

寄生蜂调控寄主害虫免疫与发育机理的研究新进展*

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摘 要 寄生蜂是重要且种类最为丰富的膜翅目昆虫类群之一,也是极具价值的害虫生物控制因子。寄生蜂携带有不同类型的活性因子,包括毒液、多分 DNA 病毒类病毒颗粒、卵巢蛋白、畸形细胞及幼虫分泌物等,用于调控寄主害虫的免疫反应、发育等重要生理过程,以确保成功寄生并确保其子代在寄主害虫体内(内寄生蜂)或体表(外寄生蜂)正常发育,最终可导致寄主害虫死亡,从而有效控制寄主害虫种群数量。目前已有诸多与寄生蜂调控寄主害虫内在机理相关的研究报道,该领域也已成为昆虫寄生学与生理学的研究热点之一。本文仅从寄生蜂寄生因子多样性、寄生蜂调控寄主害虫免疫及发育的机理等方面,对相关的最新研究进展作一概述。

关键词 寄生蜂; 寄生因子; 寄主害虫; 免疫; 发育

Recent advances in research on the mechanisms through which parasitoid wasps regulate host immunity and development

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Abstract Parasitoid wasps transmit various kinds of bioactive substances, including venom, polydnavirus, virus-like particles, teratocytes, ovarian proteins, and larval secretions, to their hosts. These substances play significant roles in regulating host physiological processes, such as immunity and development, thereby facilitating the development of the parasitoid's offspring, either inside (endoparasitoid), or outside (ectoparasitoid), the host's body. This regulation ultimately results in the death of the host. Since many hosts are important agricultural pests, parasitoid wasps are important biological control agents. There has recently been an increase in research on the mechanisms through which parasitoid wasps regulate their hosts' physiology. In this article, we review the latest progress in research on the range of substances transmitted by parasitoid wasps, and the mechanisms through which wasps regulate the immunity and development of their hosts.

Key words parasitoid wasps; parasitism factors; host pests; immunity; development

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寄生蜂是重要且种类最为丰富的膜翅目昆虫类群之一,也是害虫的关键自然控制因子和有效的生物防治作用物。寄生蜂已知种类有 10 万余种,据估测仍有 50 余万种未被发现或鉴定 (Heraty, 2009),其物种多样性远超其它膜翅目昆虫。寄生蜂通常携带有寄生因子,在其产卵或胚胎与幼虫发育过程中会将这些因子释放至寄主体内,用来调控寄主体内的重要生理过程 (图 1),以确保其成功寄生寄主害虫,及其子代的正常发育 (Pennacchio and Strand, 2006; Asgari and Rivers, 2011; Moreau and Asgari, 2015)。这些寄生因子包括:多分 DNA 病毒 (Polydnavirus, PDV) (Tan *et al.*, 2018)、毒液 (Lin *et al.*, 2019)、类病毒颗粒 (Virus-like particle, VLP) (Heavner *et al.*, 2017)、卵巢蛋白 (Mateo Leach *et al.*, 2009) 等雌蜂携带因子,以及畸形细胞 (Teratocyte) (Wang *et al.*, 2018) 等由胚胎或幼虫携带或释放的寄生因子 (Richards and Edwards, 2001; Richards, 2012)。有关寄生蜂

寄生因子的研究,多集中于毒液和 PDV 两类因子。寄生蜂毒液与其他多数动物毒液类似,它是由蛋白源和非蛋白源化合物共同组成的混合物 (Moreau and Asgari, 2015)。目前有许多比较内外寄生蜂毒液组成模式的研究,结果显示其组成上虽然存在显著差异,但其中还是存在部分保守的蛋白组分 (Asgari and Rivers, 2011)。其中,外寄生蜂毒液含有行使麻痹寄主的功能组分 (短期或长期),以保证其后代在寄主体外取食的安全性 (Kaiser *et al.*, 2019);内寄生蜂毒液则主要起到直接干扰寄主害虫重要生理学过程,或对其它雌蜂所携寄生因子 (如 PDV) 起增效作用,以确保其能成功寄生 (Teng *et al.*, 2016)。PDV 是一类基因组较大的双链 DNA 病毒。其隶属多分 DNA 病毒科 (Polydnaviridae),下分两属,分别为 *Bracovirus* (BV) 及 *Ichnovirus* (IV) 属 (Strand and Burke, 2012)。PDV 病毒颗粒对寄生蜂并无致病性 (Gundersen-Rindal *et al.*, 2013),且病毒基因在蜂体内转录水平极低 (Burke and

