Modulation of immune responses to parasitoids by polydnaviruses

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SUMMARY

Parasitoids are parasites that invariably kill their host. Polydnaviruses are injected by parasitoid wasps into the body cavity of their insect host and cause immunosuppression, allowing the parasitoid to develop in the absence of encapsulation. One of the targets of the polydnaviruses are the haemocytes of the host, which undergo significant changes in response to entry of the virus. In some systems, haemocyte apoptosis is induced, or haemocyte clumping may be seen; in others, the cells round up and fail to adhere to a substrate. Effects on haemocytes may be transitory or permanent (cell death). Various polydnavirus gene products have been identified that interfere with normal haemocyte function. Phenoloxidase activity also is inhibited during parasitism, and the effect is inducible by polydnavirus. In some systems, venom components may act synergistically with polydnavirus in mediating the virally-induced effects on the host immune system. Polydnaviruses are powerful influences on the host immune system, which serve to permit successful development of the parasitoid without triggering the host immune response.

Key words: Invertebrate immune response, haemocyte, polydnavirus, parasitoid.

INTRODUCTION

When a metazoan parasite invades an insect host, encapsulation may occur if the host is a non-habitual one. In this process, blood cells or haemocytes from the haemocoel engulf the parasite to form a capsule (Strand & Pech, 1995*a*; Lavine & Beckage, 1995). The parasite then dies encased within multiple layers of haemocytes. If the parasite finds itself in a habitual host, then encapsulation is prevented, and the parasite(s) survives to maturity. The encapsulation process involves three phases (Strand & Pech, 1995*a*): recognition of the parasite as foreign, strong adhesion between haemocytes when forming a capsule, and killing of the parasitoid. Following encapsulation, the capsule may or may not be melanized, due to the action of phenoloxidases, which catalyse the formation of melanin from tyrosine and dopa. The encapsulated, melanized parasites then often attach themselves to internal tissues such as the fat body, Malpighian tubules, salivary glands or gut. This phenomenon may be due to the action of humoral agglutinins, which agglutinate the encapsulated parasites. Alternatively, the haemocytes themselves may be the source of the sticky proteins, which are exposed on the surface of the capsule.

Parasitoids are insects that parasitize other insects, resulting in the death of the host (Quicke, 1997). Parasitoids achieve successful development in a host either by suppressing the immune response of the host or by passive immunoevasion, which results from a failure to be recognized as foreign. Both processes may be used by a single parasitoid during its lifetime, at different phases of its life cycle. Mechanisms of immunosuppression will be stressed in this review.

Some of the most potent weapons wasp parasitoids utilize in disarming their host's defense mechanisms are polydnaviruses (PDVs, for polydisperse DNA viruses) (Stolz *et al.* 1984; Vinson, 1990; Schmidt & Theopold, 1991; Beckage, 1997, 1998). These viruses are characterized by complex, superhelical DNA genomes, which are comprised of multiple circles or segments of double stranded DNA (see Fleming, 1992; Stoltz, 1993 for reviews). The mature virions are present in the reproductive tracts of adult females of endoparasitic species of wasps belonging to the families Braconidae and Ichneumonidae. They are injected into the prospective host larva during oviposition, along with eggs and proteins produced in the calyx region of the ovary, and are present in the ovarian calyx fluid. Proteins secreted by the calyx epithelium may also influence the immune response of the host. Once delivered to the lepidopteran host, viral genes are expressed but the viruses do not replicate.

These viruses are integrated into the genomes of the respective wasp which carries them, and they are transmitted vertically via the genome of the wasp as proviruses. The immature stages of the parasitoids carry only the integrated genomic sequences of viral genes. Chromosomal localization of the viral sequences has been established for both bracoviruses (Gruber *et al.* 1996; Savary *et al.* 1997) and ichnoviruses (Fleming & Summers, 1986; Stoltz, 1990; Xu & Stoltz, 1991), which are present in braconids and ichneumonids, respectively. Gruber

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et al. (1996) showed that the polydnavirus of *Chelonus inanitus* is integrated in the wasp's genome and excised during a specific stage in the adult development of the wasp. After excision, the genomic DNA is then rejoined. Savary *et al.* (1997) have also documented that excision of the viral genome occurs preceding viral replication of the polydnavirus in *Cotesia congregata*. Viral replication appears to be stimulated by release of ecdysteroid (Webb & Summers, 1992) during a specific stage of development following pupation (Webb & Summers, 1992; Albrecht *et al.* 1994).

