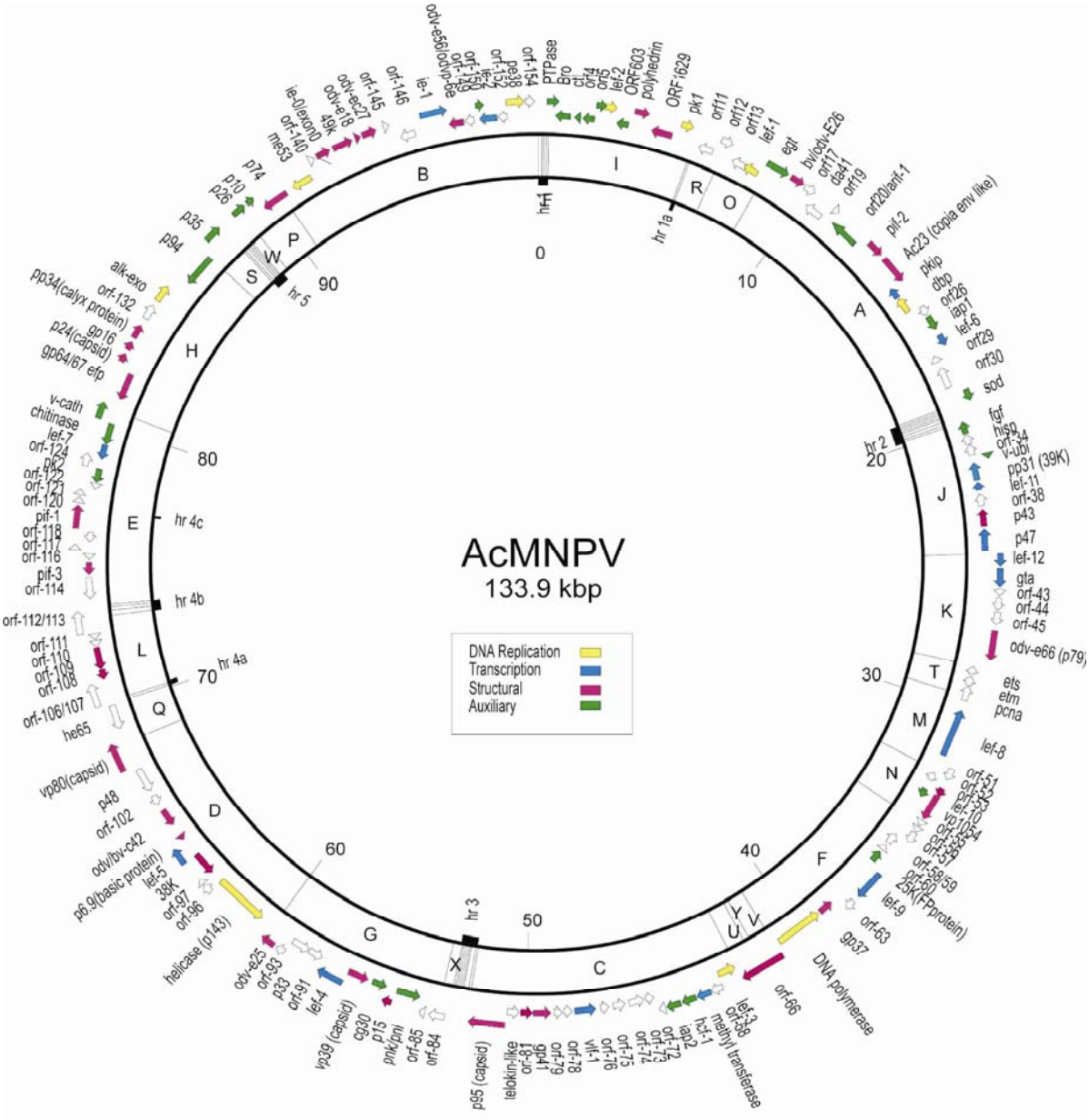

Fig. 1. Genetic and physical map of the AcMNPV genome. The different colors indicate the categorization of genes in four *functional classes*: genes for DNA replication and transcription, structural and auxiliary genes. The physical map is based on the *Eco*RI restriction sites. The figure was adjusted from (258).

Table 1. ORFs of *Autographa californica* MNPV for which published information is available

ORF	Gene	Function / Description	Needed for:		Category	Gene knock-out	Ref.
			Progeny virus	DNA replication			
1	*ptp/bvp*	Involved in wandering behavior of the host; RNA phosphatase	No	No	A	No enhanced locomotion of the host	(107, 122, 154)
2	*bro*	Might be involved in host specificity; shuttling transporter	No	No	A	N-terminal deletion of protein results in reduced ODV	(123)
3	*ctl*	Homolog to conotoxin in snails; block specific Ca2+-channels	No	No	A	No effect	(57)
4	*ac4*	Involved in nuclear localization of G-actin; enhancer activity			A		(202)
5	*ac5*	Together with *lef-2* enhance promoters			A		(1, 162)
6	*lef-2*	Essential for (plasmid) DNA replication	Yes	Yes	R	Deficient in very late gene expression	(169, 184)
7	*orf 603*	Pathogenicity factor	No	No	A	Increased time to death	(72, 224)
8	*polh*	Polyhedrin, OB protein	No	No	A	No effect on DNA or BV production	(236)
9	*orf 1629*	P78/83, nuclear actin polymerization	Yes	No	S		(220)
10	*pk-1*	Transcription factor of *polh* promoter	No	No	T	Inhibition of *polh* gene expression	(190)
14	*lef-1*	DNA primase	Yes	Yes	D	No DNA replication	(133)
15	*egt*	Prevents molting	No	No	A	Decreased time of death	(200)
16	*ac16*	Associates with intracellular membranes and viral DNA or DNA-binding proteins	Yes	Yes	S	No null mutant allowed in BmNPV	(24)
17	*ac17*	Activated by IE-1					(7, 161)
18	*ac18*		No	No		Non-essential, deletions occur spontaneous	(275)
20/21	*arif-1*	Early gene product; rearranges actin skeleton	No	No	A	No notable difference in viral progeny	(53, 237)
22	*pif-2*	Required for *per os* infection	No	No	A	No *in vivo* infection *per os*	(20, 203)
23	*ac23*	Pathogenicity factor	No	No	A	Wild type shows faster mortality in infected insects	(173)
24	*pkip*	Stimulates activation of viral protein kinase-1	Yes	No	A	No formation of plaques or occlusion bodies; reduction in VP39 protein	(182)
25	*dbp*	Protection of ssDNA against hydrolysis	Yes	No	D	Unable to produce BV	(231, 267)
27	*iap1*	Inhibitor of apoptosis	No	No	A	Replication advantage over wild type	(181)
28	*lef-6*	Involved in late and very late gene expression	No	No	A	Delayed and reduced production of BV	(156)
31	*sod*	Removes active oxygen radicals	No	No	A	No replication disadvantage	(263)
32	*fgf*	Enhances cell migration	No	No	A	Delay in mortality in insect; associated with migration of virus through insect	(49)
35	*v-ubi*	Signalling protein degradation	No	No	A		(197)
36	*pp31*	Late gene expression factor	No	No	T	Decreased BV production; down-regulation of subset of early and late genes	(287)
37	*lef-11*	Required for expression of late genes	Yes	No	T	No viral propagation	(157)
38	*ac 38*				T	Reduced BV production	(70)
39	*p43*	ODV protein			S		(20)
40	*p47*	RNA polymerase subunit	Yes		T		(88)
41	*lef-12*	Stimulates late gene expression	No	No	T	Reduced viral yield	(85)

Table 1 (continue)

42	*gta*	ATP-dependent DNA unwinding			D		(142)
45	*ac45*	Putative enhancer of *lef-12* (ac41)			T		(149)
46	*odv-e66*	Contains sorting motif at C-terminus	No		S	Not essential for BV production	(238)
47	*ets*	See *pcna*					
48	*etm*	See *pcna*					
49	*pcna*	Proliferating cell nuclear anitgen	No	No		No difference with wild type	(198)
50	*lef-8*	RNA polymerase subunit			T		(88)
53	*ac53*	Likely involved in nucleocapsid formation	Yes	No	S	Affects BV production, incomplete capsids	(160)
53a	*lef-10*	Unclear	No	No	A		(97)
54	*vp1054*	Nucleocapsid	Yes	No	S	No nucleocapsids; infection limited to a single cell	(209)
61	*fp/25k*		No	No	A	Reduced ODV yield; altered intranuclear envelopes; increased BV production	(94)
62	*lef-9*	Subunit of RNA polymerase complex	Yes	No	T		(168)
64	*gp37*	Component of ODV in OpMNPV	No	No	S	No effect on virus replication or kinetics	(34)
65	*dnapol*	DNA duplication	Yes	Yes	D	No DNA replication	(269)
66	*ac66*	Present in nucleocapsids	Yes	No	S	No BV production	(126)
67	*lef-3*	ss-DNA binding protein			D		(112)
69	*ac69*	Putative methyl transferase	No	No	T	No effect on virus replication	(283)
70	*hcf-1*	Involved in late and very late gene expression	Yes	Yes	T	No viral and DNA replication in *T.ni* larvae or cell culture,	(170)
71	*iap2*	Inhibitor of apoptosis (non-functional)	No	No	A	No effect on virus replication	(79)
77	*vlf1*	Involved in expression of p10 and polh genes	Yes	No	T	No BV, nucleocapsids, No ODVs production	(153, 268)
80	*gp41*	Tegument protein	Yes	No	S	Single cell infection; no BV production	(210)
81	*ac81*	Putative envelope protein in BmNPV	Yes	Yes	S	No DNA replication; reduced capsid formation	(71)
82	*tlp*						(232)
83	*p95*				S		(240)
86	*pnk/pnl*		No	No	A	No effect on virus replication or protein production	(55)
87	*p15*				S		(171)
88	*cg30*		No	No	A	Wild type has slight growth advantage in cell culture	(215)
89	*vp39*	Involved in rearrangement and polymerisation of actin		No	S		(28, 29)
90	*lef-4*	RNA polymerase subunit	Yes	No	T		(84)
92	*p33*	Putative regulator of apoptosis			S		(36)
94	*odv-e25*	ODV envelope protein			S		(104)
95	*helicase*	Unwinding DNA	Yes	Yes	D		(133)
98	*38k*	Required nucleocapsid assembly	Yes	No	S	No BV production or nucleocapsid formation	(282)
99	*lef-5*	Transcription initiation factor			T		(95)
100	*p6.9*	Involved in condensation and packaging of dsDNA genome			S		(68)
101	*p40*	Subunit of protein complex	Yes	No	S	No virus replication; no nucleocapsid formation	(270)
102	*p12*	Involved in nuclear localization of G-actin	Yes			No virus replication	(166)

Table 1 (continue)

103	*p48*		Yes			No virus replication	(166)
104	*vp80*	ODV and BV protein	Yes		S	No BV production; no nucleocapsid maturation	(256)
105	*he65*	Mediates nuclear localization of G-actin					(202)
108	*ac108*				S	Homologs associated with ODV	(32, 247)
109	*ac109*	Associated with ODV			S		(20)
115	*pif-3*	Putative function in infection process			S		(249)
119	*pif-1*	Mediates binding of ODV to midgut			S		(203)
123	*pk2*	Putative inhibitor of host stress	No	No	A	No effect	(152)
125	*lef-7*	Late gene expression factor	No	No	T	Decreased BV and ODV production; decreased DNA replication	(30)
126	*chitinase*	Dissolution of chitin skeleton	No	No	A	No effect on virus replication	(120)
127	*v-cath*	Cathepsin protease, liquefaction of host	No	No	A	No effect on virus replication	(120)
128	*gp64*	Required for fusion with host cell	No	No	S	Infection is unable to move from cell to cell	(193)
129	*p24*		No		S	No effect on virus replication	(242, 280)
130	*gp16*	Associated with envelope of BV			S		(81)
131	*pe/pp34*	Involved in morphogenesis of polyhedral envelope	No	No	S	Absence of electron-dense spacers around ODV	(294)
133	*an*	Involved in DNA recombination and replication	Yes	No	D	No BV production; reduced formation of normal nucleocapsids	(206, 207)
134	*94k*	Contains *non-hr*	No	No	A	No effect	(32)
135	*p35*	inhibitor of apoptosis/late expression factor	No	No	A	Not essential	(77)
136	*p26*		No	No	A	No effect on virulence	(248)
137	*p10*	Triggers release of polyhedral	No	No	A	Non essential	(25)
138	*p74*	*Per os* infectivity factor, binds to midgut epithelium	No	No	S	Essential for primary infection in midgut	(67)
139	*me53*	DNA synthesis regulator	Yes	Yes	D	No DNA replication	(285)
141	*exon0*	Egress of nucleocapsids from the nucleus to cytoplasm	No	No	A	Required for BV production	(159)
142	*49k*	Required for BV production	Yes	No	S	Essential for BV production and nucleocapsid formation	(178, 270)
143	*odv- e18*	ODV envelope protein	Yes	No	S	Depleted BV production; no effect on DNA replication and ODV formation	(179)
144	*odv- e27*	Involved in DNA processing, packaging and nucleocapsid formation	Yes	No	S	Affects nucleocapsid assembly; diminished BV production	(270)
147	*ie-1*	Transcriptional transactivator	Yes		T	Essential for virus replication, late gene expression and production of BV and ODV	(243)
148	*odv-e56*	Present in ODV envelope			S		(20)
150	*ac150*	Putative *per os* infection factor	No	No	A	Less efficient in primary infection	(291)
151	*ie-2*	Transactivator of early promoters	No	No	T	Delay in DNA synthesis, late gene expression, BV/ODV production	(227)
152	*ac152*	Localisation of G-actin; transactivator of *ac102* and *he65*			T		(202)
153	*pe38*	Transcriptional transactivation; DNA replication	No	No	T	Important but not essential for BV production and DNA synthesis	(189)

Categories: A: Auxiliary gene; D: DNA replication; S: Structural protein; T: Transcription

Table 2. Homologues of AcMNPV in Alphabaculoviruses

Alphabaculovirus-Ⅰ

AcMNPV	AdhoNPV	AdorNPV	AgipMNPV	AgseNPV	AnpeNPV	AgMNPV	BmNPV	CfMNPV	CfDefNPV	ChchNPV	ClbiNPV	EcobNPV	EppoNPV	HearMNPV	HearNPV	HearNPV G4
1			31	27	9	9	130	9	8				7			
2	84	81	83	123	108	7	131		108	114	105	89	104	82	105	105
3	86	83			8	30		131	131	74	53	47		99	99	
4				32	6	2	133	5	5				7	64		
5					5	4	134	4	4				5		117a	
6[a]	**100**	**95**	**17**	**13**	**4**	**3**	**135**	**3**	**3**	**136**	**109**	**103**	**4**	**13**	**117**	**117**
7											106					
8[d]	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**
9[d]	**4**	**4**	**2**	**2**	**147**	**152**	**2**	**146**	**149**	**2**	**2**	**2**	**136**	**2**	**2**	**2**
10[f]	**5**	**5**	**3**	**3**	**146**	**151**	**3**	**145**	**148**	**3**	**3**	**3**	**135**	**3**	**3**	**3**
11					10	10	4	10	9				8			
12																
13[f]	**125**	**121**	**21**	**16**	**12**	**20**	**5**	**12**	**18**	**137**	**122**	**125**	**10**	**30**	**123**	**123**
14[a]	**124**	**120**	**22**	**17**	**13**	**19**	**6**	**13**	**17**	**138**	**123**	**124**	**11**	**29**	**124**	**124**
15[d]	**122**	**118**	**32**	**28**	**14**	**18**	**7**	**14**	**16**	**141**	**125**	**122**	**12**	**33**	**126**	**126**
16					15	17		15	15				13			
17	120	116	34	30	16	16	9	16	14	143	127	120	14	35		
18	92	88	50	45	17	15	10	17	13	125	116	92	15	49		
19[d]	**91**	**87**	**49**	**44**	**18**	**14**	**11**	**18**	**12**	**126**	**115**	**91**	**16**	**48**	**115**	**115**
20/21			41	35	19	13	12	19	11	147			17	41	131	131
22[a]	**95**	**90**	**42**	**36**	**20**	**12**	**13**	**20**	**10**	**148**	**107**	**106**	**18**	**42**	**132**	**132**
23[c]	**118**	**114**	**12**	**8**	**21**	**22**	**14**	**21**	**21**	**150**	**129**	**118**	**19**	**8**	**133**	**133**
24[d]	**98**	**93**	**38**	**33**	**39**	**43**	**15**	**39**	**39**	**146**	**108**	**104**	**36**	**39**	**130**	**130**
25[b]	**28**	**27**	**146**	**139**	**38**	**42**	**16**	**38**	**38**	**22**	**27**	**27**	**35**	**148**	**25**	**25**
26			145	138	37	41	17	37	37	23	15		34	147	26	26
27[e]	**88**	**85**	**128**	**119**	**36**	**40**	**18**	**36**	**36**	**39**		**54**	**27**	**131**	**103**	**103**
28[f]	**29**	**28**	**147**	**140**	**35**	**39**	**19**	**35**	**35**	**21**	**17**	**16**	**32**	**149**	**24**	**24**
29	49	46	148	141	34	38	20	34	34	20	18	17	31	150		23
30					33	37	21	33	33				30			
31	106	101	57	54	29	32	23	28	29	115	102	109		57	106	106
32[e]	**112**	**117**	**45**	**39**	**27**	**29**	**24**	**27**	**28**	**130**	**118**	**95**	**25**	**45**	**113**	**113**
33			63	60		28			27	106	55	114		63		
34[d]	**18**	**17**	**143**	**136**	**26**	**27**	**25**	**26**	**26**	**25**	**21**	**20**	**24**	**146**	**27**	**27**
35[e]	**16**	**16**	**142**	**135**	**25**	**26**	**26**	**25**	**25**	**26**	**22**	**21**	**23**	**145**	**28**	**28**
36[f]	**13**	**13**	**139**	**132**	**24**	**25**	**27**	**24**	**24**	**28**	**24**	**24**	**22**	**143**	**31**	**31**
37[e]	**12**	**12**	**138**	**131**	**23**	**24**	**28**	**23**	**23**	**29**		**25**	**21**	**142**	**32**	**32**
38[f]	**11**	**11**	**137**	**130**	**22**	**23**	**29**	**22**	**22**	**30**	**25**	**26**	**20**	**141**	**33**	**33**