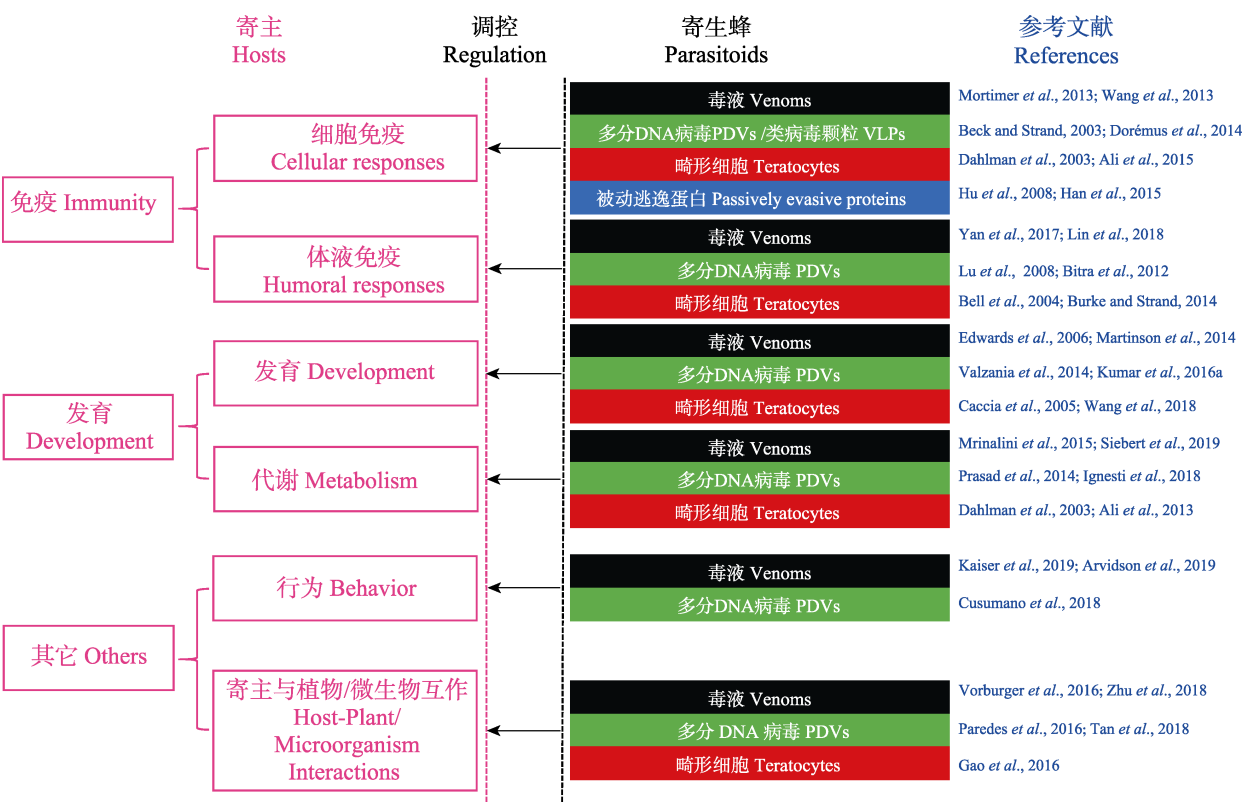


图 1 寄生蜂不同种类寄生因子对寄主害虫重要生物学过程的调控
Fig. 1 Regulations of the key biological processes of host pests by various kinds of parasitism factors from parasitoid wasps

Strand, 2014)。当其随寄生蜂产卵被注入寄主害虫体内时,它能在寄主体内迅速扩散并感染寄主细胞,其毒性相关基因被表达,并发挥功能(Burke and Strand, 2012; 2014)。

通过长期协同演化,寄生蜂及其寄主间已经形成了一套稳定的互作体系(Pennacchio and Strand, 2006; Asgari and Rivers, 2011)。寄生蜂可利用其寄生因子成功寄生寄主害虫,而寄主害虫则可通过自身的防御系统来成功避免或攻克寄生蜂寄生(Poirié *et al.*, 2009)。而这种紧张且强有力的选择压最终导致寄生蜂寄生策略的适应多样性,进而有效保证其寄生成功率(Gauthier *et al.*, 2018)。寄生蜂为了确保其后代能够在寄主害虫体内顺利完成发育,通常会采用一定手段完全抑制寄主害虫发育(抑性寄生 Idiobiont parasitism),或允许寄主继续发育(容性寄生 Koinobiont parasitism)(Whitfield, 2003)。但无论哪类寄生蜂,其寄主害虫的生理过程或多或少均受其调控,这也导致寄主在行为、内分泌、营养、生长与发育、免疫及代谢等水平上产生显著变化(Poirié *et al.*, 2009)。就寄生蜂调控寄主害虫而言,其内在机理十分复杂,目前有关该方面已有不少研究报道。有鉴于此,本文将从寄生蜂寄生因子多样性,及其调控寄主害虫免疫与发育的机理等方面,对有关最新研究进展作一概述。

1 寄生因子的多样性

寄生蜂将卵产于寄主害虫体内或体表,其后代在寄主中(或上)取食、发育,并最终致死寄主(Whitfield, 2003; Pennacchio and Strand, 2006; 严智超等, 2017)。为使寄生蜂后代在寄主中顺利发育,往往需要多种寄生因子协同作用,抑制寄主免疫,调节寄主发育,甚至调控寄主的神经和行为(Poirié *et al.* 2009; Asgari and Rivers, 2011; Kaiser *et al.*, 2019)。至今,已报道的寄生蜂主要寄生因子至少有 5 大类(含雌蜂毒液、PDV 或 VLP、卵巢蛋白、胚胎畸形细胞及幼虫分泌物)(Richards and Edwards, 2002; Strand, 2014; Strand and Burke, 2014; Mrinalini and Werren, 2016)。此外,首次从寄生蜂体蝶蛹金

小蜂 *Pteromalus puparum* 中发现一种新型负义单链 RNA 病毒 PpNSRV-1(为单分子负链 RNA 病毒目 Nyamiviridae 科下的一个新属),寄生蜂感染该病毒可显著延长成蜂寿命,并能通过减少雌性后代数量达到调控寄生蜂后代性比之目的(Wang *et al.*, 2017)。另,从一种瓢虫茧蜂 *Dinocampus coccinellae* 体内发现并鉴定获得一种新型 RNA 病毒(*D. coccinellae* 麻痹病毒 DcPV),其储存于雌蜂卵巢管内,在寄生蜂幼虫体内复制,并能被传递至寄主瓢虫 *Coleomegilla maculata* 体内。DcPV 可在瓢虫神经系统内复制,进而调控瓢虫行为,使其产生麻痹表型(Dheilly *et al.*, 2015)。上述结果表明,除了可携带 DNA 病毒外,寄生蜂还可携带 RNA 病毒,其不仅可调控寄生蜂本身的生物学特性,也极有可能是潜在的寄生因子,调控寄主害虫行为。

现有结果表明,不同种类寄生蜂其所携带的寄生因子种类及其丰富度有所不同。如,中红毁侧沟茧蜂 *Microplitis demolitor* 雌蜂携带有 PDV、毒液,而其胚胎则能释放畸形细胞(Bitra *et al.*, 2012; Burke and Strand *et al.*, 2014; Chevignon *et al.*, 2018); 斑痣悬茧蜂 *Meteorus pulchricornis* 雌蜂则携带有 VLP 及毒液(Suzuki and Tanaka, 2006; Suzuki *et al.*, 2008); 双斑镶颚姬蜂 *Hyposoter didymator* 雌蜂携带有 PDV 和毒液,尽管其毒液对寄生成功率并无显著作用(Dorémus *et al.*, 2013); 丽蝇蛹集金小蜂 *Nasonia vitripennis* 和蝶蛹金小蜂则仅含有雌蜂毒液这一种关键寄生因子(Yan *et al.*, 2017; Martinson *et al.*, 2019)。上述结果表明,所列举的茧蜂和姬蜂科寄生蜂所携带寄生因子种类较金小蜂科更为丰富。迄今,有关寄生因子多样性的研究多集中于寄生蜂毒液和 PDV,下面将以这两种因子为例,探讨其组成的多样性。