The mature adult female wasp thus emerges with a full complement of virus along with eggs in the calyx of the ovary, ready for oviposition. During this process, a complex cocktail of eggs, polydnavirus, venom, and wasp ovarian proteins is injected into the host larva. The latter three components have all been found to influence the host's immune response to the parasitoid eggs.

Haemocytes appear to be some of the primary cells targeted by polydnaviruses, which show an altered behaviour(s) after entry of the viruses (Strand & Pech, 1995*a*; Lavine & Beckage, 1995). The viruses also enter other tissues such as the fat body (Buron & Beckage, 1992). In haemocytes, effects may be transitory or permanent (i.e. apoptosis or cell death). Encapsulation is the main process which is invoked against metazoan parasites in insect hosts. The most commonly reported effect of polydnaviruses on haemocytes is that the cells 'round up' and fail to adhere to a substrate (Davies, Strand & Vinson, 1987; Strand & Noda, 1991; Strand & Pech, 1995*a*). In this condition, they are unable to spread to encapsulate foreign objects including parasitoid eggs.

No general pattern emerges regarding the effects of parasitism on host haemocytes and their function. The effects of polydnaviruses, venom, and ovarian proteins appear to be relatively species-specific. In some species, such as *Pseudoplusia includens*, the granulocytes are believed to be the specific targets of the virus (Strand & Pech, 1995*b*). These cells undergo apoptosis in response to entry of the polydnavirus of *Microplitis demolitor* (MdPDV) and are no longer available to participate in encapsulation. Characteristics of apoptosis seen in these cells include condensation of chromatin, cell surface blebbing, and fragmentation of the cellular DNA into a 200 bp ladder (Strand & Pech, 1995*b*). A large number of apoptotic granulocytes is seen at 24 h post-oviposition or post-injection of PDV into non-parasitized larvae. The haemocyte count drops precipitously. The virus does not replicate in host *P. includens* larvae (Strand *et al.* 1992); hence the effects elicited are induced by viral gene expression in the absence of replication. The plasmatocytes round up and fail to spread.

POLYDNAVIRUS GENE PRODUCTS

Recent efforts have concentrated on examining viral gene expression and the molecular events accompanying host haemocyte dysfunction. A summary of the major PDV gene products which have been shown to be required for successful parasitism is shown in Table 1. Strand (1994) showed that expression of a 1·6 kb *Microplitis demolitor* PDV (Md PDV) mRNA occurred in haemocytes from parasitized hosts as detected by *in situ* hybridization beginning at 2 h post-parasitization, and the transcript was detectable for 6 days after oviposition. He proposed that the effect on cells was mediated directly by infection of the haemocytes by MdPDV. Strand, Witherell & Trudeau (1997) showed that two *M. demolitor* polydnavirus mRNAs are expressed in haemocytes of newly parasitized *Pseudoplusia includens* larvae and both contain a cysteine-rich domain. They identified two mRNAs that are expressed in plasmatocytes and granulocytes and isolated corresponding cDNAs from a MdPDV-infected haemocyte cDNA library. Both mRNAs are expressed in granular cells and plasmatocytes, the primary classes of haemocytes involved in the insect immune response against parasites. The predicted peptides have a cysteine-rich region at their 5′ ends (Strand, Witherell & Trudeau, 1997).

Other investigators have also isolated polydnavirus-encoded gene products following parasitization or injection of PDV into non-parasitized larvae. Hayakawa *et al.* (1994) reported that 48 h following injection of the PDV of *Cotesia kariyai*, viral DNA was detected in all tested larval tissues of the armyworm host, including haemocytes, fat body, nerve cord, and brain; haemocytes contained the most viral DNA and RNA. The polydnavirus also causes developmental arrest of the host larva, via production of a growth blocking peptide (GBP) which is stimulated by PDV (Hayakawa, 1995). The virus causes an elevation in dopamine levels which is hypothesized to be mediated by the elevation in GBP. The elevation in dopamine levels disturbs the neuroendocrine control of metamorphosis thereby suppressing pupation of the host via induction of a transient decline in the level of haemolymph juvenile hormone esterase (Noguchi, Hayakawa & Downer, 1995). PDV also causes developmental arrest of other species of caterpillars (Strand & Dover, 1991) including the tobacco hornworm (Dushay & Beckage, 1993). Thus, the developmental programme as well as the immune system is affected by PDV.