Table 2 (continue)

AcMNPV	AdhoNPV	AdorNPV	AgipMNPV	AgseNPV	AnpeNPV	AgMNPV	BmNPV	CfMNPV	CfDefNPV	ChchNPV	ClbiNPV	EcobNPV	EppoNPV	HearMNPV	HearNPV	HearNPV G4
39	89	86					30				96					
40[a]	**10**	**10**	**134**	**126**	**40**	**44**	**31**	**40**	**40**	**33**	**36**	**29**	**37**	**137**	**35**	**35**
41					41	45	32	41	41		34		38		36	36
42					42	46	33	42	42				39			
43			132	124	43	47	34	43	43	35	33	30	40	135	37	37
44					44	48	35	44	44				41			
45							36									
46[e]	**50**	**47**	**71**	**125**	**45**	**49**	**37**	**45**	**45**	**101**		**31**	**42**	**70**	**96**	**96**
47					46		38									
48					47	50		46	46				44	4		
49					48			47		66						
50[a]	**49**	**46**	**130**	**121**	**49**	**51**	**39**	**48**	**47**	**37**	**32**	**32**	**45**	**133**	**38**	**38**
51			129	120	50	52	40	49	48	38	31	33	46	132	39	39
52	46	43		118			41			40	29	34	131		42	42
53[f]	**47**	**44**	**126**	**117**	**51**	**53**	**42**	**50**	**49**	**41**	**28**	**35**	**47**	**129**	**43**	**43**
53a	43	40	123	114	52	54	42a	51	50	44		38	48	126	46	46
54[a]	**42**	**39**	**122**	**113**	**53**	**55**	**43**	**51**	**51**	**45**	**39**	**39**	**49**	**125**	**44**	**47**
55[d]	**41**	**38**	**121**	**112**	**54**	**56**	**44**	**53**	**52**	**46**	**41**	**40**	**50**	**124**	**45**	**48**
56	40	37	120	111		57	45	54	53	47		41	51	123	46	49
57			119	110	55	58	46	55	54	48	43	42	52	122	47	50
58/59[d]	**39**	**36**	**118**	**109**	**56**	**59**	**47**	**56**	**55**	**49**	**44**	**43**	**53**	**121**	**48**	**51**
60[d]	**38**	**35**	**117**	**108**	**57**	**60**	**48**	**57**	**56**	**50**	**45**	**44**	**54**	**120**	**49**	**52**
61[f]	**36**	**34**	**114**	**106**	**58**	**61**	**49**	**58**	**57**	**51**	**46**	**45**	**55**	**117**	**53**	**53**
62[a]	**35**	**33**	**113**	**105**	**59**	**62**	**50**	**59**	**58**	**52**	**47**	**46**	**56**	**116**	**52**	**55**
63							51			31		28			121	121
64			30	26	60		52	60	60	67	56	49	57	31	58	58
65[a]	**58**	**55**	**106**	**100**	**61**	**65**	**53**	**61**	**61**	**58**	**67**	**58**	**58**	**107**	**67**	**67**
66[d]	**57**	**54**	**105**	**99**	**62**	**66**	**54**	**62**	**62**	**59**	**66**	**57**	**59**	**106**	**66**	**66**
67[d]	**56**	**53**	**104**	**98**	**63**	**67**	**55**	**63**	**63**	**60**	**65**	**56**	**60**	**105**	**65**	**65**
68[a]	**55**	**52**	**103**	**97**	**64**	**68**	**56**	**64**	**64**	**61**	§	**55**	**61**	**104**	**64**	**64**
69	54	51	102	96	65	69	57	65	65		64		62	103	63	63
70											57					
71[f]	**53**	**50**	**101**	**95**	**66**	**70**	**58**	**66**	**66**	**62**	**63**	**54**	**63**	**102**	**62**	**62**
72					67	71	58a	67	67				64			
73					68	72	59	68	68				65			
74					69	73	60	69	69				66		68	68
75[f]	**59**	**56**	**107**	**101**	**70**	**74**	**61**	**70**	**70**	**57**	**68**	**59**	**67**	**108**	**69**	**69**
76[f]	**60**	**57**	**108**	**102**	**72**	**75**	**61**	**71**	**71**	**56**	**69**	**60**	**68**	**109**	**70**	**70**
77[a]	**61**	**58**	**99**	**97**	**73**	**76**	**63**	**72**	**72**	**76**	**71**	**61**	**69**	**98**	**71**	**71**
78[f]	**62**	**59**	**98**	**92**	**74**	**77**	**64**	**73**	**73**	**77**	**72**	**62**	**70**	**97**	**72**	**72**

Table 2 (continue)

AcMNPV	AdhoNPV	AdorNPV	AgipMNPV	AgseNPV	AnpeNPV	AgMNPV	BmNPV	CfMNPV	CfDefNPV	ChchNPV	ClbiNPV	EcobNPV	EppoNPV	HearMNPV	HearNPV	HearNPV G4
79	99	94	29		75	78	65	74	74				71	15		
80[a]	**63**	**60**	**97**	**91**	**76**	**79**	**66**	**75**	**75**	**78**	**73**	**63**	**72**	**96**	**73**	**73**
81[a]	**64**	**61**	**96**	**90**	**77**	**80**	**67**	**76**	**76**	**79**	**74**	**64**	**73**	**95**	**74**	**74**
82[f]	**65**	**62**	**95**	**89**	**78**	**81**	**68**	**77**	**77**	**80**	**75**	**65**	**74**	**94**	**75**	**75**
83[a]	**66**	**63**	**94**	**88**	**79**	**82**	**69**	**78**	**78**	**81**	**76**	**66**	**75**	**93**	**76**	**76**
84				24						75						
85									79							
86					98	103										
87						84	70	79	80							
88			93	87	80	85	71	80	81		77	67	76	92	77	77
89[a]	**67**	**64**	**92**	**86**	**81**	**86**	**72**	**81**	**82**	**82**	**78**	**68**	**77**	**91**	**78**	**78**
90[a]	**68**	**65**	**91**	**85**	**82**	**87**	**73**	**82**	**83**	**83**	**79**	**69**	**78**	**90**	**79**	**79**
91					83		74	83	84				79			
92[a]	**69**	**66**	**89**	**83**	**84**	**89**	**75**	**84**	**85**	**84**	**80**	**71**	**80**	**88**	**80**	**80**
93[f]	**70**	**67**	**88**	**82**	**85**	**90**	**76**	**85**	**86**	**85**	**81**	**72**	**81**	**87**	**81**	**81**
94[f]	**71**	**68**	**87**	**81**	**86**	**91**	**77**	**86**	**87**	**86**	**82**	**73**	**82**	**86**	**82**	**82**
95[a]	**72**	**69**	**86**	**80**	**87**	**92**	**78**	**87**	**88**	**87**	**83**	**74**	**83**	**85**	**84**	**84**
96[a]	**73**	**70**	**85**	**79**	**88**	**93**	**79**	**88**	**89**	**88**	**84**	**75**	**84**	**84**	**85**	**85**
97																
98[a]	**74**	**71**	**81**	**74**	**90**	**94**	**82**	**91**	**90**	**91**	**85**	**77**	**85**	**80**	**86**	**86**
99[a]	**75**	**72**	**80**	**73**	**91**	**95**	**83**	**92**	**91**	**92**	**86**	**78**	**86**	**79**	**87**	**87**
100[a]	**76**	**73**	**79**	**72**	**92**	**96**	**84**	**93**	**92**	**93**	§	**79**	**87**	**78**	**88**	**88**
101[f]	**77**	**74**	**78**	**71**	**93**	**97**	**85**	**94**	**93**	**94**	**87**	**80**	**88**	**77**	**89**	**89**
102[e]	**78**	**75**	**77**	**70**	**94**	**98**	**86**	**95**	**94**	**95**	**88**	**81**	**89**	**76**	**90**	**90**
103[b]	**79**	**76**	**76**	**69**	**95**	**99**	**87**	**96**	**95**	**96**	**89**	**82**	**90**	**75**	**91**	**91**
104[d]	**80**	**77**	**75**	**68**	**96**	**100**	**88**	**97**	**96**	**97**	**90**	**83**	**91**	**74**	**92**	**92**
105			25	20	97	102	89		98	73				26	61	61
106/107[f]	**110**	**105**	**62**	**59**	**99**	**104**	**90**	**98**	**100**	**107**	**97**	**116**	**93**	**62**	**101**	**101**
108[f]	**83**	**80**	**72**	**65**	**100**	**106**	**91**	**99**	**102**	**100**	**93**	**86**	**94**	**71**	**95**	**95**
109[a]	**82**	**79**	**73**	**66**	**101**	**107**	**92**	**100**	**103**	**99**	**92**	**85**	**95**	**72**	**94**	**94**
110[d]	**81**	**78**	**74**	**67**	**103**	**109**	**92a**	**101**	**105**	**98**	**91**	**84**	**96**	**73**	**93**	**93**
111					104	110	93	102	106	71	58		97		116	116
112/113				75							95	90				
114					106	114	94	105	109				100			
115[a]	**108**	**103**	**59**	**56**	**107**	**114**	**95**	**106**	**111**	**110**	**100**	**111**	**102**	**59**	**98**	**98**
116							95a									
117			55	51	109	116	96	109	113		104		104	54	110	110
118																
119[a]	**117**	**113**	**43**	**37**	**111**	**117**	**97**	**110**	**114**	**131**	**120**	**98**	**106**	**43**	**111**	**111**
120	113	108	44		112	118	98	111	115				107			

Table 2 (continue)

AcMNPV	AdhoNPV	AdorNPV	AgipMNPV	AgseNPV	AnpeNPV	AgMNPV	BmNPV	CfMNPV	CfDefNPV	ChchNPV	ClbiNPV	EcobNPV	EppoNPV	HearMNPV	HearNPV	HearNPV G4
121							98a									
122					113	120	99	112	117							
123							100									
124					114	121	101	113	118				108			
125				21	116	123	102	115	120				109			
126			27	23	117		103	117	121	65	59	50	110	18	41	41
127	52	49	23	19	118		104	118	122	64	60	51	111	27	56	56
128					119	124	105	119	123				112			
129[f]	**102**	**97**	**15**	**11**	**120**	**125**	**106**	**122**	**124**	**134**	**111**	**101**	**114**	**11**	**118**	**118**
130	103	98	14	10	121	126	107	123	125	133	113	99	115	10	119	119
131[d]	**104**	**99**	**54**	**49**	**122**	**127**	**108**	**124**	**126**	**121**	**114**	**108**	**116**	**53**	**120**	**120**
132					123	128	109	125	127	123			117			
133[a]	**2**	**2**	**47**	**41**	**124**	**129**	**110**	**126**	**128**	**127**	**117**	**93**	**118**	**47**	**114**	**114**
134			115		126	131	110a							118		
135							112									
136	31	30	149	142	127	132	113	128	130	19	19	18	119	151	22	22
137	32	31	150	143	128	133	114	129	131	18	114	19	120	152	21	21
138[a]	**27**	**26**	**151**	**144**	**129**	**134**	**115**	**130**	**132**	**17**	**14**	**14**	**121**	**153**	**20**	**20**
139[f]	**26**	**25**	**10**	**7**	**131**	**136**	**116**	**132**	**133**	**8**	**12**	**13**	**122**	**7**	**16**	**16**
140																
141[d]	**25**	**24**	**161**	**152**	**132**	**137**	**117**	**134**	**134**	**10**	**11**	**12**	**123**	**161**	**8**	**8**
142[a]	**24**	**23**	**160**	**151**	**133**	**138**	**118**	**135**	**135**	**11**	**10**	**11**	**124**	**160**	**9**	**9**
143[a]	**23**	**22**	**158**	**150**	**15**	**139**	**119**	**136**	**136**	**12**	§	**10**	**125**	**159**	**10**	**10**
144[a]	**22**	**21**	**156**	**149**	**14**	**140**	**120**	**137**	**137**	**13**	**9**	**9**	**126**	**158**	**11**	**11**
145[b]	**21**	**20**	**155**	**148**	**136**	**141**	**121**	**138**	**138**	**14**	§	**8**	**127**	**157**	**12**	**12**
146[f]	**20**	**19**	**154**	**147**	**137**	**142**	**122**	**139**	**139**	**15**	**8**	**7**	**128**	**156**	**13**	**13**
147[d]	**19**	**18**	**153**	**146**	**138**	**143**	**123**	**140**	**140**	**16**	**7**	**6**	**129**	**155**	**14**	**14**
148[a]	**8**	**8**	**9**	**6**	**139**	**144**	**124**	**141**	**141**	**7**	**6**	**5**	**130**	**6**	**15**	**15**
149							125									
150	21		18	103	102		126									
151					141	145	127	142	143				131			
152			7												5b	
153					144	148	128	144	146				133			
154							129									

[a]Homologues belong to the baculovirus core genes. [b]Homologues in all baculoviruses except for Deltabaculoviruses. [c]Homologues in all baculoviruses except for Gammabaculoviruses. [d]Homologues present in all Alphabaculoviruses. [e]Homologues present in all Betabaculoviruses. [f]Homologues present in all Alpha- and Betabaculoviruses. § Genes not officially assigned in ClbiNPV (GenBank NC_008293). An *ac68* homolog is present between c*lbi64* and c*lbi65* (*lef-3*), and partially overlaps the *lef-3* gene. An *ac10*0 homolog is located between c*lbi86* en c*lbi87*. For *ac143* (*odv-e18*), a homolog is located between c*lbi9* en c*lbi10* (van Oers, pers. comm) and for *ac145* between *clbi8*

Table 2 (continued)

	Alphabaculovirus-Ⅱ																
AcMNPV	HearNPV NNg1	HzSNPV	HycuNPV	LseNPV	LdMNPV	MacoNPV-A	MacoNPV-B	MaviMNPV	OpMNPV	OrleNPV	PlxyMNPV	RoMNPV	SeMNPV	SfMNPV	SpltNPV	SpltNPV II	TnSNPV
1			142					123	10		1	1	26	25	23		132
2	108	108	144	58	153	90	89		116	61	2			69	125	73	108
3			143		149	107	105		136	106	3						
4			145			73	72	124	8		4	2					
5			146					125	7		5	3					
6[a]	**123**	**121**	**147**	**137**	**137**	**14**	**13**	**126**	**6**	**114**	**6**	**4**	**12**	**16**	**114**	**14**	**128**
7											7	5					
8[d]	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**3**	**1**	**8**	**6**	**1**	**1**	**1**	**1**	**1**
9[d]	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**9**	**7**	**2**	**2**	**2**	**2**	**2**
10[f]	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**1**	**3**	**10**	**8**	**3**	**3**	**3**	**3**	**3**
11			141		35			4	11	47	11	9					
12					151						12	10					
13[f]	**130**	**127**	**140**	**149**	**122**	**36**	**31**	**5**	**12**	**133**	**13**	**11**	**13**	**17**	**128**	**15**	**129**
14[a]	**131**	**128**	**139**	**150**	**123**	**35**	**30**	**6**	**13**	**132**	**14**	**12**	**14**	**18**	**129**	**16**	**130**
15[d]	**133**	**130**	**138**	**145**	**125**	**39**	**33**	**7**	**14**	**130**	**15**	**13**	**27**	**26**	**121**	**24**	**133**
16			137					8	15		16						
17			135	142	129	41	36	9	16		17	15		28	119		
18			134	136	158	56	50	10	17	123	18	16	43	41	113	44	117
19[d]	**118**	**118**	**133**	**135**	**159**	**55**	**49**	**11**	**18**	**122**	**19**	**17**	**42**	**40**	**112**	**43**	**118**
20/21	139	135	132	162	118	47	42	12	19		20	18	34	33	134		140
22[d]	**140**	**136**	**131**	**163**	**119**	**48**	**43**	**13**	**20**	**112**	**21**	**19**	**35**	**34**	**135**	**36**	**141**
23[c]	**141**	**137**	**130**	**166**	**130**	**9**	**8**	**14**	**21**	**128**	**22**	**20**	**8**	**12**	**136**	**10**	**143**
24[d]	**138**	**134**	**111**	**159**	**110**	**45**	**40**	**15**	**44**	**113**	**23**	**21**	**32**	**31**	**133**	**32**	**139**
25[b]	**24**	**24**	**112**	**31**	**47**	**155**	**154**	**16**	**43**	**53**	**24**	**22**	**126**	**127**	**30**	**132**	**22**
26	25	25	113	32	36	154	153	17	42		25	23	125	126	31	131	23
27[e]	**106**	**106**	**114**	**40**	**139**	**139**	**137**	**18**	**35**	**16**	**26**	**24**	**110**	**111**		**116**	**35**
28[f]	**23**	**23**	**115**	**30**	**38**	**156**	**154**	**19**	**40**	**18**	**27**	**25**	**127**	**128**	**29**	**133**	**21**
29	22	22	116		39	157	155	20	39	19	28	26	128	130	28	134	20
30			117					21	38		29	27					
31	109	109	122	129	145	66	65	22	29	105	31	28	48	48	-	51	109
32[e]	**116**	**116**	**124**	**146**	**156**	**51**	**46**		**27**	**125**	**32**	**29**	**38**	**37**	**122**	**39**	**122**
33				120	138	72	71			98	33	30	54	53	100	57	101
34	27	27	125	18	42	153	152	23	26	60	34	31	124	125	18	-	24
35[e]	**28**	**28**	**126**		**43**	**152**	**151**	**24**	**25**	**58**	**35**	**32**	**123**	**124**	**32**	**129**	**25**
36[f]	**31**	**31**	**127**	**36**	**44**	**150**	**149**	**25**	**24**	**56**	**36**	**33**	**120**	**121**	**33**	**126**	**26**
37[e]	**32**	**32**	**128**	**37**	**45**	**149**	**148**	**26**	**23**	**55**	**37**	**34**	**119**	**120**	**34**	**125**	**27**
38[f]	**33**	**33**	**129**	**38**	**46**	**148**	**147**	**27**	**22**	**54**	**38**	**35**	**118**	**119**	**35**	**124**	**28**
39								28			39	36					
40[a]	**35**	**35**	**110**	**41**	**48**	**145**	**143**	**29**	**45**	**52**	**40**	**37**	**115**	**116**	**36**	**121**	**31**