毒液为大部分寄生蜂所保守共有,是多种寄生蜂成功寄生寄主害虫的关键因子(Asgari and Rivers, 2011; 严智超等, 2017)。寄生蜂雌蜂毒器官十分微小,其内毒液含量极低,这使得寄生蜂毒液组分尤其蛋白组分的分离与鉴定面临巨大困难。基因组、转录组测序技术与生物大分子

质谱鉴定技术的迅速发展,为寄生蜂毒液蛋白组分鉴定创造了有利条件。近年来,已有多种寄生蜂毒液蛋白组分被全息解析。例如,蝶蛹金小蜂 (Yan *et al.*, 2016)、丽蝇蛹集金小蜂 (de Graaf *et al.*, 2010; Sim and Wheeler, 2016)、二化螟盘绒茧蜂 *Cotesia chilonis* (Teng *et al.*, 2017)、毁侧沟茧蜂 *M. mediator* (Lin *et al.*, 2019)、椰心叶甲啮小蜂 *Tetrastichus brontispae* (Liu *et al.*, 2018; Tang *et al.*, 2019)、白蛾周氏啮小蜂 *Chouioia cunea* (Xin *et al.*, 2017), 及优雅歧脉跳小蜂 *Diversinervus elegans* (Liu *et al.*, 2017a) 等。总体而言,寄生蜂毒液蛋白的组成较非寄生性膜翅目昆虫,如胡蜂、蜜蜂的毒液蛋白更为复杂。就寄生蜂毒液蛋白种类而言,大多数为酶类,其次是富半胱氨酸结构域蛋白/肽,如蛋白酶抑制剂、识别/结合蛋白等 (Asgari, 2006; Asgari and Rivers, 2011; 严智超等, 2017)。虽然,部分类别蛋白,如丝氨酸蛋白酶、金属蛋白酶、酯酶、钙网蛋白、抗原蛋白等为多种寄生蜂毒液蛋白组成所共有,但毒液蛋白组成在不同寄生蜂类群中仍存在显著差异,其常含有种间特异的未知毒液蛋白 (Crawford *et al.*, 2008; de Graaf *et al.*, 2010; Vincent *et al.*, 2010; Colinet *et al.*, 2013a; Dorémus *et al.*, 2013; Goecks *et al.*, 2013; Heavner *et al.*, 2013; Burke and Strand 2014; Colinet *et al.*, 2014; Perkin *et al.*, 2015; Yan *et al.*, 2016)。毒液蛋白组成在近缘种中也存在快速变异。如,丽蝇蛹集金小蜂和吉氏金小蜂 *N. giraulti* 的毒液蛋白组成存在显著差异 (Martinson *et al.*, 2017); 又如,近缘种波氏匙胸瘿蜂 *Leptopilina boulardi* 和隆脊匙胸瘿蜂 *L. heterotoma* 几乎没有共有的主要毒液蛋白组分 (Colinet *et al.*, 2013a)。另,即使是同一种寄生蜂,其毒液组成在群体水平也存在多样性 (Colinet *et al.*, 2013a, 2013b)。寄生蜂毒液蛋白组成上的多样性,可能与寄主害虫多样性及寄生蜂与寄主间长期协同演化关系有关。

与毒液不同,PDV 或 VLP 仅存在于少部分类群的寄生蜂中 (Strand and Burke, 2015)。PDV 基因组被整合于寄生蜂染色体上并以病毒前体形式存在。PDV 可通过寄生蜂进行垂直传播。

正是由于 PDV 的这种特殊生物学属性,使其系统发生与起源值得被研究。要研究 PDV 系统发生与起源,首先须获得高质量的 PDV 基因组序列。目前,已有 8 个 BV 和 5 个 IV 的全基因组完成测序 (Espagne *et al.*, 2004; Choi *et al.*, 2005; Webb *et al.*, 2006; Lapointe *et al.*, 2007; Tanaka *et al.*, 2007; Desjardins *et al.*, 2008; Chen *et al.*, 2011; Djoumad *et al.*, 2013; Jancek *et al.*, 2013; Dorémus *et al.*, 2014; Yu *et al.*, 2016)。根据基因组测序结果,发现 PDV 具有共性的结构属性,这也预示 PDV 间存在趋同进化。BV 和 IV 之间,在序列相似性上并无共同的基因家族存在,这说明两类 PDV 很可能拥有各自独立的起源 (Strand and Burke, 2014, 2015; Ye *et al.*, 2018)。BV 推测其起源于 1 亿年前裸病毒 Nudivirus 在雌蜂生殖系统中的整合 (Bézier *et al.*, 2009; Wang and Jehle, 2009; Wetterwald *et al.*, 2010; Thézé *et al.*, 2011; Herniou *et al.*, 2013)。而 IV 则很可能起源于另一未知病毒的整合 (Volkoff *et al.*, 2010; Thézé *et al.*, 2011), 这是因为 IV 中的基因与已知病毒相关基因的序列均不存在相似性。另有报道,云杉卷蛾雕背姬蜂 *Glypta fumiferanae* 和阿里山潜蝇茧蜂 *Fopius arisanus* 的 PDV 与 BV、IV 均不同源,是一个相对近期的独立起源事件 (Lapointe *et al.*, 2007; Burke *et al.*, 2018)。而在仓蛾圆柄姬蜂 *Venturia canescens* 中,其姬蜂 PDV 发生丢失,并发生了裸病毒重新整合,形成一类全新的 VLP,其 VLP 结构中并不具有 DNA (Pichon *et al.*, 2015)。另,有报道表明,隆脊匙胸瘿蜂所携带的 VLP,经蛋白质鉴定,发现其并不具备病毒来源的蛋白组成,而是一种分泌型微囊泡结构 (Heavner *et al.*, 2017)。由于 PDV 和 VLPs 分别具有多个独立进化来源,其基因组中所包含的毒性基因的组成也迥异不同,不同类别间存在显著差异 (Drezen *et al.*, 2017; Whitfield *et al.*, 2018)。即使进化来源相同,其基因组成上亦表现出显著变异 (Strand and Burke, 2012)。以 BV 为例,其不同种类间虽共有保守的 PDV 病毒颗粒组装相关的基本基因原件,但其寄生相关的毒性基因亦呈现出快速变