Other PDV gene products also act on the haemocytes directly. In *Heliothis virescens* larvae parasitized by *Campoletis sonorensis*, the VHv1·1 polydnavirus gene produces a protein which binds to haemocytes *in vitro* and *in vivo*, and is endocytosed by haemocytes (Li & Webb, 1994). This 34 kDa

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Table 1. PDV gene products that have been shown to be important during parasitism of insect hosts by parasitoids

Species/PDV gene product	Effect on host immune system	Reference
Microplitis demolitor		
Cysteine-rich PDV-encoded proteins	Plasmatocytes round up; granulocytes undergo apoptosis	Strand, Witherell & Trudeau (1997)
Campoletis sonorensis		
VHv1·1 gene product	Glycoprotein is endocytosed by haemocytes; protein inhibits encapsulation response	Li & Webb (1994), Soldevila, Heuston & Webb (1997)
Cotesia rubecula		
CrV1 gene product	mRNA is produced 4–8 h post-parasitization; haemocyte actin cytoskeleton is disrupted	Asgari, Hellers & Schmidt (1997)
Cotesia kariyai		
2·0 kb PDV encoded mRNA	Expressed in haemocytes when immune system is compromised 2–4 h post-parasitization	Yamanaki *et al.* (1996)

glycoprotein has been implicated in suppressing the host insect immune response, and has been expressed in baculovirus cell cultures and *in vivo* in *H. virescens* larvae using a recombinant poly-histidine baculovirus vector (Soldevila, Heuston & Webb, 1997). This gene belongs to the cysteine-rich gene family which has been isolated from *C. sonorensis* polydnavirus (Cui & Webb, 1996).

In *Manduca sexta* larvae parasitized by *Cotesia congregata*, the cells first undergo blebbing followed by clumping in the haemolymph of the host. Within the first few hours after the host is parasitized, in as few as 2 h post-parasitization, clumps of cells are evident in the haemolymph and by 24–48 h, large clumps of dead and dying cells are seen (Lavine & Beckage, 1995). Thus, the cells become sticky and adhere to each other; the cell membranes between cells seem to disappear. At the present time, it is unclear which cell types form the clumps, since the cells have not spread, thus making it difficult to distinguish plasmatocytes and granulocytes. Use of monoclonal antibodies to the different cell types (Willott *et al.* 1994) should facilitate this type of cell identification within a clump.

In addition, the haemocytes of newly parasitized *M. sexta* larvae are significantly less capable of encapsulating abiotic implants such as Sephadex beads. If beads are implanted within the first few days after parasitization, the percentage of beads encapsulated is very low in comparison to the percentage encapsulated in unparasitized larvae (Lavine & Beckage, 1996). By comparison, if beads are implanted 8 days post-parasitization they are readily encapsulated, indicating that the host immune response has recovered by that time. Bead melanization rarely occurs in newly parasitized larvae whereas it frequently occurs in non-parasitized larvae, so melanization as well as encapsulation is affected. An explanation for the reappearance of an immune response several days post-parasitization may be that new haemocytes are differentiated from prohaemocytes, thus allowing the haemocyte population to recover in terms of numbers of functional cells.

Stoltz & Guzo (1986) similarly reported that parasitism inhibits encapsulation of parasitoid eggs and Sephadex beads in *Malacosoma disstria* larvae parasitized by *Hyposoter fugitivus*. In addition, clearing of yeast cells is markedly inhibited, such that parasitized larvae injected with the yeast *Saccharomyces cerevisiae* die prior to emergence of the parasitoids from the host. Thus, the antifungal response in the insect host is greatly reduced due to the action of PDV. Injection of what are normally non-pathogenic bacteria into parasitized *M. sexta* larvae also causes their mortality (Ross & Dunn 1989); hence, parasitized larvae are rendered dramatically more susceptible to other agents due to their immunocompromised state. Not surprisingly, infections with viruses also spread faster if the animal is injected with polydnavirus at the time of oral administration of baculoviruses such as *Autographa californica* MNPV (Washburn, Kirkpatrick & Volkman 1996). The latter authors showed that in *H. zea*, a normally nonpermissive host for the AcMNPV, parasitism by *Campoletis sonorensis* rendered the host susceptible to the baculovirus. The immunocompromised state of the host induced by the polydnavirus allows the viral pathogen to invade host tissues much faster.