Table 2 (continued)

AcMNPV	HearNPV NNg1	HzSNPV	HycuNPV	LeseNPV	LdMNPV	MacoNPV-A	MacoNPV-B	MaviMNPV	OpMNPV	OrleNPV	PlxyMNPV	RoMNPV	SeMNPV	SfMNPV	SpltNPV	SpltNPV II	TnSNPV
41	36	36	109	42				30	46	50	41	38			37		
42			108						47		42	39					
43	37	37	107			143	142	31	48	48	43	40	113	114		119	32
44								32	49		44	41	84				
45								33			45	42					
46[e]	**98**	**99**	**106**	**113**	**131**	**78**	**77**		**50**	**119**	**46**	**43**	**57**	**57**	**98**	**61**	**96**
47			105					34	51		47	44					
48			104						52		48	45					
49			103						53		49	46					63
50[a]	**38**	**38**	**102**	**43**	**51**	**141**	**140**	**35**	**54**	**45**	**50**	**47**	**112**	**113**	**38**	**118**	**33**
51	39	39	101	44		140	139	36	55	44	51	48	111	112	39	117	34
52	42	43			53			37		42	52	49	109	110	44	115	37
53[f]	**43**	**44**	**98**	**60**	**54**	**137**	**136**	**38**	**56**	**41**	**53**	**50**	**108**	**109**	**45**	**114**	**38**
53a	46	47	97	63	56	134	133	39	57		54	51	106	106	48	111	41
54[a]	**47**	**48**	**96**	**64**	**57**	**133**	**132**	**40**	**58**	**38**	**55**	**52**	**105**	**105**	**49**	**110**	**42**
55[d]	**48**	**49**	**95**	**65**	**58**	**132**	**131**	**41**	**59**	**37**	**56**	**53**	**104**	**104**	**50**	**109**	**43**
56	49	50	94			131	130	42	60	36	57	54	103	103		107	44
57	50	51	93	69	60	130	129		61	35	58	55	102	102	51	106	45
58/59[d]	**51**	**52**	**92**	**71**	**61**	**129**	**128**	**43**	**62**	**34**	**59**	**56**	**101**	**101**	**52**	**105**	**4**
60[d]	**52**	**53**	**91**	**71**	**62**	**128**	**127**	**44**	**63**	**33**	**60**	**57**	**100**	**100**	**53**	**104**	**47**
61[f]	**53**	**54**	**90**	**76**	**63a**	**125**	**124**	**45**	**64**	**32**	**61**	**58**	**98**	**98**	**57**	**102**	**48**
62[a]	**55**	**56**	**89**	**78**	**64**	**124**	**123**	**46**	**65**	**31**	**62**	**59**	**97**	**97**	**59**	**101**	**49**
63	128	125			117			47			63	60					29
64	58	59	86	35	68	37	32	48	69	29	64	61	25	24	32	22	64
65[a]	**69**	**69**	**85**	**84**	**83**	**115**	**114**	**49**	**70**	**67**	**65**	**62**	**95**	**92**	**69**	**97**	**54**
66[d]	**68**	**68**	**84**	**83**	**82**	**114**	**113**	**50**	**71**	**66**	**66**	**63**	**92**	**91**	**68**	**96**	**55**
67[d]	**67**	**67**	**83**	**82**	**81**	**113**	**112**	**51**	**72**	**65**	**67**	**64**	**91**	**90**	**67**	**95**	**56**
68[a]	**66**	**66**	**82**	**81**	**80**	**112**	**111**	**52**	**73**	**64**	**68**	**65**	**90**	**89**	**66**	**94**	**57**
69	65	65	81			111	110	53			69	66	89	88	65	93	
70											70	67					
71[f]	**64**	**64**	**80**	**80**	**79**	**110**	**109**	**54**	**74**	**63**	**71**	**68**	**88**	**87**	**64**	**92**	**58**
72			79					55	75		72	69					
73			78	64		93		56	76		73	70					
74	70	70	77					57	77		74	71			71		
75[f]	**71**	**71**	**76**	**87**	**84**	**116**	**115**	**58**	**78**	**68**	**75**	**72**	**94**	**93**	**72**	**98**	**53**
76[f]	**72**	**72**	**75**	**88**	**85**	**117**	**116**	**59**	**79**	**69**	**76**	**73**	**95**	**94**	**73**	**99**	**52**
77[a]	**73**	**73**	**74**	**89**	**86**	**106**	**105**	**60**	**80**	**70**	**77**	**74**	**82**	**84**	**74**	**88**	**70**
78[f]	**74**	**74**	**73**	**90**	**87**	**105**	**104**	**61**	**81**	**71**	**78**	**75**	**81**	**83**	**75**	**87**	**71**
79			72			17	15	62	82		79	76					
80[a]	**75**	**75**	**71**	**91**	**88**	**104**	**103**	**63**	**83**	**72**	**80**	**77**	**80**	**82**	**76**	**86**	**72**
81[a]	**76**	**76**	**70**	**92**	**89**	**103**	**102**	**64**	**84**	**73**	**81**	**78**	**79**	**81**	**77**	**85**	**74**

Table 2 (continued)

AcMNPV	HearNPV NNg1	HzSNPV	HycuNPV	LeseNPV	LdMNPV	MacoNPV-A	MacoNPV-B	MaviMNPV	OpMNPV	OrleNPV	PlxyMNPV	RoMNPV	SeMNPV	SfMNPV	SpltNPV	SpltNPV II	TnSNPV
82[f]	**77**	**77**	**69**	**93**	**90**	**102**	**101**	**65**	**85**	**74**	**82**	**79**	**78**	**80**	**78**	**84**	**75**
83[a]	**78**	**78**	**68**	**94**	**91**	**101**	**100**	**66**	**86**	**75**	**83**	**80**	**77**	**79**	**79**	**83**	**76**
84											84	81					62
85									87		85	82					
86												83					
87			67						88		86	84					
88	79	80	66	95		100	99		89	76	87	85	76	78	80	82	
89[a]	**80**	**81**	**65**	**96**	**92**	**99**	**98**	**67**	**90**	**77**	**88**	**86**	**75**	**77**	**81**	**81**	**77**
90[a]	**81**	**82**	**64**	**97**	**93**	**98**	**97**	**68**	**91**	**78**	**89**	**87**	**74**	**76**	**82**	**80**	**78**
91			63						92		90	88					
92[a]	**82**	**83**	**62**	**98**	**94**	**96**	**95**	**69**	**93**	**80**	**91**	**89**	**73**	**75**	**83**	**79**	**79**
93[f]	**83**	**84**	**61**	**99**	**95**	**95**	**94**	**70**	**94**	**81**	**92**	**90**	**72**	**74**	**84**	**78**	**80**
94[f]	**84**	**85**	**60**	**100**	**96**	**94**	**93**	**71**	**95**	**82**	**93**	**91**	**71**	**73**	**85**	**77**	**81**
95[a]	**86**	**87**	**59**	**101**	**97**	**93**	**92**	**72**	**96**	**83**	**94**	**92**	**70**	**72**	**86**	**76**	**82**
96[a]	**87**	**88**	**58**	**102**	**98**	**92**	**91**	**73**	**97**	**84**	**95**	**93**	**69**	**71**	**87**	**75**	**83**
97																	
98[a]	**88**	**89**	**55**	**103**	**99**	**88**	**87**	**75**	**99**	**85**	**96**	**94**	**67**	**67**	**88**	**71**	**86**
99[a]	**89**	**90**	**54**	**104**	**100**	**87**	**86**	**76**	**100**	**86**	**97**	**95**	**66**	**66**	**89**	**70**	**87**
100[a]	**90**	**91**	**53**	**105**	**101**	**86**	**85**	**77**	**101**	**87**	**98**	**96**	**65**	**65**	**90**	**69**	**88**
101[f]	**91**	**92**	**52**	**106**	**102**	**85**	**84**	**78**	**102**	**88**	**99**	**97**	**64**	**64**	**91**	**68**	**89**
102[e]	**92**	**93**	**51**		**103**	**84**	**83**	**79**	**103**	**89**	**100**	**98**	**63**	**63**	**92**	**67**	**90**
103[b]	**93**	**94**	**50**	**108**	**104**	**83**	**82**	**80**	**104**	**90**	**101**	**99**	**62**	**62**	**93**	**66**	**91**
104[d]	**94**	**95**	**49**	**109**	**105**	**82**	**81**	**81**	**105**	**91**	**102**	**100**	**61**	**61**	**94**	**65**	**92**
105	63	63		68		32	27	82			103	101					
106/107[f]	**104**	**104**	**48**	**123**	**140**	**71**	**70**	**83**	**107**	**99**	**104**	**102**	**53**	**52**	**101**	**56**	**102**
108[f]	**97**	**98**	**47**	**112**	**108**	**79**	**78**	**84**	**108**	**94**	**105**	**103**	**58**	**58**	**97**	**62**	**95**
109[a]	**96**	**97**	**46**	**111**	**107**	**80**	**79**	**85**	**109**	**93**	**106**	**104**	**59**	**59**	**96**	**63**	**94**
110[d]	**95**	**96**	**45**	**110**	**106**	**81**	**80**	**86**	**111**	**92**	**107**	**105**	**60**	**60**	**95**	**64**	**93**
111	122	120	44	48	76			87	112		108	106					66
112/113					109					96	109	107					
114			40					88	114		110	108					
115[a]	**101**	**101**	**39**	**131**	**143**	**68**	**67**	**89**	**115**	**102**	**111**	**109**	**50**	**49**	**107**	**53**	**105**
116											112	110					
117	113	113	37			62	62	90	117	108	113	111	47	46		48	
118											114	112					
119[a]	**114**	**114**	**35**	**148**	**155**	**49**	**44**	**91**	**119**	**126**	**115**	**113**	**36**	**35**	**124**	**37**	**123**
120			34					92	120		116	114		36			
121											117						
122			33						121		118	115					
123											119	116					
124			32					93	122		120	117					

Table 2 (continued)

AcMNPV	HearNPV NNg1	HzSNPV	HycuNPV	LeseNPV	LdMNPV	MacoNPV-A	MacoNPV-B	MaviMNPV	OpMNPV	OrleNPV	PlxyMNPV	RoMNPV	SeMNPV	SfMNPV	SpltNPV	SpltNPV II	TnSNPV
125			31			16		94	123		121	118		21			
126	41	41	30	57	70	22	19	95	124	24	122	119	19	22	42	18	61
127	56	57	29	74	78	33	28	96	125	22	123	120	16	20	54	17	60
128			28					97	126		124	121					
129[f]	**125**	**122**	**27**	**139**	++	**12**	**11**	**98**	**127**	**116**	**125**	**122**	**10**	**14**	**116**	**12**	**126**
130	126	123	26			11	10	99	128	118	126	123	9	13		11	125
131[d]	**127**	**124**	**25**	**158**	**136**	**60**	**61**	**100**	**129**	**109**	**127**	**124**	**46**	**45**	**132**	**47**	**113**
132			24					101	130		128	125					115
133[a]	**117**	**117**	**23**	**134**	**157**	**54**	**47**	**102**	**131**	**124**	**129**	**126**	**41**	**39**	**109**	**42**	**119**
134						126	124				130	127	99	99		103	
135				75				103			131	128			55		
136	21	21	21	20	40	158	157	104	132	20	132	129	129	131		135	19
137	20	20	20	21	41	159	158	105	133	21	133	130	130	132	19	136	18
138[a]	**19**	**19**	**19**	**24**	**27**	**160**	**159**	**106**	**134**	**15**	**134**	**131**	**131**	**134**	**21**	**137**	**17**
139[f]	**16**	**16**	**17**	**27**	**23**	**7**	**7**	**107**	**137**	**14**	**135**	**132**	**7**	**10**	**27**	**8**	**9**
140																	
141[d]	**8**	**8**	**16**	**8**	**21**	**168**	**167**	**109**	**138**	**13**	**136**	**133**	**138**	**142**	**8**	**147**	**10**
142[a]	**9**	**9**	**15**	**11**	**20**	**167**	**166**	**110**	**139**	**12**	**137**	**134**	**137**	**141**	**11**	**146**	**11**
143[a]	**10**	**10**	**14**	**12**	**19**	**166**	**165**	**111**	**140**	**11**	**138**	**135**	**136**	**140**	**12**	**145**	**12**
144[a]	**11**	**11**	**13**	**13**	**18**	**165**	**164**	**112**	**141**	**10**	**139**	**136**	**135**	**139**	**13**	**144**	**13**
145[b]	**12**	**12**	**12**	**14**	**17**	**164**	**163**	**113**	**142**	**9**	**140**	**137**	**134**	**138**	**14**	**143**	**14**
146[f]	**13**	**13**	**11**	**15**	**16**	**163**	**162**	**114**	**144**	**8**	**141**	**138**	**133**	**137**	**15**	**142**	**15**
147[d]	**14**	**14**	**10**	**16**	**15**	**162**	**161**	**115**	**145**	**7**	**142**	**139**	**132**	**136**	**16**	**141**	**10a**
148[a]	**15**	**15**	**9**	**17**	**14**	**6**	**6**	**116**	**146**	**6**	**143**	**140**	**6**	**8**	**17**	**7**	**8**
149								117			144	141					
150						118	117	118			145	142		68	22		
151			6					119	151		146	143					
152	5				8	8		120			147	144					
153			5					121	152		148	145					
154								122			149	146					

++ The LdMNPV p24 gene is lacking in the sequenced strain, but is present in other natural LdMNPV strains (251).

with the wandering behaviour of infected larvae (107), similarly to the closely related Bombyx mori (Bm) NPV ptp gene (122). RNA-triphosphatase activity is also encoded by the AcMNPV *lef-4* gene (*ac*90), which in addition encodes guanyltransferase activity (154).

Ac2: *bro,* baculovirus repeated ORF

This gene belongs to the baculovirus repeated ORF (*bro*) family, which has members in many other baculoviruses either as a single gene or in multiple copies. A similar gene is also present in entomopoxvirus (3, 11). The AcMNPV *bro* gene is present as a single copy and encodes a protein with a predicted mass of

Table 3. AcMNPV homologues in Beta-, Gamma and Deltabaculoviruses #

	Betabaculovirus										Gamma-baculovirus			Delta-baculovirus
AcMNPV	AdorGV	AgseGV	ChocGV	CrleGV	CpGV	HearGV	PhopGV	PlxyGV	SpltGV	XecnGV	NeabNPV	NeleNPV	NeseNPV	CuniNPV
1				89										
2						133	9		111	60				1
3						130				127				5
4		46						40	80					
5				91	100									
6[a]	**32**	**35**	**29**	**38**	**41**	**33**	**37**	**32**	**32**	**35**	**57**	**57**	**57**	**25**
10[f]	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**6**	**3**	**3**				
13[f]	**61**	**63**	**54**	**65**	**73**	**79**	**65**	**54**	**61**	**81**				
14[a]	**62**	**64**	**55**	**66**	**74**	**80**	**66**	**55**	**62**	**82**	**68**	**65**	**68**	**45**
15	118	123	115	128	141		129	118		22				
22[a]	**39**	**43**	**35**	**45**	**48**	**42**	**44**	**37**	**39**	**45**	**55**	**52**	**55**	**38**
23[c]	**23**	**25**	**23**	**30**	**31**	**26**	**27**	**26**	**24**	**27**				**104**
25[b]	**68**	**69**	**61**	**72**	**81**	**87**	**73**	**61**	**70**	**89**	**6**	**14**	**22**	
27[e]	**88**	**106**	**84**	**16**	**17**	**139**	**86**	**98**	**106**	**137**	**21**	**11**	**17**	
28[f]	**67**	**68**	**60**	**71**	**80**	**86**	**72**	**60**	**69**	**88**				
29		16	16	19	19	15	111	17		16				
30		132							127	138				
31	51	54	44	57	59	63	54	47		68				
32[e]	**117**	**128**	**114**	**127**	**140**	**145**	**128**	**104**	**116**	**144**				
33		14		15	16		14							
35[e]	**45**	**47**	**39**	**52**	**54**	**47**	**49**	**42**	**45**	**52**				
36[f]	**49**	**51**	**42**	**55**	**57**	**50**	**52**	**45**	**48**	**55**				
37[e]	**50**	**52**	**43**	**56**	**58**	**51**	**53**	**46**	**49**	**56**				
38[f]	**59**	**61**	**51**	**62**	**69**	**77**	**62**	**52**	**59**	**79**				
40[a]	**58**	**60**	**50**	**61**	**68**	**74**	**68**	**51**	**58**	**78**	**49**	**46**	**49**	**73**
46[e]	**28**	**33**	**27**	**35**	**37**	**150**	**33**	**30**	**125**	**149**				
47		124												
50[a]	**110**	**118**	**107**	**119**	**131**	**149**	**121**	**109**	**121**	**148**	**83**	**78**	**81**	**26**
53[f]	**111**	**122**	**109**	**121**	**134**	**169**	**122**	**112**	**127**	**171**				
53a		126	112	124	137	172	125			174				
54[a]	**115**	**127**	**113**	**125**	**138**	**173**	**126**	**115**	**130**	**175**	**88**	**83**	**85**	**8**
60[d]		**84**				**103**			**84**	**102**				
61[f]	**101**	**108**	**97**	**108**	**118**	**141**	**110**	**100**	**109**	**140**				
62[a]	**100**	**107**	**96**	**107**	**107**	**140**	**109**	**99**	**107**	**139**	**39**	**37**	**40**	**59**
64					13	109				107				
65[a]	**94**	**101**	**90**	**101**	**111**	**134**	**103**	**93**	**101**	**132**	**12**	**20**	**28**	**91**
66[d]				**31**		**135**								
68[a]	**97**	**104**	**93**	**104**	**114**	**137**	**106**	**96**	**104**	**68**	**40**	**38**	**41**	**58**
69													5	
71[f]	**89**	**53**	**84**	**16**	**17**	**139**	**108**	**98**	**106**	**137**				