异, 毒性基因家族在近缘种间亦存在显著差异, 在远源种间则几乎没有共用的毒性基因家族 (Strand and Burke, 2012, 2015)。PDV 的这种属性与寄生蜂毒液蛋白的特性极为类似, 这也预示着寄生蜂所携带的寄生因子在其与寄主相互作用及协同演化过程中, 发生了快速演化, 以使寄生蜂适应其寄主。此外, 毒液蛋白组分及 PDV 基因组成上的多样性也预示了寄生蜂寄生因子的不同组分在功能上亦有可能存在多样性。

2 寄生蜂调控寄主免疫

昆虫天然免疫主要包括体液免疫和细胞免疫。针对寄生蜂卵和幼虫这类个体较大而无法通过吞噬或结节反应清除的外源物, 昆虫主要采用包裹反应将其杀死并清除 (Schmidt *et al.*, 2001; Lavine and Strand, 2002)。昆虫在包裹反应发生的同时, 通常也会伴有不同程度的黑化反应发生。寄生蜂在与寄主长期协同演化过程中也演化出一系列调控或适应寄主免疫反应的方式, 可分为主动抑制和被动逃避。主动抑制指寄生蜂通过自身携带的寄生因子抑制寄主免疫系统, 使之不能发挥正常功能。被动逃避指寄生蜂被动逃避来自寄主免疫系统的攻击, 例如通过一些卵或胚胎表面成分躲避寄主的“非我”识别 (Non-selfrecognition), 或将卵产在寄主免疫系统无法触及之处 (如神经节或中肠), 或产于免疫能力较弱时期 (如卵期) (Beckage and Gelman, 2004; Kraaijeveld and Godfray, 2009)。此处将从寄生因子角度对寄生蜂调控寄主免疫反应的内在机理作一概述。

PDV 采用降低血淋巴中游离血细胞数量, 抑制血细胞免疫能力以及改变免疫相关基因表达等手段来降低寄主血细胞的包裹能力 (Dorémus *et al.*, 2014)。棉铃虫齿唇姬蜂 *Campoletis chlorideae* 萼液 (含 PDV) 可明显降低寄主棉铃虫幼虫血细胞数量, 抑制血细胞粘附能力, 进而降低其包裹能力 (Han *et al.*, 2015)。PDV 可以通过促进血细胞凋亡来降低寄主血淋巴中免疫血细胞的数量。毁侧沟茧蜂 PDV 可以通过表达蛋白酪氨酸磷酸酶-H2 (PTP-H2) 诱导寄主

大豆夜蛾 *Pseudoplusia includens* 颗粒血细胞凋亡 (Suderman *et al.*, 2008)。黑头折脉茧蜂 *Toxoneuron nigriceps* 的 PDV 基因编码的蛋白 TnBV1 和 TnBVANK1 可引起寄主烟芽夜蛾 *Heliothis virescens* 血细胞类凋亡样细胞程序性死亡或凋亡 (Lapointe *et al.*, 2005; Salvia *et al.*, 2017)。双斑侧沟茧蜂 *M. bicoloratus* 的 PDV 基因编码蛋白可诱导寄主斜纹夜蛾血细胞中 cyclophilin A 基因表达上调, 并抑制其转录起始因子 eIF4A 表达, 从而导致血细胞凋亡 (Dong *et al.*, 2017; Tian *et al.*, 2019)。此外, 菜蛾盘绒茧蜂 *C. plutellae* 的 PDV 表达的类 EP-1 基因也可降低寄主小菜蛾幼虫血淋巴中血细胞数量 (Kwon and Kim, 2008)。多种寄生蜂, 如菜蛾盘绒茧蜂、棉铃虫齿唇姬蜂和二化螟盘绒茧蜂 PDV 都可明显抑制寄主幼虫颗粒细胞和浆细胞延展行为 (Yu *et al.*, 2007; Han *et al.*, 2015; Teng *et al.*, 2016)。PDV 对寄主血细胞粘附能力的抑制主要体现在对肌动蛋白纤维 (F-actin) 的影响上。菜蛾盘绒茧蜂 PDV 编码的 CpBV-CrV1d 蛋白可与寄主中靶标分子甘油醛-3-磷酸脱氢酶 GAPDH 相结合, 引起寄主血细胞骨架 F-actin 去稳定, 进而抑制血细胞延展 (Kumar and Kim, 2016)。索诺齿唇姬蜂 *C. sonorensis* 的 PDV 通过解聚 F-actin 或者抑制 actin 表达降低 F-actin 和 G-actin 在寄主烟芽夜蛾血细胞中表达, 从而影响血细胞包裹反应 (Turnbull *et al.*, 2004)。该蜂也可通过 PDV 的 cys-motif 基因家族成员之一 WHv1.6 基因的表达产物与寄主血细胞细胞膜和其它细胞器互作, 进而抑制血细胞在外源物表面延展粘附 (Gill and Webb, 2013)。此外, 双斑侧沟茧蜂 PDV 表达的 vinnexins 可抑制寄主斜纹夜蛾血细胞细胞间隙连接的形成, 推测其可能具有抑制血细胞包裹的作用 (Pang *et al.*, 2015)。毁侧沟茧蜂 MdBV 的 Glc1.8 和菜蛾盘绒茧蜂 PDV 的 CpBV H4 蛋白也可诱导寄主血细胞失去粘附或吞噬能力 (Beck and Strand, 2003, 2005; Gad and Kim, 2008)。微红盘绒茧蜂 *C. rubecula* 的 PDV 编码蛋白在寄主菜粉蝶血细胞受到免疫刺激时, 可抑制其表面 lectin 结合位点的暴露和

微粒形成, 进一步抑制寄主血细胞包裹反应发生; 此外, 该蜂 PDV 病毒还编码一种与 C-type lectin 同源的新型蛋白, 推测该蛋白可能与寄主血淋巴中的免疫因子相互作用, 通过竞争反应来抑制寄主免疫反应 (Glatz *et al.*, 2003)。