Concomitant with the cellular changes seen in parasitized *M. sexta*, parasitization triggers production of early parasitism-specific proteins (EPs) which circulate in the blood (Beckage *et al.* 1987). In parasitized *Heliothis virescens* larvae, a new glycoprotein is similarly produced, which is induced by the polydnavirus of *Campoletis sonorensis* (Cook, Stoltz & Vinson, 1984).

In the tobacco hornworm, the EPs represent roughly 15% of the total haemolymph protein; hence, they are abundant proteins. One of these proteins (EP1) has been confirmed to be a poly-

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dnavirus gene product (Harwood *et al.* 1994). The protein is heavily glycolsylated and is 190 kDa, with subunits in the 33–35 kDa range. Synthesis of the mRNA encoding this protein begins within 30 minutes after the host is parasitized, and continues for several days. The fat body and haemocytes both contain the EP1 mRNA. The EP1 protein appears later and continues to be detectable in the blood for 6 days post-parasitization (Harwood & Beckage, 1994; Harwood *et al.* 1994). Two other EP proteins (EP2 and 3), also in the 30–40 kDa range, are also produced in the host (Harwood *et al.* 1994), as well as several lower MW < 20 kDa polypeptides which are seen only in the haemolymph of newly parasitized larvae. The unresolved question is whether any of the EP proteins have a functional role in disrupting the insect host immune response. Their synthesis is intriguingly temporally correlated with induction of the major detrimental effects on the immune system but an experimental demonstration that the EP proteins play a role in suppressing the immune response still eludes us.

The scenario in *Heliothis virescens* larvae parasitized by *Campoletis sonorensis* offers additional insights. Eggs washed free of virus are avidly encapsulated (Edson *et al.* 1980). Wasp ovarian proteins, of non-viral origin, are secreted by the epithelial cells lining the reproductive tract (Webb & Luckhart, 1994, 1996; Luckhart & Webb, 1996). These proteins act to protect the egg during the earliest phases of parasitism, within the first few hours post-oviposition. Later, the polydnavirus begins viral gene expression at 4 h post-oviposition, and viral gene products are available to protect the developing parasitoid beginning at that point. Alterations in haemocytes are seen at 1·5 h, before PDV gene expression begins.

Polydnavirus gene products also cause a translational block of haemolymph arylphorin (storage protein) production, as well as inhibition of synthesis of other host proteins such as juvenile hormone esterase, as examplified by *Heliothis virescens* larvae parasitized by *Campoletis sonorensis* (Shelby & Webb, 1994, 1997). The virus literally takes over the translational machinery of the cell, resulting in production of polydnavirus gene products at the expense of host proteins. Another interpretation is that this effect shunts host resources away from larval growth and adult development, which makes them available to the developing endoparasitoid. However, the process is selective as not all endogenous host proteins are affected. The synthesis of proteins such as the iron-binding proteins transferrin and ferritin, and juvenile hormone binding protein, continues unabated (Shelby & Webb, 1997). Exactly how the selective blockage in translation is effected remains to be demonstrated.

A cysteine-rich gene family is present in the polydnavirus of *C. sonorensis*, and several related proteins are produced by these genes (Dib-Hajj, Webb & Summers, 1993). These studies followed up earlier work (Blissard *et al.* 1986, 1989; Fleming *et al.* 1983; Theilmann & Summers, 1988) suggesting that polydnavirus genes are expressed following parasitization of host *H. virescens* larvae. The VHv1·1 gene product has been produced from baculovirus expression systems (Soldevila & Webb, 1996; Soldevila *et al.* 1997), and polyclonal antisera react with a 30 kDa protein from haemocytes, cell-free plasma, and fat body of parasitized larvae. This protein binds to granulocytes and plasmatocytes, and is endocytosed by the cells (Li & Webb, 1994). Expression of the VHv1·1 gene product reduces the encapsulation response to washed parasite eggs, indicative of a role in the host immune response. In 1996, a new CsPDV gene encoding an abundant 1·4 kb mRNA expressed in parasitized insects was isolated (Cui & Webb, 1996). The VHv1·4 cDNA has two conserved domains that presumably result from duplication of a portion of the gene. A functional role for this protein has yet to be identified. The VHv1·4 and VHv1·1 proteins are 62% identical overall, indicative of a close genetic relationship among genes in this cysteine-rich family (Cui & Webb, 1996).