Table 3 (continued)

AcMNPV	AdorGV	AgseGV	ChocGV	CrleGV	CpGV	HearGV	PhopGV	PlxyGV	SpltGV	XecnGV	NeabNPV	NeleNPV	NeseNPV	CuniNPV
75[f]	**93**	**100**	**89**	**99**	**108**	**129**	**101**	**92**	**100**	**126**				
76[f]	**92**	**99**	**88**	**98**	**107**	**128**	**100**	**91**	**99**	**125**				
77[a]	**91**	**97**	**86**	**97**	**106**	**126**	**99**	**89**	**97**	**123**	**45**	**42**	**45**	**18**
78[f]	**90**	**96**	**85**	**96**	**105**	**125**	**98**	**88**	**96**	**122**		**43**	**46**	
79					65	69				75				
80[a]	**88**	**95**	**83**	**95**	**104**	**124**	**97**	**87**	**95**	**121**	**47**	**44**	**47**	**33**
81[a]	**87**	**94**	**82**	**94**	**103**	**123**	**96**	**86**	**94**	**120**	**48**	**45**	**48**	**106**
82[f]	**86**	***93***	***81***	***93***	***102***	***122***	***95***	***85***	***93***	***119***				
83[a]	**85**	**91**	**80**	**92**	**101**	**121**	**94**	**84**	**92**	**118**	**87**	**82**	**84**	**35**
86		41							108		17	24	39	
88				25	24	13			124	14				
89[a]	**81**	**86**	**76**	**87**	**96**	**113**	**88**	**79**	**87**	**111**	**92**	**88**	**89**	**24**
90[a]	**80**	**85**	**75**	**86**	**95**	**112**	**87**	**78**	**86**	**110**	**62**	**59**	**62**	**96**
92[a]	**79**	**83**	**74**	**84**	**93**	**100**	**85**	**76**	**83**	**101**	**8**	**16**	**24**	**14**
93[f]	**78**	**82**	**73**	**83**	**92**	**99**	**84**	**75**	**82**	**100**				
94[f]	**77**	**81**	**72**	**82**	**91**	**98**	**83**	**74**	**81**	**99**				
95[a]	**76**	**79**	**71**	**81**	**90**	**97**	**82**	**72**	**80**	**98**	**61**	**58**	**61**	**89**
96[a]	**75**	**78**	**70**	**80**	**89**	**96**	**81**	**71**	**79**	**97**	**60**	**57**	**60**	**90**
97														
98[a]	**74**	**77**	**69**	**79**	**88**	**95**	**80**	**70**	**77**	**96**	**59**	**56**	**59**	**87**
99[a]	**73**	**76**	**68**	**78**	**87**	**94**	**79**	**69**	**76**	**95**	**58**	**55**	**58**	**88**
100[a]	**72**	**75**	**67**	**77**	**86**	**93**	**78**	**67**	#	**94**	**28**	**28**	**36**	**23**
101[f]	**71**	**74**	**66**	**76**	**85**	**92**	**77**	**66**	**75**	**93**				
102[e]	**70**	**73**	**65**	**75**	**84**	**91**	**76**	**64**	**74**	**92**				
103[b]	***69***	***72***	***64***	***74***	***83***	***90***	***75***	***63***	***73***	***91***	***34***	***31***	***33***	
105		132		61		62				67				
106/107[f]	**43**	**46**	**37**	**50**	**52**	**45**	**47**	**42**	**42**	**50**				
108[f]	**47**	**49**	**41**	**54**	**56**	**49**	**51**	**44**	**47**	**54**				
109[a]	**46**	**48**	**40**	**53**	**55**	**48**	**50**	**43**	**46**	**53**	**71**	**67**	**70**	**69**
110[d]	**44**		**38**	**51**	**53**	**46**	**48**	**41**	**43**	**51**				
111				29					126	160				
112/113						148			120	147				
115[a]	**26**	**29**	**26**	**34**	**35**	**30**	**31**	**29**	**27**	**32**	**69**	**66**	**69**	**46**
119[a]	**63**	**65**	**56**	**67**	**75**	**82**	**67**	**7**	**64**	**84**	**79**	**76**	**79**	**29**
125						132				129				
126		32			10	105				103				
127		31		11	11					58				
129[f]	**60**	**62**	**52**	**63**	**71**	**78**	**63**	**53**	**60**	**80**				
130	69			50										
133[a]	**107**	**115**	**104**	**115**	**125**	**146**	**114**	**106**	**117**	**145**	**36**	**33**	**31**	**54**
134						20				21				

Table 3 (continued)

AcMNPV	AdorGV	AgseGV	ChocGV	CrleGV	CpGV	HearGV	PhopGV	PlxyGV	SpltGV	XecnGV	NeabNPV	NeleNPV	NeseNPV	CuniNPV
135			15											75
136														
137	13		45		22	5		21	4	5				
138[a]	**53**	**56**	**46**	**58**	**60**	**72**	**55**	**49**	**56**	**77**	**50**	**47**	**50**	**74**
139[f]	**119**	**131**	**116**	**129**	**143**	**178**	**130**	**120**	**134**	**180**				
141[d]		**13**				**13**		**15**	**12**	**14**				
142[a]	**11**	**12**	**13**	**14**	**15**	**12**	**13**	**14**	**11**	**13**	**63**	**60**	**63**	**30**
143[a]	**10**	**11**	**12**	**13**	**14**	**11**	**12**	**13**	**10**	**12**	**65**	**62**	**65**	**31**
144[a]	**82**	**87**	**77**	**88**	**97**	**114**	**89**	**80**	**88**	**112**	**66**	**63**	**66**	**32**
145[b]	**8**	**10**	**9**	**8**	**9**	**10**	**8**	**12**	**9**	**11**	**67**	**64**	**67**	
146[f]	**7**	**9**	**8**	**7**	**8**	**9**	**7**	**11**	**8**	**10**				
148[a]	**12**	**15**	**14**	**17**	**18**	**14**	**16**	**16**	**13**	**15**	**16**	**23**	**38**	**102**
150						19			9	11				
153				25	24		24							

AcMNPV ORFs without homologues in Beta-, Gamma- and Deltabaculoviruses are not shown. [a]Homologues belong to the baculovirus core genes. [b]Homologues in all baculoviruses except for Deltabaculoviruses. [c]Homologues in all baculoviruses except for Gammabaculoviruses. [d]Homologues present in all Alphabaculoviruses. [e]Homologues present in all Betabaculoviruses. [f]Homologues present in all Alpha- and Betabaculoviruses.

37.8 kDa (328 aa) with unclear function. Disruption of the *bro* gene has no effect on virus replication in cultured cells or on the lethal dose in insect larvae when injected as BV or *per os* with ODV. However, disruption of the N-terminal part of the BRO protein reduced the number of OBs (15). In contrast to AcMNPV, BmNPV contains five *bro* genes, *bro-a* till *bro-e*. The BmNPV *bro-d* gene is essential for virus replication in cell culture and *bro-a* and *bro-c* genes can complement each other (124). However, the absence of *bro* genes in several baculoviruses suggests that the requirement for *bro* genes may depend on the host species (15). In BmNPV, the BRO proteins reside in the nucleus until 4 h post infection (p.i.). After that time point, the proteins are found in both cytoplasm and nucleus (123). Furthermore, mutation in the leucine-rich N-terminal part of the protein results in accumulation of proteins, which suggest that this region serves as a CRM1-dependent nuclear export signal (123).

Ac3: *ctl,* conotoxin-like peptide

The *ctl* gene encodes a conotoxin-like peptide, which has a molecular mass of 5.6 kDa (53 aa). Conotoxins are neurotoxins that are present in the venom of marine snails, belonging to the genus *Conus* (257). Ω-conotoxins block specific types of Ca^{2+}-channels in neurons (180), while another sub-class of conotoxins have a behavioural and anticonvulsant effect in DBA/2 mice (114). Infection with a mutant AcMNPV virus – with either a disruption or a null mutant of the gene – was not significantly different in infectivity in Sf21 cells or in virulence *S. frugiperda* larvae (57).

Ac4: *ac4,* putative enhancer activity

ORF 4 of AcMNPV is an early gene and together with

five other early genes of AcMNPV, *ac102, he65 (*ac*105*), *ie-1 (ac147*), *ac152*, and *pe38 (ac153*) respectively, is needed to accumulate G-actin into the nucleus of Tn-368 cells (202). The expression of *ac4*, *ie-1,* and *pe38* starts before the expression of *ac102* or *he65*. The gene *ac4* codes for a protein of 17.6 kDa (83 aa.) which has not been characterized thoroughly, but it has enhancer activities for cellular and viral promoters (162).

Ac5: *ac5,* enhancer

In BmNPV, a region upstream of the polyhedrin promoter corresponding to the 5'-ends of *ac4* and *ac5* of AcMNPV was shown to have enhancer capabilities (1). This enhancer activity was confirmed as the homologous region in AcMNPV resulted in increased promoter activity in luciferase-assays in combination with several full or minimal promoters: *hsp70*, CMVm and *p35* minimal promoter in insect cells (162). In AcMNPV *ac5* encodes a hypothetical protein (12.4 kDa, 109 aa), however no transcripts have been detected (287).

Ac6: *lef-2*, late expression factor 2

The *lef-2* gene codes for late expression factor-2 (LEF-2), (23.9 kDa, 210 aa). This protein is essential for the expression from *vp39* and *polh* promoters (216). In addition, LEF-2 as well as five other gene products (IE-1, LEF-1 LEF-3, DNA polymerase, and helicase) are required for replication of plasmid DNA containing an AcMNPV origin of replication (133). Protein-protein interaction between LEF-1 and LEF-2 is essential for this DNA replication (61) and LEF-2 binds to DNA (187). A point mutation changing an aspartic acid into an asparagine residue at amino acid 178, showed no difference in plasmid replication between mutant and wild type virus infections but showed deficiency in very late gene expression (184). *Lef-2* is a baculovirus core gene.

Ac7: *orf603,* ORF603 peptide

The *orf603* gene encodes a hitherto uncharacterized protein of 23.6 kDa (201 aa). Partial deletion of the *orf603* gene did not affect BV yield in cell culture nor the dose to kill insects (72). However, a truncation of ORF603 decreased the time to death in *S. frugiperda* larvae (224).

Ac8: *polh*, major occlusion body protein

The *polh* gene encodes the 28.6 kDa polyhedrin protein (245 aa), which is the major component of OBs in NPVs. It was the first baculovirus gene to be characterised (105). AcMNPV polyhedrin has a mosaic structure, which makes it unsuitable for phylogenetic analysis (117). *polh* is the most conserved gene in baculoviruses. The gene is described very late after infection from a canonical TAAG motif. The function of the polyhedra is to protect and spread the virus outside the host. Upon ingestion by the host, the polyhedra dissociate due to the alkaline environment of the midgut and release the virions (129). The gene is not essential for virus replication in cell culture and its promoter is used extensively to drive the expression of foreign genes. For a more detailed review see (236).

Ac9: *orf1629*, P78/83 capsid protein

The *orf1629* gene codes for the essential P78/83 structural protein of BVs and ODVs (226). The protein with a calculated mass of 60.7 kDa (543 aa) has a phosphorylated and a non-phosphorylated isoform, and is present at one end of the mature nucleocapsid (272). P78/83 resembles Wiscott-Aldrich Syndrome proteins (WASP) and is, together with the host protein complex ARP2/3, responsible for actin polymerization in the nucleus of infected cells (74, 175). By deleting

part of *orf1629* from the AcMNPV genome, a new method was developed to obtain recombinant baculoviruses by dominant selection with almost 100% recombination efficiency (130).

Ac10: *pk-1*, protein kinase

The protein product of this gene, PK-1 (32.0 kDa, 272 aa), has high similarity to serine-threonine protein kinases and phosphorylates histone H1 in rabbit reticulocyte lysates (233). The gene is expressed from the beginning of the late throughout the very late phase of the viral infection (233). PK-1 is required for transcription of the very late *polh* gene, presumably through phosphorylation of LEF-8 (*ac50*), which is required in the (very) late transcription complex (190, 191). PK-1 interacts with PKIP (*ac24*), which stimulates PK-1 activity (62).

Ac11: *ac11,* unknown function

The *ac11* gene encodes a hypothetical protein with a predicted mass of 40.1 kDa (340 aa). Homologs found in many Alphabaculoviruses (Table 2) together form the DUF1386 family (176), but no particular motifs point towards a specific function.

Ac12: *ac12,* unknown function

This ORF encodes a hypothetical protein of 25.4 kDa (217 aa) with unknown function (9). The gene is not conserved among the Alphabaculoviruses; only in the related virus *Rachoplusia ou (*Ro)MNPV and in *Lymantria dispar (*Ld)MNPV homologous genes can be found. In the former the homologous gene is 25 codons shorter than in AcMNPV (92). Microarray analysis revealed transcripts of the gene, but its function remains unknown (287).

Ac13: *ac13,* unknown function

Ac13 codes for a hypothetical protein with a predicted mass of 38.7 kDa (327 aa). Homologs are conserved among all Alphabaculoviruses and are present in a few granuloviruses (Table 2 and Table 3). Transcripts were found by microarray analysis (287), but no function was assigned.

Ac14: *lef-1,* late expression factor 1

The gene product LEF-1 with a calculated mass of a 30.8 kDa (266 aa) is essential for DNA replication (133) and forms a complex with LEF-2 (*ac6*) (61). This interaction is required as non-interacting mutants of LEF-1 and LEF-2 do not promote transient DNA replication (61). LEF-1 contains a primase-like motif (61) and its primase activity was confirmed (187) based on the oligonucleotide synthesis on a poly (dT) template, which then allowed initiation of DNA synthesis by an exogenous DNA polymerase (Klenow enzyme). *Lef-1* is a baculovirus core gene.

Ac15: *egt,* ecdysteroid UDP-glucosyl transferase

The *egt* gene encodes the enzyme ecdysteroid UDP-glucosyl transferase (EGT) (23.6 kDa, 201 aa). The gene is lost in some baculovirus lineages (100). This enzyme prevents insect molting by inactivating ecdysteroid hormones through transfer of glucosyl groups to these hormones (199). The presence of EGT during infection leads the development of larger insects, a longer time to death and a higher yield of progeny virus (41). Deletion of the *egt* gene makes baculovirus-based insecticides more effective by an early reduction of the feeding damage (200).

Ac16: *bv/odv-e26*; structural protein

The ORF *ac16* encodes a structural protein (25.9 kDa, 225 aa) present in the envelopes of BVs and ODVs, named BV/ODV-E26 or briefly E26 (14). *Ac16* is an early gene and transcripts accumulate rapidly after infection (213). *Ac16* transcription initiates from a cryptic promoter sequence (87). When the *ac16*

locus (previously called DA26) was disrupted-maintaining the N-terminus - a virus with a few polyhedra (FP) phenotype was produced, which was still infectious and showed no difference in protein synthesis when mutant and wild type virus were compared (201). However, deletion of the *ac16* homolog in BmNPV (*Bm8) was* not successful, indicating that this ORF may be essential (24). Multiple isoforms of E26 are present in infected cells, one isoform associates with viral DNA or DNA-binding proteins, a second one associates with intracellular membranes, likely due to palmityolation (24).

More recently, it has been shown that Ac16 contains a subdomain within the acidic transcriptional activation domain for binding with IE0 and IE1. Deletion of the *ac16* gene results in an increased ratio of IE0 to IE1, but there was no effect on temporal production of these proteins nor on BV production nor on DNA replication (195).

Ac17: *ac17,* unknown function

Ac17 gene transcripts are present from the early to the very late phases and the encoded protein (18.5 kDa, 164 aa) localized in the cytoplasm of infected cells from 6 h p.i. (7). The gene *ac17,* together with *pe38 (ac153*), *he65 (ac105*), *gp64 (ac128*), *ie2 (ac151*), *ac16, ac25* and *pcna (ac49*), is activated by the trans-activator IE1 in the mammalian cell line Vero E6 (161). The function of the gene remains unknown, although transcriptional control is most likely. Deletion mutants of *ac17* are infectious (139).

Ac18: *da41*, unknown function

The *ac18* gene (*da41*) is expressed as a 40.9 kDa (353 aa) protein. The gene is not essential for virus infection and replication at least *in vitro* as viable *ac18* mutants are formed in bioreactors (139). The lethal dose was not affected by deleting *ac18*, but time to death was increased (275). Which role *ac18* plays, is still unclear.

Ac19: *ac19,* unknown function

This gene encodes a hypothetical protein with a calculated mass of 12.2 kDa (108 aa). Although homologs are found in other baculoviruses (Table 2), the function of the gene product is unknown. This gene is represented in the transcriptome (287).

Ac20/21: actin rearrangement inducing factor-1

The gene *ac20* was identified in 1994 (9) and had the potential to encode a partial homolog of *ac21*. Resequencing of these ORFs showed that *ac20* and *ac21* in fact form one ORF (92). The *ac20/ac21* fusion gene codes for the 47.7 kDa (417 aa) actin rearrangement inducing factor 1 (ARIF-1). The gene is expressed after transactivation by IE-1, weakly from 2 h p.i., more abundantly after 4-6 h p.i., and not detectably at 12 h p.i. (237). ARIF-1 is a tyrosine phosphorylated protein and induces rearrangement of the actin skeleton (237) by interacting with filamentous actin (F-actin) at the plasma membrane (53). Deletion of ARIF-1 interfered with F-actin accumulation at the plasma membrane, but not with the formation of early actin cables and nuclear F-actin accumulation (53, 237). Homologs are only present in Alphabaculoviruses (Table 2).