寄生蜂 PDV 可抑制寄主原酚氧化酶激活级联, 进而影响其黑化反应。毁侧沟茧蜂 PDV 编码两个隶属富半胱氨酸蛋白家族的成员, Egfl.0 和 Egfl.5。其中 Egfl.0 的蛋白序列与小丝氨酸蛋白酶抑制剂 (Small serpin) 的胰蛋白酶抑制剂样 (Trypsin inhibitor like) 结构域相似, 可通过抑制酰胺化阻断原酚氧化酶激活蛋白酶 (Prophenoloxidase-activating proteinase, PAP) PAP1 和 PAP3 的合成, 同时也可阻止丝氨酸蛋白酶同源物 (Serine proteinase homolog, SPH) SPH1 和 SPH2 的合成, 进而阻断原酚氧化酶激活级联反应 (Beck and Strand, 2007; Lu *et al.*, 2008)。除具有延长的 C-末端重复域外, Egfl.5 与 Egfl.0 结构相似, 二者功能亦相似 (Lu *et al.*, 2010)。此外, 寄生蜂 PDV 还可通过表达核因子 NF- κ B 的抑制因子 I- κ B, 进而影响 NF- κ B 信号途径, 抑制寄主体内抗菌肽基因表达。如毁侧沟茧蜂 PDV 能表达 I- κ B 型 ankyrin, 其中 Ank-H4 和 Ank-N5 可以通过抑制 Relish 复合体形成, 从而扰乱寄主 IMD 信号途径, 影响包括 Cecropin 和 Lebocin 等抗菌肽在寄主大豆夜蛾脂肪体中的合成 (Thoetkiattikul *et al.*, 2005; Bitra *et al.*, 2012)。集聚盘绒茧蜂 *Cotesia congregata* 的 PDV 也表达多个 ankyrin, 但其对寄主烟草天蛾 Relish1 蛋白的转录激活因子活性的抑制能力与其在细胞中的空间分布有关, 有的 V-ankyrins 只分布在细胞质, 而有的则同时分布在细胞质与细胞核 (Magkrioti *et al.*, 2011)。菜蛾盘绒茧蜂 PDV 中也可表达两个 ankyrin, CvBV-ank1, CvBV-ank12 (Chen *et al.*, 2008)。双斑侧沟茧蜂 PDV 病毒感染 Spli221 细胞后, 可检测到多个病毒片段, 包括 vank86、vank92 和 ptp109 在 Spli221 细胞中表达, 它们共同作用并抑制 NF- κ B 信号通路, 降低抗菌肽基因 attacin 在细胞中表达 (徐沙等, 2017)。

而在已知携带 IV 的姬蜂中, 毒液对寄主免疫反应几乎不起作用 (Asgari, 2012; Dorémus *et al.*, 2014)。例如半闭弯尾姬蜂 *Diadegma semiclausum* 毒液仅在寄生后 24 h 内短暂抑制寄主血细胞延展, 之后血细胞延展能力和吞噬作用都恢复正常 (黄芳等, 2011)。但在携带 BV 的茧蜂中, 不同体系结果略有不同。二化螟盘绒茧蜂毒液单独并不能对寄主二化螟血细胞免疫能力产生显著影响, 但它可抑制寄生后 6 h 内寄主体液的黑化反应, 同时协同萆液 (含 PDV) 降低寄主幼虫血淋巴中血细胞总数, 抑制血细胞粘附、包裹和血淋巴黑化能力 (Teng *et al.*, 2016)。而在一些寄生体系中, 毒液可对寄主免疫反应起明显抑制作用, 多种毒液成分在此过程中起重要作用。毁侧沟茧蜂毒液源金属蛋白酶同源物 VRF1 的活性部分可进入寄主棉铃虫血细胞与 Dorsal 结合, 而影响寄主 Toll 途径的信号转导, 进而影响血细胞对蜂卵包裹 (Lin *et al.*, 2018)。微红盘绒茧蜂毒液钙网蛋白 (Calreticulin) CrCRT 可抑制寄主血细胞粘附能力 (Zhang *et al.*, 2006)。微红盘绒茧蜂毒液蛋白 Vn50 可抑制寄主菜粉蝶的血淋巴黑化反应 (Asgari *et al.*, 2003; Zhang *et al.*, 2004)。但菜粉蝶盘绒茧蜂 *C. glomerata* 的毒液对寄主菜粉蝶幼虫的血淋巴黑化反应无显著影响, 寄生后寄主酚氧化酶活性降低可能来源于萆液的作用 (Zhu *et al.*, 2011)。

在不携带 PDV 的寄生蜂中, 毒液对寄主免疫反应的影响主要体现在降低寄主血细胞数量, 抑制血细胞粘附及包裹能力, 以及抑制寄主血淋巴黑化反应等方面。如, 蝶蛹金小蜂毒液可以显著增加寄主菜粉蝶蛹血细胞总数, 抑制其血细胞延展, 降低其包裹和吞噬能力, 并降低其黑化能力 (Fang *et al.*, 2011a; Zhang *et al.*, 2012)。白蛾周氏啮小蜂毒液可抑制美国白蛾蛹颗粒细胞和浆血细胞包裹作用和吞噬作用, 且随毒液浓度增加, 两种血细胞免疫能力均显著下降 (辛蓓等, 2016)。白蛾黑基啮小蜂 *T. nigricoxae* 毒液对寄主杨小舟蛾蛹血细胞包裹反应有明显抑制作用 (于艳华等, 2015)。啮小蜂 *Tetrastichus* sp. 毒液对亚洲玉米螟蛹血细胞免疫反应也有显著抑