In *Pieris rapae* larvae parasitized by *Cotesia rubecula*, the wasp's polydnavirus causes a transient change in the host's haemocytes, in that they 'round up' as described earlier, but then their appearance returns to normal. Thus, the effect of the polydnavirus is transitory, and is believed to be invoked by a single polydnavirus gene product expressed in haemocytes between 4 and 8 h post-parasitization (Asgari, Hellers & Schmidt, 1996). The actin cytoskeleton and adhesive properties of the cell are altered as a result of polydnavirus gene expression. In the absence of actin polymerization the cells cannot extend their filopodia. Several hours later the haemocytes' behaviour returns to normal. In this species, the protection of the parasitoid can be divided into three distinct phases (O. Schmidt, personal communication): (1) an initial protection of the egg by a protective layer on the surface; (2) transient suppression of the host defense system by the polydnavirus-encoded immune suppressor; and (3) the surface protection of the parasitoid larva after the recovery of the host's cellular defense mechanisms.

Yamanaka *et al.* (1996) isolated five cDNA clones encoding *C. kariyai* polydnavirus mRNAs transcribed in host larvae of *Pseudaletia separata*. A 2·0 kb mRNA was detected mainly in haemocytes. This RNA increased in relative abundance after 2 and 4 h post-parasitization when the immune response of the host first appeared compromised, leading to speculation about its possible involvement in immunosuppression.

Parasitized hosts of *Drosophila melanogaster* parasitized by *Leptopilina heterotama* contain low

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numbers of haemocytes called lamellocytes, the primary haemocyte class involved in encapsulation in *Drosophila*. A substance called lamellolysin from the accessory gland fluid of the adult female wasp was implicated as causing haemocyte death (Rizki & Rizki, 1984), though virus-like particles have also been found in this species which have also been implicated in causing host immunosuppression (Rizki & Rizki, 1990). In the absence of normal numbers of lamellocytes, encapsulation cannot occur, and the parasitoid escapes encapsulation.

EFFECTS ON PHENOLOXIDASES

Another process which is affected by polydnaviruses is the rate of haemolymph melanization and conversion of tyrosine to dopa and subsequently the conversion of dopa to dopachrome and melanin. In tobacco hornworm larvae parasitized by *Cotesia congregata*, the rate of haemolymph melanization is markedly diminished during parasitism, beginning when the host is first parasitized and continuing until the wasps emerge from the host. In nonparasitized insects injected with *Cotesia congregata* polydnavirus, a similar effect is seen (Beckage *et al.* 1989). Since melanization is thought to be one of the primary humoral immune mechanisms, the finding that the rate of melanization is reduced is significant. In the absence of melanization, toxic radicals and reactive oxygen intermediates do not form, thus protecting the parasitoid. Stoltz & Cook (1983) reported a similar phenomenon in host tent caterpillar larvae parasitized by wasps belonging to the genus *Hyposoter* as did Sroka & Vinson (1978) in *Heliothis virescens* larvae parasitized by *Campoletis sonorensis*. Thus, this effect appears widespread among parasitized insects.

ROLE OF PARASITOID VENOMS

In braconid wasps, venom frequently has a synergistic effect with the polydnavirus, allowing the virus to act at much lower doses than it would normally. Stoltz *et al.* (1988) proposed that the venom of *Cotesia melanoscela* promotes the entry and uncoating of the polydnavirus of the wasp, thereby allowing the virus to act on haemocytes, thus having a facilitative effect. Guzo & Stoltz (1987) observed that in *C. melanoscela*, both virus and venom were necessary to suppress encapsulation and cause a reduction in total haemocyte count, the appearance of debris in the haemocoel, and the appearance of nuclear pycnosis in the haemocytes, all of which normally occur following parasitization. As outlined by Strand & Pech (1995*a*), at superphysiological dosages, virus alone may be sufficient to alter haemocyte behaviour, but at a lower physiological dose more haemocytes are affected when hosts are injected with virus plus venom compared to hosts injected with virus alone. Thus, the venom may allow the wasp to parasitize a host with a smaller dose of virus than it could otherwise. Along the same lines, Wago & Tanaka (1989) reported synergistic effects of virus and venom of *Apanteles kariyai* on the granular cells of the host larva, *Pseudaletia separata*. Synergistic effects of venom are not seen in all systems, however, and in tobacco hornworm larvae parasitized by *C. congregata*, no effect of the venom is discernable.