Ac22: *pif-2, per os* infectivity factor 2

Ac22 encodes the 43.8 kDa (382 aa) PIF-2 protein conserved in all baculoviruses and essential for oral infectivity of midgut cells (223). Hence, PIF-2 is a *per os* infectivity factor. PIFs are not needed when the virus is injected into the hemolymph (as for all four known baculovirus PIF proteins). Proteomic analysis showed the presence of PIF-2 in ODVs (20) and it has

a predicted N-terminal membrane anchor (249). PIF-2 is thought to be involved in binding of ODVs to midgut epithelial cells, and possibly associates with PIF-1 (203). PIF-2 is a highly conserved protein belonging to the baculovirus core genes and is often used in baculovirus phylogeny.

Ac23*: ac23,* copia-like envelope protein

The gene *ac23* is a truncated, non-functional homolog of the baculovirus F-protein present in group II NPVs of the Alphabaculoviruses and in Beta-, and Deltabaculoviruses. The F-protein homolog or F-like protein Ac23 (79.9 kDa, 690 aa) does not function as fusion protein, as it lacks a functional furin cleavage site, but it may have other functions (219). An AcMNPV-mutant lacking *ac23* showed that the gene is not essential for either infection, virus propagation or BV production, but the mutant killed *T. ni* larvae slower than wild type virus, suggesting that the F-like Ac23 protein is a viral pathogenicity factor *in vivo* (173).

Ac24: *pkip,* protein kinase interacting protein

The gene *ac24* or *pkip* is a late gene and encodes a protein kinase-interacting protein (PKIP; 19.2 kDa, 169 aa) (62). PKIP interacts with PK-1 (see *ac10*) in virus-infected cells and stimulates activity of PK-1 (62). A temperature sensitive *pkip* mutant showed neither BV production nor VL gene expression, but intracellular nucleocapsids of this mutant structurally resembled those of the wild type AcMNPV (182).

Ac25: *dbp, ss*DNA-binding protein

Homologs of the *dbp* gene have been identified in all sequenced baculovirus genomes, except the dipteran CuniNPV (205). DBP (36.6 kDa, 316 aa) is expressed as an early gene product (204), which is essential for the production of viable virions. However, it is not required for synthesis of viral DNA nor for expression of viral genes (231, 267). DBP has a tight association with subnuclear structures and has high affinity for ssDNA. It has both DNA unwinding and renaturation activities and may be involved in the processing of replication intermediates (188).

Ac26: *ac26,* unknown function

The *ac26* gene encodes a protein with a theoretical molecular mass of 14.6 kDa (129 aa) and has a conserved domain with unknown function in the NCBI Conserved Domain Database (CDD) (176). The gene appears to be transcribed (287), but the function remains unclear. The majority of the homologs can be found in Alphabaculoviruses (Table 2).

Ac27: *iap-1,* inhibitor of apoptosis

The gene *iap-1* encodes a protein (33.3 kDa, 286 aa) containing an imperfect 70-amino acid repeat, called a baculovirus IAP repeat (BIR) at the N-terminus and an additional Cys_3-His-Cys_4 (C3HC4) zinc or RING-finger-like motif at the carboxyl-terminus (79). *Ac27* was named *iap-1* on the basis of homology to the *Cydia pomonella* (Cp) GV *iap* gene (43). Expression of *iap-1* does not block the induction of apoptosis by AcMNPV *p35 (ac135)* deletion mutants (36). The gene is transcribed early and late after infection as a part of a bicistronic mRNA, which also includes *lef-6* (*ac28*) sequences (214). Spontaneous deletion in the *Pst*I-I fragment harbouring the *iap-1* gene occurs during serial passage of the virus (139). Three spontaneous recombinant viruses with different mutations showed no abnormalities in the rate of replication and the amount of BV and ODV produced in cell culture (181). However, in competition-assays, the mutant lacking *iap-1* has a replication advantage over wild type AcMNPV in TN-368, but not in Sf21 cells (181).

Ac28: *lef-6,* late expression factor 6

Lef-6 is transcribed into a monocistronic mRNA at 9 h p.i. and at 12 h p.i, but *lef*-6 is transcribed together with *iap-1* as a bicistronic mRNA at 12 h p.i. (214). LEF-6 is most abundant between 12 and 24 h p.i. (156). Furthermore, LEF-6 (calculated mass 20.4 kDa, 173 aa) is localized in the nuclei of infected cells (156) and is involved in expression of L and VL genes (214). LEF-6 is not essential for viral reproduction, DNA replication or late transcription in Sf9 cells. However, late gene transcription and the production of BVs were delayed and reduced (156).

Ac29: *ac29,* unknown function

The gene *ac29* encodes a hypothetical protein with calculated mass of 8.6 kDa (71 aa). The gene is transcribed (287), but its function is not described in the literature. Homologous genes are present in the majority of Alphabaculoviruses (Table 2).

Ac30: *ac30,* unknown function

The *ac30* gene codes for a protein (54.7 kDa, 463 aa) with unknown function. Transcripts are present during viral infection (287). Homologous are present in some but not all Alpha- and Betabaculoviruses (Table 2 and Table 3).

Ac31: *sod,* superoxide dismutase

Transcription of the *sod* gene results in two RNAs of 1.4 and 1.5 kb which are detectable at 24-48 h and 12-48 h p.i., respectively (263). The encoded superoxide dismutase (16.2 kDa, 151 aa) is not essential for virus replication in cell culture or in larvae (263). Homologs are found in almost every Alphabaculovirus and in a few Betabaculoviruses (Table 2 and Table 3). The *sod* gene, therefore, may have an important function in the Alphabaculovirus' life cycle (109).

Ac32: *fgf,* fibroblast growth factor

The *fgf* gene encodes a fibroblast growth factor homolog (FGF; 20.6 kDa, 181 aa) and homologs are only present in baculoviruses that infect lepidopteran insects (Alpha- and Betabaculoviruses) (48). FGFs have an important role in angiogenesis, cell proliferation, differentiation, and cell migration (110). AcMNPV FGF is also functional in cell culture, as it is secreted and able to enhance cell migration (48). An *fgf* deletion mutant showed no differences in production of infectious BV nor in DNA replication in Sf21 cells nor did the mutant have a replication advantage (50). In insect larvae of *S. frugiperda* and *T. ni* death was delayed compared to the wild type virus with oral feeding, but not with intrahemocoelic injection (49). These results suggest that FGF plays a role in the systemic spread of the virus from the midgut (49).

Ac33: *hisp,* histidinol-phosphatase

The gene *hisp* codes for a protein (20.8 kDa, 182 aa) with putative histidinol-phosphatase activity due to the presence of a conserved haloacid dehalogenaselike hydrolase domain. The function of histidinolphosphatase is to catalyze the dephosphorylation of L-histidinol phosphate and such enzymes have been characterized mainly in prokaryotes (211). This gene is represented in the transcriptome (287).

Ac34: *ac34,* unknown function

The gene *ac43* encodes a hypothetical protein of 24.9 kDa (215 aa) with a conserved domain with unknown function according to the CDD database (176). Homologs are found in all Alphabaculoviruses except *Spodoptera litura (Splt)* NPV (Table 2).

Ac35: *v-ubi,* viral ubiquitin

The gene *v-ubi* encodes the viral ubiquitin (V-UBI) protein (8.7 kDa, 77 aa). The protein has 70% identity to eukaryotic ubiquitin proteins and is produced at

maximal levels between 14 and 18 h p.i., indicating that the gene is a late gene (82). The gene has been classified as an auxiliary gene and the encoded ubiquitin is likely involved in signaling the degradation of proteins by the 26S proteome (197). Homologs are present in all Alpha- and Betabaculoviruses except *Leucania separate (*Ls)NPV (Table 2 and Table 3).

Ac36: 39K/*pp31*, nuclear matrix associated phosphoprotein

The gene *pp31* (also known as 39K) encodes a phosphoprotein (31.3 kDa, 112 aa) that can bind in a non-specific way to ssDNA and dsDNA with equal affinity and is essential for late gene expression, *i.e.* it serves as a late expression factor (22, 86). In addition, a *pp31*-null mutant was prepared of AcMNPV, and microarray and quantitative PCR showed that *pp31* is not essential for viral DNA replication. However, the deletion resulted in a minor down-regulation of a subset of both early and late genes and, as for BmNPV (77), in decreased BV production (287).

Ac37: *lef-11*, late expression factor 11

Lef-11 codes for the late expression factor-11 (LEF-11) with a calculated mass of 13.1 kDa (112 aa). Its messenger RNA is present from 3 to 36 h p.i., while LEF-11 is detected until 72 h p.i. and localizes within a dense region of infected nuclei (158). LEF-11 is not essential for DNA replication in transient replication assays (169), but is necessary for the activity of late gene promoters (262). An AcMNPV *lef-11* null mutant was not able to replicate in Sf9 cells and late gene transcription was absent (157).

Ac38: *ac38*, ADP-ribose pyrophosphatase

The Ac38 protein (25.3 kDa, 216 aa) has homology with proteins in the *Nudix* (*nu*cleotide *di*phosphate *X*) superfamily of pyrophosphatases and contains the conserved *Nudix* motif: $GX_5EX_7REUXEEX_2U$ (U: I, L or V, and X: any amino acid). Within this superfamily, the Ac38 protein shows the closest phylogenetic relationship with ADP-ribose pyrophosphatases (ADPRases). Recombinant Ac38 indeed has *in vitro* ADPRase activity (70). Transcripts of *ac38* are detectable from 2 h p.i. and the level increases during the late stage of infection. Deletion of *ac38* decreases the yield of BV to less than 1% of the wild type virus (70). So far, the gene is conserved in all Alpha- and Betabaculoviruses (Table 2 and Table 3).

Ac39: *p43*, ODV protein of unknown function

The 43.5 kDa protein P43 (363 aa) encoded by the gene *ac39*, is present in the proteome of ODVs (20). No putative conserved domains have been detected and its function other than being an ODV protein is still enigmatic. Homologs are present in seven NPV genomes.

Ac40: *p47*, transcription regulator

The *ac40* gene product has a molecular mass of 47.5 kDa (P47;401 aa) and belongs to the group of factors required for late gene expression (262). Moreover, the gene *p47* together with three other genes *ac50, ac62* and *ac90* - coding for *lef-8, lef-9* and *lef-4*, respectively - form a RNA polymerase complex that transcribes late and very late viral genes (88), while early genes are transcribed by the host RNA polymerase II (106). P47 directly binds to all other subunits of the late viral RNA complex, as well as to itself, and P47 is required for the association of LEF-4 with LEF-8 (44). *Ac40* is a baculovirus core gene.

Ac41: *lef-12*, late expression factor 12

Ac41 encodes late expression factor 12, LEF-12 (21.1 kDa, 181 aa), which stimulates late gene expression in transient assays in a cell type specific manner

(167). In a virus context, *lef-12* is neither essential for virus replication nor for expression of late genes, but it has a stimulatory affect on late gene expression levels and virus yield (85). L*ef-12* expression depends on DNA replication and the mRNA is synthesized by 12 h p.i. LEF-12 protein is first detected 18 h p.i. and peaks at 24 to 36 h p.i., (85). The expression of *lef-12* is diminished when it is not present in *cis* with sequences present within the nearby ORF *ac45* (149).

Ac42: *gta*, global transactivator-like protein

The *ac42* gene encodes a putative 59.1 kDa (506 aa) global transactivator-like protein (GTA) and homologs are found only in group I NPVs (Table 2). Baculovirus GTA proteins contain conserved regions belonging to the SNF2-N terminal domain and the helicase C-terminal domain superfamilies (142). The presence of these domains suggests a role in ATP-dependent DNA unwinding. In *Choristoneura fumiferana* (Cf) MNPV, the region upstream of the *gta* gene has an early CAGT promoter motif and a transcript is detectable at 6 h p.i. (142). Baculovirus consensus promoter motifs are absent in the AcMNPV *gta* upstream sequence.

Ac43: *ac43,* unknown function

Ac43 represents a small ORF, that contains the code for a late gene product of 8.8 kDa (77 aa) (9). Microarray analysis showed transcripts from this part of the genome (287).

Ac44: *ac44,* zinc finger protein with unknown function

Ac44 is a putative early gene encoding a 15.0 kDa (131 aa) protein with a zinc finger motif (9), suggesting a role in DNA binding. Transcripts from this ORF have been demonstrated by microarray analysis (287). The homolog in BmNPV (Bm35) contains a region rich in C and H residues, resembling RING-finger motifs. Such motifs are found in ubiquitin-ligase (E3), but Bm35 may have a different function since it tested negative for E3 activity (111).

Ac45: *ac45,* unknown function

Ac45 encodes a predicted protein of 22.7 kDa (192 aa) with unknown function. The presence of the *ac45* ORF stimulates expression of *lef-12 (ac41)* (149). This stimulatory effect is only observed when provided in *cis*, suggesting that the *ac45* region acts either as an enhancer of *lef-12* transcription or produces an as yet unobserved protein as a result of mRNA splicing, combining *ac45* and *lef-12* sequences (149).

Ac46: *odv-e66*, occlusion-derived virus envelope protein

ODV-E66 (predicted mass 79.1 kDa, 704 aa) is an integral ODV envelope protein that like ODV-E25 (*ac94*), is N-terminally anchored in the envelope (104, 239). ODV-E66 is not required for BV production (240). The N-terminal region of AcMNPV ODV-E66 enables trafficking of marker proteins to intranuclear membranes and the ODV envelope (104). This region has two features: (*i*) a hydrophobic sequence of 18 aa and (*ii*) positively charged amino acids close to the C-terminal end of the hydrophobic sequence. The latter may comprise a sorting motif for selection of proteins to the inner nuclear membrane (21).

Ac47: *ets*, unknown function

The 88-codon *ets* ORF has the ability to encode a 10.5 kDa protein (88 aa), and shows sequence homology to a small part of the vesicular stomatitis virus RNA polymerase gene (similarity 50% for a 250 bp region) (42). The *ets* gene represents the smallest ORF in a polycistronic unit in the *Eco*RI-T fragment (hence its name). The other ORFS in this unit are with ORFs *ac48* or *etm,* the medium-sized ORF, and *ac49*

(*etl/pcl)* for the largest ORF in the unit), as further described below in the context of *ac49.*

Ac48: *etm*, unknown function

The gene *etm* encodes a putative 12.9 kDa (113 aa) hydrophobic protein with unknown function (42). It is part of a polycistronic unit with ORFs *ac48* and *ac49*, as outlined in detail under *ac49.*

Ac49: *pcna,* proliferating cell nuclear antigen

The *pcna* gene (previously *etl*) encodes a 28.6 kDa protein (256 aa) with 42% amino acid identity to rat proliferating cell nuclear antigen (198). The gene *pcna* forms the largest ORF in a putative polycistronic unit comprising *pcna*, *etm* (*ac48)* and *ets (ac47*). The largest and most predominant transcript from this region is an early 1.7 kb poly $(A)^+$ RNA, which contains each of the three tandem, non-overlapping ORFs. Smaller (0.5 kb) heterogeneous transcripts are also observed from the cistron, corresponding to *ets (ac47)*. Both the 1.7 and 0.5 kb transcripts are present at 4 h p.i.. Whilst the 1.7 kb transcripts are shut off at 12 h p.i., the levels of the smaller transcript persist until late after infection (42). Cellular PCNAs colocalize with viral DNA replication sites and complement viral PCNA in *pcna*-defective viruses (113). In transient replication assays, PCNA did not stimulate DNA replication (133, 149), nor is it essential for virus replication, at least in proliferating cell cultures (198).

Ac50: *lef-8,* late expression factor 8

The gene *lef-8* encodes the late expression factor 8 (101.8 kDa, 876 aa), which is the largest subunit of the RNA polymerase complex (see *ac40*). LEF-8 harbors a conserved sequence motif GXKX4HGQ/NKG found in DNA-directed RNA polymerases (217). LEF-8 directly associates with LEF-9 (*ac62*), the other protein with RNA polymerase motifs and with P47 (*ac40*) (44). LEF-8, like all other RNA polymerase subunits, is encoded by a baculovirus core gene.

Ac51: *ac51,* BJDP (unknown function)

The early gene *ac51* encodes a predicted (37.5 kDa, 318 aa) protein. A transcript has been demonstrated by microarray analysis, however its function remains unknown (287). The ortholog *splt39* from SpltNPV is a late gene and encodes a protein described as baculovirus J domain protein (BJDP). It has a predicted coiled-coil domain and RNA recognition motif, and is present in both ODVs and BVs (273). AcMNPV ODVs do not contain detectable amounts of Ac51 protein (20), which appears to be in line with the early promoter motifs of this ORF.

Ac52: *ac52,* unknown function

The gene *ac52* is putatively an early gene for a 14.9 kDa (123 aa) protein. A detectable mRNA transcript from this ORF was found in microarray analysis (287).

Ac53: *ac53,* unknown function

Ac53 is located in a gene cluster of five ORFs (*ac53, lef-10 (ac53a*)*, vp1054 (ac54*)*, ac55* and *ac56*), which all have the same clock-wise orientation. This cluster is conserved in many group I NPVs (160). In BmNPV many overlapping, 3'co-terminal mRNAs are transcribed from this region (2). Deletion of *ac53* affects BV formation. Tubular, incomplete capsid-like structures lacking nucleic acids are present, although DNA replication is not affected (160). Therefore, the encoded 17.0 kDa (139 aa) protein is most likely involved in nucleocapsid assembly and may have a role in condensation or packaging of viral DNA. Its crucial role is reflected by the presence of *ac53* orthologs in all sequenced lepidopteran and hymenopteran

baculovirus genomes (Table 2 and Table 3). The homologous protein encoded by BmNPV (Bm42) is present in BVs, but is absent in ODVs (2).