制作用(任丹青等, 2004)。果蝇寄生蜂匙胸瘿蜂 *Ganaspis* sp.1(G1)毒液中的 sarco/endoplasmic reticulum calcium ATPase (SERCA) 可抑制黑腹果蝇浆细胞细胞质中钙离子爆发, 从而影响浆细胞激活和粘附能力及寄主的细胞免疫能力 (Mortimer *et al.*, 2013)。蝶蛹金小蜂毒液可抑制寄主菜粉蝶蛹血细胞和脂肪体中 C-type lectin、cecropin、lysozyme、attacin 和 lebecin 等多种免疫相关基因的表达 (Fang *et al.*, 2010; 2011a; 2016)。其毒液钙网蛋白在抑制细胞免疫过程中起重要作用 (Wang *et al.*, 2013), 这与微红盘绒茧蜂毒液钙网蛋白功能类似。在白蛾周氏啮小蜂毒液蛋白组和亚金跳小蜂 *Aenasius arizonensis* 毒腺转录组中也鉴定到了钙网蛋白, 及其它相关酶类如金属蛋白酶、丝氨酸蛋白酶及精氨酸激酶的存在 (Shaina *et al.*, 2016; Xin *et al.*, 2017)。蝶蛹金小蜂毒液还可以抑制其寄主体内一些其它免疫相关基因如革兰氏阴性菌结合蛋白、肽聚糖识别蛋白、 β -1, 3-葡聚糖识别蛋白基因的表达, 进而影响寄主菜粉蝶蛹的天然免疫反应 (Fang *et al.*, 2010; Zhu *et al.*, 2015)。此外, 蝶蛹金小蜂毒液可以抑制菜粉蝶蛹体内清道夫受体 (Scavenger receptor) Pr-SR 基因的表达, 从而影响血细胞的吞噬和包囊能力 (Fang *et al.*, 2011b)。此外, 毒液也会影响到寄主的血淋巴黑化作用。如丽蝇蛹集金小蜂毒液中含有 Pacifastin 蛋白酶抑制剂 NVPP-1、NVPP-2 及 NvSPPI (小丝氨酸蛋白酶抑制剂的一种), 其均能显著抑制寄主家蝇蛹血淋巴中原酚氧化酶激活级联反应, 进而削弱寄主体液免疫水平 (钱岑等, 2013; Qian *et al.*, 2017)。蝶蛹金小蜂寄生后, 菜粉蝶蛹转录组中 serpin 基因的表达量显著上调 (Zhu *et al.*, 2015), 同时其毒液中还含有一种 serpin 剪接体蛋白, 它通过与寄主菜粉蝶蛹血淋巴中的原酚氧化酶激活蛋白 Pr-PAP1 形成复合物, 来抑制原酚氧化酶的激活反应, 进而抑制寄主血淋巴的黑化作用 (Yan *et al.*, 2017)。

类病毒粒子 (VLPs) 及卵巢蛋白可帮助寄生蜂卵逃避寄主的免疫反应。仓蛾圆柄姬蜂卵表面覆盖的 VLPs 具有抑制寄主血细胞粘附的功

能, 从而保护蜂卵免受寄主血细胞的包囊 (Schmidt *et al.*, 2001)。隆脊匙胸瘿蜂与生殖系统相连的附腺中含有 VLPs, 它可专一性地感染果蝇与非我识别和包囊相关的薄层细胞 lamellocytes 并诱导其凋亡, 但其对与吞噬相关的浆细胞无显著影响 (Schmidt *et al.*, 2001)。在微红盘绒茧蜂毒液中也鉴定到一种 32 ku 蛋白 (Crp32), 它由卵巢区细胞分泌, 可粘附到蜂卵或其它病毒颗粒表面, 在寄生蜂产卵时随卵进入寄主体内, 其重组蛋白可抑制寄主血细胞对外源物的包囊反应 (Asgari *et al.*, 1998)。斑痣悬茧蜂毒囊中存在一种结构与仓蛾圆柄姬蜂类病毒颗粒类似的类病毒粒子, 它可诱导寄主斜纹夜蛾幼虫血细胞尤其是颗粒细胞凋亡, 注射该粒子可明显降低斜纹夜蛾血细胞对外源物的包囊能力 (Suzuki and Tanaka, 2006)。此外, 有关蜂幼虫分泌物影响寄主免疫反应的研究相对较少。其中, 多胚发育寄生蜂佛罗州点源跳小蜂 *Copidosoma floridanum* 的两种幼虫基因表达分析结果表明, 其能表达丝氨酸蛋白酶和富半胱氨酸结构域多肽, 这些蛋白或多肽可能起到调控寄主粉纹夜蛾黑化反应或抗菌肽合成的功能, 可在抑制寄主免疫能力的同时增强寄主对病原微生物的抵抗能力 (Donnell and Strand, 2006)。

畸形细胞作为一种重要的寄生因子, 它也对寄主免疫反应起着调控作用。首先被发现的畸形细胞对寄主免疫反应的调控作用主要集中于其对寄主血淋巴黑化反应的抑制功能 (Bell *et al.*, 2004)。在菜蛾盘绒茧蜂畸形细胞基因组中, 鉴定到畸形细胞分泌的类毒液蛋白 TSVP-8 的编码基因, 其表达产物可抑制寄主血淋巴黑化反应 (Gao *et al.*, 2016)。畸形细胞对寄主细胞免疫的抑制功能首先在菜蛾盘绒茧蜂中被证实, 当小菜蛾被植入菜蛾盘绒茧蜂畸形细胞后, 其血细胞结节形成能力降低 40% 左右, 且早期畸形细胞的免疫抑制能力强于晚期 (Andrew *et al.*, 2006)。在菜蛾盘绒茧蜂畸形细胞转录组中共鉴定到 11 个丝氨酸蛋白酶编码基因和 7 个 Rho GTPase 激活蛋白 (RhoGAPs) 编码基因, 并通过 RNAi 实验验证, serpin-1, 4 和 RhoGAP-2, 5 可抑制寄

主血细胞免疫能力,降低血细胞对大肠杆菌结节的形成 (Ali *et al.*, 2015)。此外,在该蜂基因组中还鉴定到与红足侧沟茧蜂 *M. croceipes* 畸形细胞 TSP 14 蛋白同源的具 Cys-motif 结构域的 Cp-TSP13 编码基因,其编码基因重组蛋白可显著抑制寄主血细胞延展能力 (Rana *et al.*, 2002; Dahlman *et al.*, 2003; Kim and Kim, 2016)。畸形细胞也可表达抗菌肽。在菜蛾盘绒茧蜂畸形细胞转录组中鉴定到了抗菌肽 defensin-1, defensin-3 基因的表达,且寄生后小菜蛾幼虫抗菌能力要高于假寄生(不产卵,无畸形细胞产生)对照 (Gao *et al.*, 2016),该蜂 PDV 表达蛋白会抑制寄主体内抗菌肽合成,而畸形细胞表达抗菌肽则可起到代偿作用。毁侧沟茧蜂畸形细胞也可表达产生抗菌肽 hymenoptaecin,可能具有与菜蛾盘绒茧蜂畸形细胞表达抗菌肽功能类似 (Burke and Strand, 2014)。