Webb & Summers (1990) may have uncovered a molecular explanation for this synergy. They showed that polydnavirus and venom genes of the wasp *Campoletis sonorensis* share related sequences. Monoclonal antibodies raised against venom glands recognized epitopes conserved on several polydnavirus proteins. It is not surprising, then, that venom can duplicate some effects of PDV on the host. Perhaps the virus has 'captured' venom genes for exploitation, or the venom has acquired the ability to mimick the virus since they are both secreted by epithelial tissue. Webb & Summers (1990) stated that the phenomenon reflects an evolutionary relationship in which venom gene homologues were incorporated into the viral genome, thereby allowing viral expression of venom-related genes to ensure parasitoid survival. The sharing of genes by PDV and venom also brings up the possibility that the parasitoids have simply developed the capacity to encapsidate part of their genome in the form of virus-like elements. According to this interpretation, the virus represents 'genomic secretions' of the parasitoid in the form of polydnaviruses (Federici, 1991) which rapidly invade host tissues following parasitization.

PASSIVE IMMUNOEVASION TACTICS

The wasp *Venturia canescens* is unique among all parasitoids studied thus far in that the virus-like particles (VLP) contained in the ovaries lack nucleic acid. Instead of causing immune disruption by activating gene transcription in host larvae of *Ephestia kuehniella* or expressing proteins themselves, the particles provide protection by allowing the parasitoid to passively evade the immune responses of the host via a process akin to antigen mimicry. The particles attach to the surface of the egg during its passage from the ovary to oviduct (Rotherham, 1973) and the virus-like particles contain a protein which mimicks a basement membrane protein produced in the host (Feddersen, Sander & Schmidt, 1986). Thus, the parasitoid egg is cloaked in a protective layer of VLP particles during the early development of the parasitoid in the host. Four major proteins comprise the virus-like particles (Theopold, Krause & Schmidt, 1994;

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Hellers *et al.* 1996). Two alleles encode one of these virus-like particle proteins in *V. canescens* and the resulting protein variants differ by the presence or absence of eighteen amino acids (Hellers *et al.* 1996). After hatching, presumably the larval surface similarly fails to invoke a response by the insect immune system. Hence, the immune system of the host remains intact and immunosuppression is not actively induced. This is obvious from observations made in superparasitized caterpillars, in which fighting among wasp larvae causes the damaged larvae to become encapsulated by the host. Thus, the encapsulation response is not inhibited and the host remains capable of mounting a response.

In *Cardiochiles nigriceps*, the eggs of the parasitoid are thought to evade encapsulation by a passive process due to the presence of a protective fibrous layer which prevents activation of the immune response (Davies & Vinson, 1986). In the parasitoid *Cotesia rubecula*, a calyx fluid protein that is structurally related to a virus protein has been identified on the egg surface of the parasitoid which provides passive protection until the polydnavirus causes immunosuppression of the host (Asgari & Schmidt, 1994). The protein layer provides a passive protection during the temporal gap between oviposition and inactivation of the host immune system by polydnaviruses. In tobacco hornworm larvae parasitized by *Cotesia congregata*, late first instar parasitoids can be transferred to unparasitized larvae lacking PDV and complete their development and emerge normally (Adamo, Linn & Beckage, 1997; Lavine & Beckage, 1996). Hence, in contrast to earlier stages, the PDV is not necessary for suppression of the host immune response during the final stages of parasitism when the parasitoids probably evade the host immune response via a passive mechanism. Aside from these studies, little is known about mechanisms of passive immunoevasion in insect hosts.

Surely, polydnaviruses are some of the most intriguing elements which interface with the insect immune system and they offer the opportunity to explore how one organism, the parasitoid, exploits another, the host, via its unique viral partner. We are only just now beginning to scratch the surface to uncover the mechanisms whereby PDVs inhibit the host immune system with respect to both cellular and humoral components. The viruses also play a role in the community ecology of parasitoids and how they interact with their respective host in defining the host range of a parasitoid (Whitfield, 1993).

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