Ac53a: *lef-10,* late expression factor 10

The gene *lef-10* belongs to the group of 18 genes that support late gene expression (262). The exact function is unclear, but the LEF-10 protein (8.6 kDa, 78 aa) might be involved in promoter recognition, stabilization of late transcripts or could be associated with the virus-induced RNA polymerase complex (169). The gene has been classified as an auxiliary factor in the transcription process (97).

Ac54: *vp1054*, VP1054 viral capsid-associated protein

The *vp1054* region produces multicistronic mRNAs from early to very late times after infection (209). VP1054 is a 42.1 kDa (365 aa) structural protein present in both BVs and ODVs required for nucleocapsid formation (209). VP1054 interacts with the 38K protein (*ac98*) in infected cells (281) and is encoded by a baculovirus core gene

Ac55: *ac55,* unknown function

Ac55 is an early gene for a hitherto unidentified 8.2 kDa (73 aa) protein without known domains. A mRNA from this ORF has been demonstrated (287).

Ac56: *ac56,* unknown function

Ac56 encodes a small putative protein of 9.9 kDa (84 aa) protein for which no conserved domains have been found. A transcript from this ORF was found by microarray analysis (287).

Ac57: *ac57,* unknown function

Ac57 is a putative early gene encoding a 19.0 kDa.(161 aa) protein. Microarray studies revealed a transcript from this ORF (287). The Ac57 protein and its orthologs in other Alphabaculoviruses form the DUF918 superfamily (176), but this gives no further clues concerning its function.

Ac58/59: *ac58/59*, ODV protein of unknown function:

In the closely related *Rachoplusia ou* (Ro)MNPV the *ac58* and *ac59* orthologs are fused into one ORF of 172 codons (92). This is also the case in *e.g.* BmNPV. Partial resequencing of the AcMNPV C6 strain confirmed that *ac58* and *ac59* are in fact one ORF (92). *Ac58/59* encodes a 20.3 kDa (172 aa) protein. Ac58/59 specific peptides were found within or associated with the ODVs by proteomic analysis (20). Ac58/59 belongs to the ChaB superfamily, originally known in *E. coli* in combination with ChaA, a cation transporter. The role of ChaB proteins in baculoviruses is unclear.

Ac60: *ac60,* unknown function

Ac60 was predicted by sequence analysis to potentially encode a 10.1 kDa (87 aa) protein (9). Transcript levels from this ORF were reduced by 72% in a *pp31* (*ac36*) deletion mutant (287). As in the Ac58/59 protein, Ac60 contains a ChaB superfamily domain.

Ac61: *fp/25k,* FP protein

FP25K (25.2 kDa, 214 aa) is a structural protein of BVs and ODVs (16). *Ac61* mutants show a reduction in polyhedrin transcripts, but have wild type *p10* expression levels (93). Mutations in FP25K also reduce *ODV-e66* expression and transport of ODV- E66 protein to the nucleus is inhibited (16). A more general role has been proposed for FP25K in targeting and intracellular transport of viral proteins during infection (16). In BmNPV it has been shown that FP25K is required for maintaining transcriptional regulation and efficient secretion of V-CATH and maintaining a steady-state level expression during secretion (125).

During serial passage of AcMNPV in cultured insect cells spontaneous mutants occur having the "few polyhedral" (FP) phenotype. This is the result of frequent transposon insertions in this area (10). These mutants have typical characteristics (94), including a reduced number of occlusion bodies, no envelopment of nucleocapsids within the nucleus and enhanced BV production.

Ac62: *lef-9,* late expression factor 9

The protein LEF-9 has a molecular mass of 59.3 kDa (516 aa) and is required for late and very late gene expression (168). LEF-9 contains RNA polymerase motifs and is an essential subunit of the RNA polymerase complex encoded by AcMNPV. Mutations in the conserved RNA polymerase motif showed the requirement of conserved asparagine residues (44) LEF-9 and LEF-8 interact directly (44) (see also *ac40*).

Ac63: *ac63*, unknown function

The Ac63 protein has a predicted mass of 18.5 kDa (155 aa) and does not contain any known conserved domains. Homologs are present in several Alphabaculoviruses (Table 2).

Ac64: *gp37,* spindle body protein or GP37

ORF ac63 encodes a glycoprotein with a predicted molecular mass of 34.8 kDa (P34.8, 302 aa) and is a homolog of the OpMNPV spindlin, which in that virus is a component of OBs (80). Baculovirus GP37 proteins are homologous to entomopoxvirus fusolins (221). Disrupting the gene in AcMNPV showed that the gene is not essential for virus replication nor affects virulence or speed of kill (34).

Ac65: *dnapol,* DNA polymerase

The *ac65* gene codes for DNA polymerase (114.3 kDa, 984 aa) and is conserved among all baculoviruses. It is disputable whether it is essential for DNA replication in transient replication assays (133) or only stimulatory (169). Vanarsdall *et al*. (269) have shown using quantitative PCR (qPCR) that an AcMNPV-bacmid lacking *dnapol* cannot replicate its DNA in Sf9 cells.

Ac66: *ac66,* desmoplakin-like (ODV protein of unknown function)

The gene *ac66* encodes a protein of 94.0 kDa (808 aa) and contains two conserved domains: a viral desmoplakin N-terminal domain and a CorA-like Mg^{2+}-transporter region, respectively. Desmoplakin is the major component of desmosomes (253), which have a strong adhesive nature. They are involved in intercellular adhesion and participate in cell proliferation, differentiation and morphology (69). The CorA family consists of a group of membrane transporters of metal ions, abundant in prokaryotes, which can also be found in humans and yeast (196). The protein has been found in ODV nucleocapsids, but the exact localization is unknown (20). An *ac66*-null mutation resulted in depleted BV production due to inefficient transport of nucleocapsids from the nucleus to the cytoplasm. However, *ac66* is not required for the formation of the nucleocapsids, but appears to be involved in pre-occluded virion and occlusion body formation (126).

Ac67: *lef-3,* late expression factor 3

The *lef-3* gene is essential for DNA replication in transient replication assays (133). The 44.6 kDa (385 aa) LEF-3 protein binds to ssDNA (90). LEF-3 forms, together with P143 (helicase; see *ac95*) and IE-1 (see *ac147*), complexes with viral chromatin in infected cells (112). It has been proposed that LEF-3 interacts with P143 to stabilize the formed ssDNA after

unwinding by the P143 helicase (112). LEF-3 also mediates nuclear localization of P143 (284) due to a nuclear localization signal domain which is required for interaction between LEF-3 and P143 (8).

Ac68: *ac68,* unknown function

All baculovirus genomes sequenced to date carry a homolog of the AcMNPV *ac68* gene (Table 2 and Table 3), suggesting that it performs an important role in baculovirus biology. The conserved sequence is assigned as DUF708 domain, with unknown function (176). *Ac68* is transcribed from 3 to 96 h p.i. and the gene product (22.3 kDa, 192 aa) was detected from 36 to 96 h p.i. (148). Deletion of *ac68* did not affect production of infectious BVs, nucleocapsid or OB formation, nor did deletion of *ac68* change the time to kill *in vivo* (148).

Ac69: *mtase1*, MTase1

Ac69 is a late gene (283) and its 30.4 kDa (262 aa) product stimulates late gene expression *in vitro* (149). The protein is homologous to *E. coli* FtsJ (148), an RNA methyltransferase and also has an S-adenosylmethionine (AdoMet)-methyltransferase domain. The protein binds AdoMet *in vitro* and has (nucleoside 2′-O)-methyltransferase activity, allowing coupling of methyl groups to RNA (283). Disruption of the *ac69* gene does not affect virus replication in single-step growth curves (283), but the effect *in vivo* has not been analyzed.

Ac70: *hcf-1,* host cell-specific factor 1

The gene *hcf-1* encodes a 34.4 kDa (290 aa) protein involved in the expression of late and very late gene promoters. HCF-1 is absolutely required for virus replication and late gene expression in TN-368 cells, and its absence is accompanied by a block in cellular and viral protein synthesis (170). In *T. ni* larvae a *hcf-1* mutant, shows a reduced speed of kill. In Sf21 cells and in *S. frugiperda* larvae replication of *hcf-1* mutants is not different from that of the wild type virus, hence the name host cell-specific factor (170).

Ac71: *iap-2,* apoptosis inhibitor

The gene *iap-2* encodes a putative apoptosis inhibitor (28.6 kDa, 249 aa). It contains the conserved RING-finger like-motifs present in all *iap* genes, but not a BIR repeat region (79). Deletion of either *iap-1* (*ac27*) or *iap-2,* or the simultaneous deletion of both genes did not have an effect on the replication of the virus in Sf21 cells (79). Whether it has a role in inhibiting apoptosis remains unclear. In other NPVs IAPs have been shown to inhibit apoptosis (36).

Ac72: unknown function

Homologs of *ac72* are only found in genomes of Alphabaculoviruses (Table 2). The role of this transcribed gene encoding a 7.1 kDa (60 aa) protein (287) is not known.

Ac73: *ac73,* unknown function

Homologs of the predicted gene *ac73* (11.5 kDa, 99 aa protein) are present in genomes of several other members of the genus *Alphabaculovirus* (Table 2). Information about the (putative) function of *ac73* in the viral life cycle is not available, but transcripts are made (287).

Ac74: *ac74,* unknown function

Homologs of *ac74* (30.6 kDa, 265 aa) are present in many but not all Alphabaculoviruses (Table 2), but the function of *ac74* remains unknown. RNA copies have been found for this ORF (287).

Ac75: *ac75,* unknown function

Homologs of *ac75* can only be found in genomes of Alphabaculoviruses (Table 2). The predicted gene product has a molecular mass of 15.5 kDa (133 aa)

and transcripts have been detected with micro-arrays (287). There is no publication about the role of *ac75* in baculovirus biology.

Ac76; *ac76,* unknown function

Homologs of *ac76* can be found in genomes of all Alphabaculoviruses (Table 2). The predicted gene is transcribed (287) and encodes a hypothetical protein of 9.4 kDa (84 aa). No data about the role of *ac76* in the baculovirus replication cycle are available.

Ac77: *vlf-1,* very late expression factor 1

Ac77 or the *vlf-1* gene is involved in the expression of the very late genes *p10* and *polh* (183, 288). The gene is transcribed in the late phase of infection – from 15 to 24 h p.i. The VLF-1 protein (44.4 kDa, 379 aa) is localized in the nucleus of infected cells and in nucleocapsids of both BV and ODV (289). Deletion of the *vlf-1* gene results in defective BV production, but this is not due to impaired DNA replication as the *vlf-1* mutant is still able to replicate DNA, although at a lower level (268). When infected with a *vlf-1* null mutant neither nucleocapsids nor occlusion bodies are produced (153). VLF-1 may be involved in viral DNA processing as the protein sequence of VLF-1 shows similarity to integrases and resolvases (153, 183). Integrases belong to a family of tyrosine recombinases, which can arrange DNA duplexes by site-specific recombination (60). DNA replication of most likely AcMNPV is based on concatemer formation (147) and if true, VLF-1 might be involved in processing the concatemers before the DNA is packaged into nucleocapsids (153). *Ac77* is a baculovirus core gene.

Ac78: *ac78,* unknown function

The *ac78* gene product is a hypothetical protein (12.5 kDa, 109 aa) with a conserved DUF912 domain (176), which occurs in homologous NPV proteins, but gives no indication for the function *of ac78.* The gene is conserved among all Alphabaculoviruses (Table 2).

Ac79: *ac79,* unknown function

The *ac79* gene encodes a hypothetical protein (12.2 kDa, 104 aa) with a conserved endonuclease GIYYIG catalytic domain. This domain shows similarity with bacteriophage T4 *segA-E* genes and with group I introns of fungi (245). The GIY-YIG motif belongs to the homing endonuclease family, members of which catalyze double-stranded breaks in DNA to facilitate homing of introns (235). Orthologs of *ac79* are found in several Alphabaculoviruses (Table 2), but its function in baculovirus biology remains enigmatic.

Ac80: *gp41*, tegument protein

The gene *gp41* is expressed as a late gene with transcripts starting within two consensus late transcription start sites (TAAG), located immediately upstream of the first ATG codon (276). The 41 kDa protein (predicted molecular mass 45.4 kDa, 409 aa) has O-glycosidically linked N-acetylglucosamine (GlcNAc) residues and is present between the envelope membrane and the nucleocapsids of ODVs (277). A thermosensitive (*ts) gp41* mutant causes single-cell-infections, which progress through the very late phase including the formation of OBs. However, infection does not spread to neighboring cells (210), indicating that BV production is affected in the *ts*-mutant, although GP41 is only found in ODVs (277). *Ac80* is conserved in all baculovirus genomes.

Ac81: *ac81,* unknown function

The *ac81* gene is highly conserved and belongs to the baculovirus core genes. The gene product has a predicted mass of 26.9 kDa (238 aa) and the homologous protein in BmNPV (Bm67) is detected neither in BVs nor ODVs. Immunofluoresence analysis

showed that the Bm67 protein is present in the cytoplasm and interacts with the host protein actin A3 (31). Bm67 is required for the production of infectious BV (71). *Bm67* mutations negatively affect viral DNA synthesis and the stability of nascent viral DNA. Nucleocapsids with a wild type morphology are hardly found and nucleocapsids are only occasionally exported to the cytoplasm. The envelopment of nucleocapsids is also abnormal with these *Bm67* mutants (71).

Ac82: *tlp,* telokin-like protein-20

The gene a*c82* encodes a protein with a predicted molecular mass of 20 kDa (19.8 kDa, 180 aa). In Western blot analysis it shows a size of 28 kDa and reacts with an antibody specific against the smooth muscle protein telokin, hence the name telokin-like protein or TLP (232). However, no amino acid sequence similarity exists between TLP-20 and telokin. 3-D structure analysis of TLP-20 showed a seven-stranded antiparallel β-barrel flanked on the basis by two additional β-strands and on the top by an α-helix. As such, TLP-20 does not resemble the structure of any other known protein (101).

Ac83: *p95,* viral capsid associated protein, VP91

The gene *p95* encodes a protein (96.2 kDa, 847 aa), with two conserved domains: a viral capsid protein 91 and a chitin-binding peritrophin-A domain, respectively. The *p95* gene belongs to the baculovirus core genes (Table 2 and Table 3). VP91 is associated with the capsid and envelope of ODVs (240). The second conserved domain belongs to the family of chitin peritrophic binding proteins and is able to bind chitin, which is present in a matrix lining the gut of most insects (58, 246).

Ac84: *ac84,* unknown function

The gene *ac84* codes for a hypothetical protein (21.7 kDa, 188 aa) without any known conserved domain. The gene is transcribed (287).

Ac85: *ac85,* unknown function

The *ac85* gene product is a hypothetical protein with a mass of 6.4 kDa (53 aa) and homologs are only present in RoMNPV and *Plutella xylostella* (Px) MNPV (Table 2). The *ac85* gene is transcribed (287).

Ac86: *pnk/pnl* polynucleotide kinase/ligase

The gene *pnk/pnl* is an immediate early gene encoding a protein (80.8 kDa, 694 aa) that contains two conserved domains: a kinase and a T4 RNA ligase domain (55). Deletion of *pnk/pnl* has no effect on virus replication in Sf21 cells or on protein production (55). The effect in pathogenesis in larvae is unknown.

Ac87: *p15,* unknown function

The gene *p15* codes for a 15.0 kDa protein (126 aa) of unknown function. The protein does not contain known conserved domains, but homologs can be found in eight other Alphabaculoviruses (Table 2). For BmNPV P15 a function as a viral capsid protein was proposed due to high similarity with other viral capsid proteins. The transcription of the *bm70* gene is regulated in time with a short early and a longer late transcript (171).

Ac88: *cg30;* unknown function

The *ac88* gene product (30.1 kDa, 264 aa) harbors a zinc-finger-like and a leucine zipper motif, a characteristic found in proteins involved in gene regulation (215). *cg30* is transcribed as an early monocistronic RNA and as the second cistron of an abundant late bicistronic RNA together with *vp39* (259), but a CG30-beta-galactosidase fusion protein was mainly observed early in the infection process (215). *cg30* is not essential for virus replication *in vitro* and *in vivo*,

but the wild type virus accumulated to slightly higher titers over the *cg30* deletion mutant after several passages in cell culture (215).

Ac89: *vp39,* major viral capsid protein VP39

The VP39 (39.0 kDa, 357 aa) is the most abundant structural protein of the nucleocapsid (260) with monomers arranged in stacked rings around the nucleoprotein core as reviewed in (249). VP39 is involved in the rearrangement and polymerization of host actin (28, 29). Recent results have shown that VP39 interacts with the 38K protein in infected insect cells (281). The *vp39* gene is transcribed at late time points in infection from a promoter sequence containing three A/GTAAG consensus motifs (maximal transcription 12–24 h p.i.) as a bicistronic mRNA together with *cg30* (259, 260). *Vp39* is a core gene.

Ac90: *lef-4,* late expression factor 4

The *lef-4* gene encodes the 55 kDa late expression factor 4 (predicted molecular mass 53.9 kDa, 464 aa) (54). LEF-4 is a subunit of the AcMNPV RNA polymerase (88) (see *ac40*) and is essential for late gene expression (132). LEF-4 has guanylyltransferase (84), RNA 5'- triphosphatase and ATPase activities (119), and appears to be a complete mRNA capping enzyme. The *lef-4* gene is present in all baculoviruses (Table 2 and Table 3).