部分寄生蜂并不主动抑制寄主免疫反应,而是通过被动策略进行逃避。多种寄生蜂卵表纤维层可帮助其子代逃避寄主血细胞包裹反应。黑头折脉茧蜂卵表面纤维层可保护其不被寄主烟芽夜蛾幼虫血细胞包裹 (Davies and Vinson, 1986)。微红盘绒茧蜂卵表面会粘附一种萼液蛋白,这种蛋白可在 PDV 基因表达前,被动保护其不被寄主菜粉蝶幼虫血细胞包裹 (Asgari *et al.*, 1998)。棉铃虫齿唇姬蜂卵可通过其卵表成分被动逃避寄主棉铃虫幼虫包裹反应 (Han *et al.*, 2015)。镶颚姬蜂卵可依赖其在被产入寄主体内之前就已粘附的卵表面蛋白逃避寄主血细胞包裹,经质谱分析共鉴定获得免疫相关蛋白-载脂蛋白 III 和 3 个姬蜂病毒结构蛋白编码区蛋白 (Dorémus *et al.*, 2013)。仓蛾圆柄姬蜂卵表 mucin 层载脂蛋白 III-hemomucin 复合物可帮助其逃避寄主地中海粉螟 *Ephestia kuehniella* 的包裹反应 (Kinuthia *et al.*, 1999)。腰带长体茧蜂 *Macrocentrus cingulum* 卵及胚胎表面的重糖基化蛋白 hemomucin 也可通过其表面糖修饰-Gal-GalNAc 保护它们免受寄主血细胞包裹 (Hu *et al.*, 2003, 2008, 2014)。对 61 个基因组已知的昆虫 hemomucin 基因进行分析,结果表明, hemomucin 蛋白在昆虫中广泛

存在,分为含 mucin 和不含 mucin 结构域两种形式。对 7 个内寄生蜂 hemomucin 蛋白结构分析表明, mucin 结构域只在目前已知的两种采用被动逃避策略的寄生蜂仓蛾圆柄姬蜂和腰带长体茧蜂中存在,而在其它 PDV 或毒液起重要功能的寄生蜂类群中, hemomucin 蛋白的 mucin 域均已丢失。而 Hemomucin 糖基化位点主要位于 mucin 域上。这些结果提示寄生蜂被动逃避策略可能与糖识别相关 (Yin *et al.*, 2018)。此外,采用转录组结合蛋白质组学方法,对二化螟盘绒茧蜂卵巢蛋白进行鉴定,发现其中含被动免疫逃逸蛋白 IEPs 的同源蛋白 IEP-1, IEP-2A 和 IEP-2B,以及 Crp32 的同源蛋白 Crp32A, Crp32B 和 Crp32C。其中, IEP-1 和 IEP-2A 及 Crp32A-C 均在雌蜂卵巢中高表达,且 Crp32B 只在卵巢中表达。功能研究结果表明,重组 Crp32B 蛋白能在寄主体内抑制其血细胞对 Ni 离子树脂珠子(模拟寄生蜂卵)的包裹作用,且此抑制作用呈显著剂量效应 (滕子文, 2017)。

寄生蜂调控寄主免疫反应涉及多个因子间的相互作用,在一个寄生体系中可能同时存在主动抑制和被动逃避策略。镶颚姬蜂卵可通过粘附在其表面的蛋白被动逃避寄主包裹反应,但其幼虫还需要 PDV 提供的主动抑制保护 (Dorémus *et al.*, 2013)。棉铃虫齿唇姬蜂卵亦可被动逃避寄主包裹反应,但幼虫期还需要来自 PDV 的保护 (Han *et al.*, 2015)。此外,不同寄生体系中同一因子所起作用可能不同,如在携带 PDV 的寄生蜂中,毒液大多起协同或增效作用,而在不携带 PDV 寄生蜂中,毒液则可直接起抑制包裹反应及黑化反应的功能。此外,同一类寄生因子如毒液,其中的相同组分,可能在不同寄生体系中,所起免疫抑制作用亦显著不同。如钙网蛋白,其在“蝶蛹金小蜂-菜粉蝶蛹”体系中,毒液钙网蛋白 PpCRT 可显著抑制菜粉蝶蛹血细胞延展与包裹作用 (Wang *et al.*, 2013),而它在“丽蝇蛹集金小蜂-蝇蛹”体系中,该蜂毒液钙网蛋白却起着抑制寄主血淋巴黑化反应的作用 (Siebert *et al.*, 2015) 另外,不同因子也可能在不同寄生体系中起相同作用。如 PDV 具有抑制寄主黑化

反应的功能,而毒液也就具有这个功能,但它们作用方式不同。寄生蜂在调控寄主免疫方面所表现出的这些特性可能与其对寄主高度适应性及其长期协同演化有关。

3 寄生蜂调控寄主发育

寄生蜂寄生因子除了抑制寄主免疫反应外,还会调控寄主发育,主要包括抑制或推迟寄主发育或影响其变态,调控寄主营养物质、激素及生长调节因子的含量与变化水平等。同时,寄生蜂可调控寄主体内的代谢水平,从而为其子代营造良好的生存环境。其可通过下调寄主代谢水平并麻痹寄主,来延长寄生蜂子代的取食时间,从而使其获得最佳的生存条件(Nakamatsu *et al.*, 2006; Becchimanzi *et al.*, 2017)。