Ac91: *ac91*, unknown function

Ac91 potentially encodes a 24.1 kDa (224 aa) protein expressed in the late phase of infection and the gene is transcribed (287). The protein has an N-terminus rich in hydrophobic amino acids, including a stretch of 7 iso-leucine residues, and a large central domain consisting of mainly proline, threonine and serine residues. The C-terminal domain, which is preceded by a methionine, is also present in some other baculoviruses, suggesting that the protein encoding region may be smaller than the entire ORF (not published).

Ac92: *ac92/p33,* unknown function, P33

Ac92 is a baculovirus core gene encoding a 33 kDa (predicted 30.9 kDa, 259 aa) protein (P33). Inactivation of this gene is lethal for the virus, indicating that *ac93* is an essential baculovirus gene (230). P33 forms a complex with the mammalian tumor suppressor protein P53, when AcMNPV is used as a *p53* gene expression vector, P33 also enhances P53-mediated apoptosis in insect cells (230). Flag-tagged P33 displays a diffuse cytoplasmic localization and punctuate nuclear staining in the absence of P53. In the presence of P53, P33 has an entirely nuclear localization. An insect *p53* homolog has been identified (208) and many DNA viruses encode a P53 binding protein. Mass spectrometry indicated that P33 may be present in ODV particles (20).

Ac93: a*c93,* unknown function

The *ac93* ORF is transcribed (287) and encodes a 18.4 kDa (161 aa) protein of unknown function, also named P18 in other baculoviruses. The conserved region is addressed as a DUF628 domain in the CDD (176).

Ac94: *odv-e25,* occlusion-derived virus envelope protein

ODV-E25 (25.5 kDa, 228 aa) is an integral ODV envelope protein, that is N-terminally anchored in the envelope (249). ODV-E25 is also present in BVs, but is much less abundant there than in ODVs (239). The ODV-E25 protein is initially present at a low concentrations, but is present at a higher levels from 36 h p.i. onwards (239). The N-terminal amino acid sequence of the protein (24 amino acids) is highly hydrophobic and this hydrophobic domain is sufficient

to direct ODV-E25 to virus-induced membrane microvesicles within the nucleus and the ODV viral envelope (104).

Ac95: *helicase,* DNA helicase

Ac95 is a baculovirus core gene and encodes a 143.2 kDa (1221 aa) polypeptide (P143) with a consensus NTP-binding site and six other motifs characteristic for helicase proteins. *Ac95* is a delayed early gene, which is transactivated by IE-1 (*ac147*) and PE38 (*ac153*) with a stimulatory role of IE-2 (*ac151*) (163). A *ts*-mutant showed the essential role of P143 in viral DNA replication (165) and this was further confirmed by transient replication assays (133). The AcMNPV helicase shows specificity for AcMNPV replication and cannot be exchanged with the SeMNPV helicase in transient DNA replication assays (98).

Ac96: *ac96,* unknown function

Ac96 is a baculovirus core gene encoding a 19.8 kDa (173 aa) protein. The BmNPV homolog Bm79 encodes a larger, 28 kDa protein, which is located in the ODV-envelope (ODV-E28) (286). The conserved region of Ac96 is indicated as the baculovirus 19 kDa protein superfamily domain. AcMNPV *ac96* is found within a four-gene cluster comprising of *helicase, lef-5, ac96,* and *38K (ac98).* The relative positions of these genes are conserved in all baculovirus genomes (100).

Ac97: *ac97,* unknown function

Ac97 is predicted to be an early gene encoding a 6.5 kDa (56 aa) protein. A transcript overlaps this ORF (287). Homologs of this gene with unknown function have not been found in other baculoviruses (Table 2 and Table 3).

Ac98: *38k*, 38K protein

The gene *ac98* encodes the protein 38K (38.0 kDa, 320 aa) which is synthesized in the late phase of infection. The 38K protein is localized and distributed over the cylindrical sheath of the nucleocapsid of both BVs and ODVs and is required for nucleocapsid assembly, but not for DNA replication (281, 282). Furthermore, it interacts with the nucleocapsid proteins VP1054 (*ac54*), VP39 (*ac89*), VP80 (*ac104*) and itself (281). The *ac98* belongs to the baculovirus core genes (Table 2 and Table 3).

Ac99: *lef-5,* Late expression factor 5

The gene *ac99* codes for the late expression factor LEF-5 (31.0 kDa, 265 aa), which has significant sequence similarity in a stretch of 32 C-terminal amino acids with a zinc ribbon domain in the eukaryotic transcription elongation factor TFIIS (95). Unlike the cellular TFIIS, LEF-5 functions most likely as a transcription initiation factor and stimulates transcription mediated by baculovirus RNA polymerase from late and very late viral promoters at least in *in vitro* transcription assays (83).. The N terminal 194 amino acids are involved in LEF-5:LEF-5 self interactions and the 32 C-terminal amino acids of LEF-5 contain a putative Zn^{2+}-ribbon domain (95). The acidic dipeptide DE within this domain is crucial for LEF-5 activity (83). *Lef-5* is a core gene (Table 2 and Table 3).

Ac100: *p6.9,* major DNA-binding protein

The most abundant protein in the nucleoprotein core is a small (6.9 kDa, 55 aa), very basic (pI=12), protamine-like protein named: Basic Protein or P6.9. The positively charged arginine residues of P6.9 interact with the viral DNA genome to mediate DNA condensation in the nucleocapsid (127). In infected cells P6.9 is phosphorylated, but in nucleocapsid assembly this phosphorylation is inhibited by the presence of Zn^{2+} (68). A model for this packaging has

been proposed: during packaging of viral DNA, P6.9 is dephosphorylated by cellular phosphatases followed by DNA condensation. Phosphorylation of P6.9 by a capsid-associated kinase results in unpackaging of the nucleocapsid upon entry into cells, allowing the onset of the infection cycle (68). *P6.9* is a baculovirus core gene.

Ac101: *p40*, BV/ODV-C42

The gene *ac101* is transcribed at the late stage of infection. It encodes a 42 kDa protein (41.5 kDa predicted molecular mass, 361 aa), which is a component of the nucleocapsid of both BVs and ODVs (18). There is strong evidence that ODV-C42 is capable of direct interaction with the WASP-like protein P78/83 (*ac9*) and ODV-EC27 (*ac144*) (18). ODV-C42 probably binds to the viral protein P78/83 in the cytoplasm to form a protein complex, which then migrates to the nucleus during AcMNPV infection due to the nuclear localization signal in ODV-C42 (274). A mutant virus lacking *ac101* is not able to propagate in cell culture as no mature nucleocapsids are formed, however, viral genome replication was not affected (270). Direct interaction between BV/ODV-C42 and a leucine zipper domain of EXON0 (*ac141*) enables egress of nucleocapsids from the nucleus to cytoplasm during the late phase of infection (64). Homologs of the gene *ac101* are present in all sequenced baculoviruses except CuniNPV (249) (Table 2 and Table 3).

Ac102: *p12*, transport of G-actin

The transcription of the gene coding for the 12-kDa protein (13.3 kDa predicted, 122 aa) initiates from the consensus baculovirus late transcription start site (ATAAG) (166). Attempts to prepare a *p12*-mutant were not successful, suggesting that the gene is essential for virus replication in cell culture (166). Together with the products of the genes *ie-1 (ac147*), *pe38 (ac153*), *he65 (ac105*), *ac4,* and *ac152,* P12 is involved in transport of G-actin into the nucleus during baculovirus infection (202).

Ac103: *p48,* unknown function

The 5' end of the *p48* transcript maps to consensus baculovirus late transcription start sites (ATAAG) (166). Attempts to prepare *p48* mutant viruses were not successful suggesting that the gene is essential for virus replication in cell culture (166). More recently, detailed analysis of a *p48* deletion mutant confirmed that this gene is essential for BV production and ODV envelopment (290). Homologs of *ac103* can be found in the genomes of all Alpha-, Beta- and Gammabaculoviruses (Table 2 and Table 3).

Ac104: *vp80*, capsid-associated protein VP80

A late 2.1 kb transcript was mapped to *ac104* which encodes a 79.9 kDa protein (691 aa). VP80 is a structural capsid-associated protein as confirmed with anti-BV sera (164). VP80 interacts with the viral protein, 38K (see *ac98*) (281). In BmNPV, VP80 is essential for BV production and nucleocapsid maturation. The BmNPV *vp80* could not functionally be replaced by AcMNPV *vp80* (256). In the case of *Choristoneura fumiferana* (Cf) MNPV, the VP80 protein appears as a 82 kDa protein in samples from ODVs and as an 72/82 kDa doublet from BVs (151). Homologs of the *vp80* gene are only found in Alphabaculoviruses (Table 2).

Ac105: *he65,* HE65 protein

The designation *he65* stems from the size of the predicted protein (65.6 kDa, 553 aa) and the genomic location of this ORF, being flanked by an *Eco*RI site and the *hr*4 left region. *He65* is a delayed early gene and mRNA is detectable from 2 h p.i.. Transcript

levels remain stable into the late phases of infection (12). HE65, together with Ac102, mediates nuclear localization of monomeric G-actin, a process promoting nuclear F-actin formation, which is required for progeny virus production (202). Localization of G-actin within the nucleus is a temporally regulated process. Transactivators encoded by *ie-1 (ac147*), *pe38 (ac153*), *ac4* and *ac152* are essential for expression of *he65* and *ac102* (202).

Ac106/107: *ac106/107,* unknown function

Partial resequencing of AcMNPV showed that the original *ac106* and *ac107* together form one ORF (92). The combined ORF encodes a 28.3 kDa (243 aa) protein and has homologs in all Alpha- and Betabaculoviruses (Table 2 and Table 3) (100). Together these homologs form the DUF816 superfamily (176), a family of baculovirus proteins with unknown function.

Ac108: *ac108,* P11 protein

Ac108 is a putative late gene, expressing a 11.8 kDa (105 aa) protein belonging to the baculovirus 11 kDa protein family according to the CDD database (176). Its homologs in *Antheraea pernyi* (Anpe)NPV and SpltNPV are ODV structural proteins, with envelope localization shown for SpltMNPV P11 (32, 247). Association with ODVs has not been found for Ac108 (20). *P11* is transcribed from a late promoter motif in AnpeNPV and from an early promoter in SpltNPV, with concordant differences in initiation of transcription.

Ac109: *ac109,* occlusion derived structural protein

The *ac109* gene belongs to the baculovirus core genes. It encodes a 44.8 kDa (390 aa) protein which is present within or associated with the ODV (20). Its homolog in *Helicoverpa armigera* (Hear)NPV (*ha94*) is a late gene encoding the structural ODV component ODV-EC43 (66). The conserved part of this protein is known as DUF673 domain according to the CDD database (176).

Ac110: *ac110,* unknown function

Ac110 codes for a small 6.8 kDa (56 aa) protein of unknown function. Homologs are present in all Alpha-baculoviruses and most Betabaculoviruses (Table 2 and Table 3) and the conserved part of the protein is designated as DUF1448 domain (176). Transcripts from this region have been reported (287).

Ac111: *ac111,* unknown function

The gene *ac111* is probably an early gene encoding a 8.2 kDa (67 aa) protein with undetermined function. The ORF is represented in the transcriptome of Ac-MNPV (287). Homologs of this ORF form the baculovirus 8 kDa gene family (176) with members in various Alpha- and Betabaculoviruses (Table 2 and Table 3).

Ac112/113: *ac112/113,* unknown function

The ORF *ac112* encodes a protein (30.9 kDa, 258 aa) with a zinc finger motif (9). Homologs are present in a few baculovirus genomes and in Fowl pox virus (FPF217) (4). The homologs of *ac112* and *ac113* are fused into one ORF in RoMNPV and re-sequencing showed that this is also the case in AcMNPV C6 (92). The function of this ORF is unknown.

Ac114: *ac114,* unknown function

The gene *ac114* codes for a protein with a predicted mass of 49.3 kDa (424 aa). Ac114 was detected in the capsid of ODVs (20). The gene is unique for group I NPVs and contains a conserved domain belonging to the DUF1098 superfamily of unknown function (176).

Ac 115: *pif-3, per os* infectivity factor 3

PIF-3 is a 23.0 kDa (204 aa) baculovirus core protein required for oral infectivity of larvae. It has a

predicted N-terminal transmembrane domain and is located most likely on the inside of the ODV envelopes (249). PIF-3 does not affect ODV binding or envelope fusion with larval midgut cells, but may play a crucial role further downstream in the infection process (203).

Ac116: *ac116,* unknown function

The putative gene product encoded by *ac116* is 6.4 kDa (58 aa) and homologs are only present in the closely related BmNPV, *Plutella xylostella* (Plxy) MNPV and RoMNPV (Table 2). The function of the transcribed *ac116* gene (287) is unknown.

Ac117: *ac117,* unknown function

The gene is transcribed (287) and codes for a putative protein with a molecular mass of 11.0 kDa (95 aa). Homologs are present in several other members of the genus *Alphabaculovirus* (Table 2).The function of *ac117* in the viral life cycle is not known.

Ac118: *ac118,* unknown function

The gene codes for a protein (18.7 kDa, 157 aa) with unknown function and an RNA copy was found (287). A homolog of *ac118* is only present in the genomes of the closely related PlxyMNPV and RoMNPV (Table 2).

Ac119: *pif-1, per os* infectivity factor 1

PIF-1, previously called PIF, is a low-abundant 59.7 kDa (530 aa) baculovirus core protein essential for oral infectivity in insect larvae (249). The *Spodoptera exigua* (Se)MNPV PIF-1 protein is present in ODVs (128), most likely anchored in the membrane by a conserved N-terminal transmembrane region (249). PIF-1 was not found in a proteomic analysis of AcMNPV ODVs (20), suggesting a low abundance. Together with PIF-2 it mediates binding of ODVs to epithelial midgut cells (203).

Ac120: *ac120,* unknown function

The putative gene product encoded by *ac120* has a molecular mass of 9.5 kDa (82 aa). There is no information about the role of the *ac120* product in the baculovirus life cycle. Homologs of *ac120* can only be found in genomes of several other members of the genus *Alphabaculovirus* (Table 2).

Ac121: *ac121,* unknown function

A homolog of *ac121* is only present in the genome of BmNPV (Table 2) and encodes a 6.7 kDa (58 aa) protein. There is evidence that Ac121 stimulates expression of the viral protein 39K (*ac36*) by up-regulation of IE1 (*ac147*) expression (78). Ac121 does not influence late gene expression (149).

Ac122: *ac122,* unknown function

The predicted gene *ac122* (7.2 kDa, 62 aa) is transcribed (287) and present in genomes of several other members of the genus *Alphabaculovirus* (Table 2). No information on its function is available.

Ac123: *pk2,* protein kinase 2

The gene *pk2* is transcribed early as an 1.2 kb RNA and encodes the protein PK2 (24.9 kDa, 215 aa). PK2 contains six out of eleven motifs conserved among eukaryotic protein kinases (152). Truncation of the *pk2* gene has no effect on the number, size, or appearance of viral plaques and on the kinetics of protein synthesis or protein phosphorylation profiles during virus infection in cultured Sf21 cells. PK2 mutants show no difference in infectivity or virulence in larval bioassays, neither in production of OBs as compared to wild type AcMNPV infection (152). PK2 prevents the phosphorylation of the eukaryotic translation initiation factor 2α (eIF2α). This phosphorylation is induced by stress, as caused by viral infection and inhibits protein synthesis in general (39). PK2 is a

homolog of cellular eIF2α kinases, but is an inactive, truncated enzyme. By forming hetero-dimers with the cellular eIF2α kinases their phosphorylation activity is inhibited. Wild type AcMNPV shows a reduced eIF2α phosphorylation and increased translational activity, compared to a *pk2* deletion mutant (51).

Ac124: *ac124*, unknown function

This gene encodes a protein (28.5 kDa, 247 aa) with unknown function. Homologs are present in several members of the genus *Alphabaculovirus* (Table 2). *Ac124* is transcribed (287).

Ac125: *lef-7*, late expression factor 7

The *lef-7* gene is transcribed early in infection from an initiation site 14 to 16 bp upstream of the putative translational start site and transcribed late in infection from a not determined initiation site more upstream (194). LEF-7 (26.6. kDa, 226 aa) is required for maximum late reporter gene expression (167). Deletion of *lef-7* results in decreased BV and ODV production and DNA replication compared to the wild type virus infection (30). In BmNPV deletion of *lef-7* also resulted in decreased levels of viral DNA replication (77). Furthermore, *lef-7* is required for efficient homologous recombination in the presence of all other DNA replication genes (45).

Ac126: *ac126*, chitinase (ChiA)

The AcMNPV chitinase protein (ChiA) has a predicted molecular mass of 61.4 kDa (551 aa). ChiA accumulates in the endoplasmatic reticulum due to the presence of a signal peptide and a KDEL-retention signal (241, 261). Its release upon cell death is mediated by P10 (*ac137*) (261). ChiA is - together with the protease cathepsin (V-CATH; *ac127*) - required for disruption of the chitin skeleton of the host (96). The resulting liquefaction of the insect enables the efficient spread of viral occlusion bodies. ChiA is also prerequisite for processing of v-CATH from an inactive pro-enzyme (102). As a consequence deletion of *chiA* (+/- *v-cath*) from baculovirus expression vectors is used to reduce recombinant protein degradation (120). The *chiA* genes are present in many Alphabaculoviruses and some Betabaculoviruses and may have been picked up later in baculovirus evolution (Table 2 and Table 3).

Ac127: *v-cath*, cathepsin

The protease cathepsin (V-CATH) (predicted size 36.9 kDa, 323 aa) is activated from an inactive precursor by ChiA (a*c126*) and both proteins (V-CATH and ChiA) are required for the liquefaction of the insect host to allow efficient spread of OBs (96). V-CATH is also activated by chaotropic agents like SDS and its activity is inhibited by the protease inhibitor E64 (103). As, the *chiA* genes, the *v-cath* genes are also present in many Alphabaculoviruses and some Betabaculoviruses, but not all these viruses have both *chiA* and *v-cath* genes (Table 2 and Table 3).

Ac128: *gp64*, major budded virus envelope glycoprotein

In AcMNPV-infected Sf9 cells, the gene *gp64* is transcribed both early and late in infection (116). GP64 (58.6 kDa predicted size, 512 aa) is absolutely essential for cell to cell spread of BVs. GP64 occurs as a covalently bonded trimer and is present on the surface of infected cells and is acquired by virions during budding through the plasma membrane, the final step in the release of BVs (212). GP64 is involved in host-receptor binding and is sufficient alone to mediate low-pH-triggered membrane fusion during intra-cellular trafficking (177). A domain in the N-terminal part (aa 21-159) is thought to be involved

in host-receptor binding (292) and fusion and oligomerization domains have also been identified (192). The GP64 transmembrane region plays a crucial role in membrane fusion and is also required for GP64 trafficking and the budding process (154). The crystal structure of the GP64 post-fusion form revealed structural homology with the vesicular stomatitis virus G and herpes simplex virus type 1 gB proteins (121).

Ac129: *p24,* viral capsid protein

The gene *ac129* is transcribed in the late phase of virus infection, initiated from a canonical late promoter sequence (GTAAG) situated immediately upstream of the coding sequence (75). P24 (22.1 predicted molecular mass, 198 aa) is a capsid-associated protein, which is not N-glycosylated, but its precise function is unknown. Transposon-based interruption of the *p24* gene did not affect viral propagation in cell culture (75, 242, 280). In SpltNPV, the homologous protein is associated with ODVs as a complex of 83 kDa (155). For *Lymantria dispar* (Ld)MNPV some natural variants lack *p24* sequences (251).

Ac130: *gp16,* unknown function

Ac130 has the potential to encode a protein of 12.1 kDa (106 aa). In OpMNPV, the homologous protein GP16 was detected at 24 h p.i. and its levels increased through 120 h p.i. OpMNPV GP16 is N-glycosylated and not associated with purified BVs and ODVs. It localizes to cytoplasmic lamellar-like structures close to the nuclear membrane and to envelopes of viruses on their way from the nucleus to the cell surface (81). In AcMNPV, transcription of the gene *ac130* could not be detected by microarray analysis (287).

Ac131: *pp34*, major polyhedral calyx protein

The phosphoprotein PP34 (38 kDa, predicted 29.1 kDa, 252 aa) is detected from 15 h p.i. and continues to be phosphorylated until 60–70 h p.i. inside infected insect cells. It is involved in the morphogenesis of the polyhedral envelope of baculoviruses and is part of the carbohydrate envelope of occlusion bodies called the calyx (278, 294). Electron-dense "spacers" present in wild-type AcMNPV-infected cells, are absent in *pp34*-null mutants (294).

Ac132: *ac132,* unknown function

The *ac132* gene with a predicted product of 25.1 kDa (219 aa) is transcribed (287) and homologs are present in genomes of several other members of the genus *Alphabaculovirus* (Table 2), but no function has been associated with it.

Ac133: *an,* alkaline nuclease

All sequenced baculovirus genomes encode a homolog of alkaline nuclease (AN) (Table 2 and Table 3). The predicted molecular mass of the AcMNPV AN is 48.3 kDa (419 aa). AN protein is present in two forms, one full length (53 kDa) and a shorter form (43 kDa). Both forms are found at low levels from 12 h p.i., with maximal abundance at 24 h p.i. (150). AN associates with LEF-3, the baculovirus ssDNA-binding protein (185). AN has 5' to 3'exonuclease and 5' to 3' endonuclease activity. Both these enzyme functions are involved in DNA recombination and replication (185, 186). The first attempt to produce an AcMNPV *an*-null virus was not successful, suggesting that *an is* an essential gene (150). Transfection with an AcMNPV *an*-null bacmid shows no BV production and a reduced number of normal-appearing nucleocapsids. Instead, numerous aberrant capsid-like structures are formed, indicating a defect in nucleocapsid maturation or in a DNA-processing step, that is necessary for encapsidation (206, 207).

Ac134: *94k,* unknown function

The *94k* gene encodes a protein of 94.5 kDa (803 aa). The function of the 94K is still unknown, but homologs can be found in several other baculoviruses (Table 2 and 3). In the closely related BmNPV only 151 bps correspond to *ac134* suggesting the gene might not be essential and was lost by a deletion (76). Random transposon insertions into the *94k* gene have confirmed that it is not essential for virus replication (32). The *94k* gene harbors the *non-hr* origin of replication, which is characterized by palindromes- and AT-rich regions. These motifs are essential for its ability to act as origin of DNA replication and are conserved in BmNPV (134).

Ac135: *35k/p35,* apoptosis inhibitor

The gene *p35* encodes the 34.8 kDa (299 aa) protein P35, which is a strong inhibitor of apoptosis The function of P35 and IAP proteins is extensively reviewed e.g. (36). Mutations in the *p35* gene result in apoptosis of infected Sf21 cells and abort infection (37, 146), but have a wild type appearance in Tn368 cells (38). P35 blocks apoptosis by inhibiting the activity of Sf-caspase-1 and as such works at a different point in the caspase cascade as IAPs, which block apoptosis further upstream in the pathway (5, 140). Crystal structures of the interaction between P35 and Sf-caspase-1 have been determined (56). P35 gene expression is transactivated by IE-1 the protein, which is also responsible for inducing apoptosis (243).

Ac136: *p26,* unknown function

The gene *p26* encodes a dimeric protein (monomeric 27.2 kDa, 240 aa) with unknown function, which is located primarily in the cytoplasm. Transcripts accumulate between 2-12 h p.i. (73, 248). Although conserved in most Alphabaculoviruses (Table 2) and present as two copies in several group-II NPVs, deletion of this ORF does not notably affect the virulence of the virus (248).

Ac137: *p10,* fibrillin or fibrous body protein

The *p10* gene is a non-essential, hyper-expressed very late gene, encoding a 10.3 kDa protein (94 aa). P10 forms two cytoskeletal-like structures: microtubule-associated filaments through interaction with α-tubulin and perinuclear, tubular aggregates (25, 218). The formation of these structures requires the N-terminal heptad repeat/coiled-coil domain of P10 (52). Other domains include a pro-line rich region and a positively-charged C-terminus. The nuclear filaments may play a role in occlusion body maturation via interaction with the polyhedral envelope. P10 also triggers the release of individual polyhedra from the cell nucleus (265). The *p10* promoter is-besides the polyhedrin promoter-exploited in baculovirus expression vectors.

Ac138: *p74,* occlusion-derived virus envelope protein

The AcMNPV P74 (73.9 kDa, 645 aa) was the first ODV-envelope protein found to be essential for primary infection in larval midguts (67) and is therefore also addressed as PIF-0 (review in (249)). The *p74* gene belongs together with *pif-1*, *pif-2* and *pif-3* to the baculovirus core genes. In order to be active, P74 needs to be cleaved by trypsins in the insect gut (250). P74 is exposed at its N-terminus at the ODV surface and binds to midgut epithelium (89) through a receptor not yet characterized for AcMNPV. A double C-terminal membrane anchor allows insertion into membranes, as shown by rescue of P74 negative ODVs with recombinant P74 protein (293).

Ac139: *me53,* DNA synthesis regulator

The *me53* ORF is an immediate-early gene abundantly

transcribed as early as 1 h p.i. It encodes a protein of 53 kDa (52.6 kDa, 449 aa) with a C–terminal zinc finger motif ($CX_2CX_{13}CX_2C$) suggesting a sequence-specific DNA binding capacity and the N-terminus contains a proline-rich region (131). Deletion of this essential gene prevents DNA replication (285).

Ac140; *ac140,* unknown function

The transcribed *ac140* gene (287) is translated in a hypothetical protein of 7.1 kDa (60 aa) with unknown function. No homologs have been found in any other baculovirus (Table 2).

Ac141: *exon0,* unknown function

The gene *exon0* is transcribed in the late phase of infection and encodes a 30.1 kDa (261 aa) protein with the following functional domains: The N-terminal halve of EXON-0 contains two acidic domains and a domain rich in charged amino acids, whereas the C-terminal part comprises a leucine zipper/coiled coil domain and a RING finger-like domain (46, 64). The protein EXON0 is not essential for virus replication or ODV production, but is required for the production of BVs, as it mediates the egress of nucleocapsids from the nucleus (46, 63). EXON0 interacts with the nucleocapsid protein BV/ODV-C42 and with FP25, enabling the escape of nucleocapsids from the nucleus to the cytoplasm (64). Recently, interaction of EXON0 with ß-tubulin was demonstrated (65). The *ac141* ORF is located in the 4.5 kb part of the transcript that is removed by splicing to get the immediate early *ie-0* mRNA (see *ac147*) (46). Some homologs are aberrantly referred to in literature as *ie-0*.

Ac142: *49k,* 49 kDa protein

The ORF *ac142* belongs to the core baculovirus genes and is a late gene, transcribed from 12 to 72 h p.i. The gene product, Ac142, is a 55.4 kDa (477-aa) protein with a putative transmembrane domain and is associated with the nucleopcapsids of BVs and ODVs (20, 178). *ac142* is essential for infectious BV production and for effective envelopment of ODVs to allow the subsequent packaging into occlusion bodies (178).

Ac143: *odv-e18*, occlusion-derived virus envelope protein

The gene *odv-e18* is transcribed from three late promoter motifs from 16 through 72 h p.i. ODV-E18 is a structural protein (6.6 kDa predicted, 62 aa) present in the ODV envelope and in virus-induced intranuclear membranes (19). Deletion of *ac143* prohibits the production of infectious BVs, however, the level of DNA replication and occlusion body formation are not affected (179). Homologs are found in all baculovirus genomes (179).

Ac144: *odv-ec27,* occlusion-derived virus envelope/ capsid protein

The *odv-ec27* is a late gene, transcribed from the same promoter motifs as *odv-e18 (ac143*) and its product, ODV/EC27, is localized to the ODV envelope and capsid structures (19). The protein has a cyclin-like domain, suggesting a role in cell cycle de-regulation (13). Antibodies against ODV-EC27 recognized a 27 kDa protein (33.5 kDa predicted, 292 aa) in infected cells and proteins of 27 and 35 kDa in purified ODVs. The ODV-E35 protein appears to be the result of a translational shift during ribosomal reading of the bicistronic *odv-e18/odv-27* mRNA (19). ODV-E27 interacts with ODV/BV-C42 and P78/83 (18). AcMNPV *odv-e27* deletion mutants show a diminished production of infectious BVs. DNA replication is similar as for the wild-type virus but the mutant has a defect in

nucleocapsid assembly (270). *Odv-ec27* is a baculovirus core gene.

Ac145: *ac145,* unknown function

The gene *ac145* is expressed at the late to very late phase of infection and encodes a small protein (8.9 kDa, 77 aa), present in both BVs and ODVs. Ac145 belongs to a family of proteins, which contain a C6 or peritrophin-A-like domain ($CX_{7\text{-}18}CX_5CX_{6\text{-}11}CX_{12}CX_{5\text{-}11}C$, where X represents any amino acid residue other than cysteine) (143). The function of Ac145 is not clear although it plays a role in oral infection. Deletion of *ac145* does not affect BV propagation, but leads to decreased *in vivo* infectivity compared to wild-type AcMNPV in a host dependent way (143). Homologs of the gene are conserved in all baculoviruses, except Deltabaculoviruses (Table 2 and Table 3).

Ac146: *ac146,* unknown function

The *ac146* gene codes for a protein of 22.9 kDa (201 aa) and is found in the genomes of Alpha- and Betabaculoviruses. No information about the function of *ac146* is available.

Ac147: *ie-1,* immediate early transactivator IE-1

During the early phase of infection, mRNAs of 1.9-kb and spliced 2.1-kb transcripts are present which encode IE-1 and IE-0, respectively (35). The *ie-0* transcript is the only known spliced baculovirus mRNA. IE-1 contains 582 aa (66.9 kDa) arranged into different domains, including an acidic activation domain at the N-terminus, a DNA binding domain, and an oligomerization domain at the C-terminus (47, 136). Compared to IE-1, IE-0 has 52 extra N-terminal amino acids. IE-1 is a potent transcriptional transactivator and essential for virus replication (133). A virus lacking either *ie-1* or *ie-0* could be propagated in cell culture, but a double knock-out is not viable. The *ie0-ie1* gene complex is essential for viral infection and is needed to obtain wild type levels of replication, late gene expression and BV and ODV production (243, 252). D*e novo* synthesis of IE-1 leads to virus-induced apoptosis (243). IE-1 also transactivates the expression of the *p35* gene, and in that way counteracts its own pro-apoptotic activity (243). Homologs are found in all Alphabaculoviruses (Table 2).

Ac148: *odv-e56*, occlusion-derived virus envelope protein

Transcription of the gene *odv-e56* starts from a late ATAAG promoter and transcripts are detected from 16 to 72 h p.i. (17). ODV-E56 protein (predicted 40.9 kDa, 476 aa) is present in viral-induced intranuclear microvesicles, and consequently is incorporated into ODV envelopes (17). Mutation in the 3´-end of *odv- e56* alters its location to the nucleocapsids instead of the ODV envelope, suggesting that an important localization sequence is present in the C-terminus of this protein (17).

Ac149: *ac149,* unknown function

The *ac149* ORF encodes a putative protein of 12.4 kDa (107 aa) with unknown function. Homologs are present in a few related Alphabaculoviruses (Table 2).

Ac150: *ac150,* unknown function

The gene *ac150* encodes an 11.2 kDa (99 aa) protein and is expressed in the late to very late phase of infection. The protein Ac150, is a member of a family containing peritrophin-A-like domains (see also *ac145*) - common among mucins, peritrophins and chitinases - and the protein contains an integrin-binding motif (143). Deletion of *ac150* has no effect on infectivity of the virus for *T. ni* or *H. virescens* larvae, but the mutant is less efficient in establishing a primary infection in midgut cells, although the infectivity kinetics are the same as for the wild type virus (291).

These results together suggest that *ac150* can be considered as a putative *per os* infection factor (PIF) that mediates, but is not essential for, oral infection (291). This has been confirmed as a deletion of the homologous gene (*bm126*) in BmNPV shows no difference in BV production and mean lethal dose of OBs. However the median survival time in larvae is delayed (91).

Ac151: *ie-2,* immediate early transactivator 2

The *ie-2* gene encodes the immediate early protein IE-2 (47.0 kDa, 408 aa), which functions as a trans-activator of early baculovirus promoters in transient expression assays (26). Other functions of the protein are blocking the progression of the cell cycle in a variety of cell lines (229) and augmenting the replication and stability of reporter plasmids containing hr sequences in the presence of IE-1 and four other AcMNPV gene products (133, 167). Viruses with *ie-2* mutations exhibit delays in viral DNA synthesis, late gene expression, BV production, and OB formation in Sf21 cells but not in TN-5B1-4 cells (227).

Ac152: *ac152*

The gene *ac152* encodes a protein of 10.8 kDa (92 aa). The protein Ac152 is involved in nuclear localization of G-actin in TN-368 cells and is a trans-activator (directly or indirectly) of both *ac102* and *he65* genes (202).

Ac153: *pe38*

The gene product of *pe38*, the protein PE38 (321 aa), is present during the early phase of infection as a nuclear 38 kDa protein, but during the late phase, it is modulated to or produced as a cytoplasmic 20 kDa protein in a process which is controlled by viral factors (137). PE38 is a protein with RING finger and leucine zipper motifs and is involved in transactivation of viral genes and augmenting viral DNA replication in transient replication assays (133, 137). Furthermore, PE38 is augments IE1-induced apoptosis, but is not able to induce apoptosis when expressed in Sf21 cells alone (228). PE38 is an important factor in viral DNA synthesis and BV production (189).

Ac154: *ac154,* unknown function

The gene *ac154* encodes a protein (calculated mass 9.4 kDa, 81 aa) with unknown function. Transcripts of this gene have been identified (287). Only four homologs are present in other Alphabaculoviruses (Table 2).

CONCLUSION

The research towards elucidating the function of AcMNPV genes started in the early 1980s with the assignment of *polyhedrin* and *p10*, but was enhanced by the publication of the complete genome sequence in 1994 showing originally 154 ORFs (9) to which *ac53a* (*lef-10*) was added later. Partial re-sequencing of the AcMNPV C6 strain at a later date, demonstrated that four ORF pairs were actually fused (*ac20/21*, *ac58/59*, *ac106/107*, *ac112/113*), bringing the total to 151 ORFs (92). For many ORFs, we had little or no idea about their putative function. Overtime, many ORFs were assigned (see Table 1), mainly associated with transcription, DNA replication, virion structure and pathogenesis. Nevertheless, as of January 2009, 73 ORFs still remain with an unknown function. The most striking ORFs were those involved in the inhibition of apoptosis (*p35*) and in abrogation of the molt (*egt*). These observations provoked resonance far beyond baculovirology.

Functional studies in other, closely-related baculoviruses are sometimes useful to indicate which role an encoded AcMNPV protein might have. However,

discrepancies have been found, which may reflect intrinsic differences in the viral protein under study. The discrepancies may also reflect dissimilarities in the presence or absence of other baculovirus gene products or in the interplay with host factors.

Many of the AcMNPV ORFs with unknown function encode relatively small proteins, sometimes with homologs in only a few baculoviruses, and therefore may not be functional or may not have a very crucial role. Others with unrevealed function, though, belong to the baculovirus core genes at the family level, or are represented in a whole genus, and must play key roles in baculovirus biology. Some of these genes may very well play a role in baculovirus ecology rather than in transcription, gene regulation, DNA replication, or in the assembly of BV and ODV particles. A systematic analysis of knock-out mutants would help in the further functional assignment of AcMNPV ORFs.

Detailed information on the molecular genetics and functional biology of AcMNPV ORFs will contribute to the further development, tailoring and improvement of baculoviruses as biocontrol agents, protein expression vectors and as vectors for gene therapy. This Encyclopedia of AcMNPV genes should be the starting point and further contribute to this venture.

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