就 PDV 而言,如黑头折脉茧蜂 PDV 中 Ankrin 基因家族成员 *TnBVank1*,其表达产物可通过阻断其寄主黑腹果蝇类固醇生成细胞的内吞运输,从而扰乱其前胸腺蜕皮类固醇合成(Valzania *et al.*, 2014)。同样,*TnBVank3* 的表达产物可抑制寄主前胸腺细胞类固醇合成基因的表达,同时可调控黑腹果蝇体内 insulin/TOR 信号转导途径相关基因表达,进而影响寄主体内蜕皮激素合成(Ignesti *et al.*, 2018)。上述结果可知,黑头折脉茧蜂 PDV 的 *TnBVank1* 和 *TnBVank3* 调控寄主蜕皮激素合成与变态发育的途径不同。菜蛾盘绒茧蜂 PDV 基因 *CpBV-H4*,其表达产物可抑制寄主小菜蛾体内两个核染色质重构因子(Chromatin remodeling factors),赖氨酸去甲基化酶以及 SWI/SNF 复合物编码基因的表达,进而抑制寄主胰岛素信号通路并延缓寄主发育(Kumar *et al.*, 2016a, 2016b)。在菜蛾盘绒茧蜂 PDV 基因组中共注释获得 4 个与杆状病毒 P94 蛋白基因同源的基因 *CpBV-E94Ks*,功能研究表明,该 4 个基因的表达产物均能显著抑制寄主小菜蛾发育进度(Kim and Hepat, 2016)。另,在菜蛾盘绒茧蜂 PDV 基因组中鉴定到一个选择性转录抑制因子编码基因 *CpBV15β*,该基因表达产物可抑制寄主小菜蛾体内精氨酸激酶 Px-AK 和生长因子 Px-IDGF 基因的转录水平,

进而抑制寄主变态与发育过程(Prasad *et al.*, 2014)。向小菜蛾体内注射菜蛾盘绒茧蜂 PDV 基因组片段 S27(其上含有 7 个蛋白酪氨酸磷酸酶 CpBV-PTPs),可显著降低寄主体内发育相关激素的滴度水平,进而延缓寄主发育(Kwon *et al.*, 2010)。毁侧沟茧蜂 PDV 感染寄主大豆夜蛾后能持续保持其寄主体内的保幼激素水平,并一直升高蜕皮激素滴度,最终导致寄主幼虫发育延缓,变态化蛹延迟(Pruijssers *et al.*, 2009)。索诺齿唇姬蜂 PDV 上富半胱氨酸结构域蛋白基因的重组表达产物可显著抑制烟芽夜蛾幼虫发育,减少其正常化蛹比例,增加寄主死亡率(Fath-Goodin *et al.*, 2006)。另,寄生蜂 PDV 进入寄主鳞翅目幼虫体内,PDV 上相关基因可在寄主唾液腺中发生表达,使寄主幼虫唾液组分发生改变,进而改变幼虫取食植物后所引起的植物挥发物组成,使被取食植物降低对该寄生蜂的重寄生蜂的吸引力,以保护该寄生蜂后代不受其重寄生蜂危害(Zhu *et al.*, 2018)。同时,亦有证据表明,寄生蜂 PDV 进入寄主鳞翅目幼虫体内,能抑制寄主唾液腺中葡萄糖氧化酶活性(植物防御反应的重要激发子),进而下调植物防御反应,促使寄主幼虫生长更为迅速,以更有利于寄生蜂后代生存与适应(Tan *et al.*, 2018)。

与寄生因子 PDV 类似,寄生蜂毒液蛋白亦可通过对寄主与营养代谢相关的基因或者基因网络进行调控,进而对其寄主发育起调控作用。例如,丽蝇蛹集金小蜂毒液能引起寄主棕尾别麻蝇 *Sarcophaga bullata* 与发育阻滞相关基因的差异表达(Martinson *et al.*, 2014)。通过转录组技术分析发现蝶蛹金小蜂寄生引起寄主中多个与脂肪、糖类、氨基酸等代谢相关的基因发生差异表达(Zhu *et al.*, 2015);管氏肿腿蜂寄生可引起寄主黄粉甲蛹血淋巴中的 α -淀粉酶、乙醇脱氢酶、环己-1-烯-1-羧基-CoA 水合酶等与能量代谢相关的蛋白差异表达(Zhu *et al.*, 2014);毁侧沟茧蜂寄生导致寄主棉铃虫血淋巴中 68 个与物质代谢相关的蛋白差异表达,这些差异表达蛋白中分别有 20 和 12 个与糖和脂肪酸代谢通路相关(Lin *et al.*, 2019)。寄生蜂毒液还可通过寄生

或注入毒液来调控寄主体内激素水平,进而调控其发育进度。如栉角姬小蜂 *Eulophus pennicornis* 寄生或注射毒液到番茄夜蛾 *Lacanobia oleracea* 幼虫体内后,番茄夜蛾不能蜕皮,发育停滞 (Edwards *et al.*, 2006)。另外,毒液蛋白 EpMP3 注射到 5 龄番茄夜蛾幼虫后,使其部分不能蜕皮到 6 龄而死亡,存活的幼虫发育和生长迟缓 (Price *et al.*, 2009)。蚜茧蜂 *Aphidius colemani* 注射毒液至二龄蚕豆蚜 *Aphis fabae* 后,其幼虫发育至四龄后翅芽退化,且表现出发育停滞,羽化成虫时的死亡率增加 (Kati and Hardie, 2010)。此外,寄生蜂寄生会引起寄主体内激素紊乱 (内分泌组织被破坏或靶标位点对激素信号响应受抑制),从而导致寄主发育延迟或完全停滞 (Asgari and Rivers, 2011)。栉角姬小蜂 *E. pennicornis* 毒液可通过调节寄主前胸腺活性来破坏其蜕皮类固醇生成,进而阻碍其发育 (Edwards *et al.*, 2006)。烟草天蛾被集聚盘绒茧蜂 *C. congregata* 寄生后,毒液可导致寄主血淋巴蜕皮类固醇滴度发生异常 (Beckage *et al.*, 1998)。蝶蛹金小蜂寄生或注射毒液至菜粉蝶体内,导致寄主保幼激素酯酶活性显著下降,保幼激素含量上升,蜕皮激素含量显著降低 (Zhu *et al.*, 2009)。此外,寄生蜂寄生或毒液往往对寄主脂肪体的影响尤为突出,这可能是由于寄主脂肪体中富含大量脂类物质,而某些寄生蜂成虫缺乏脂肪合成能力,其成虫阶段所需脂类物质必须由幼虫直接从寄主中获得并积累 (Visser and Ellers, 2008)。寄生蜂毒液中存在的部分酶类功能蛋白,其可能具有直接分解寄主体内物质的功能,进而为寄生蜂子代提供物质储备。例如,在蝶蛹金小蜂、管氏肿腿蜂、椰心叶甲啮小蜂等寄生蜂毒液中富含酸性磷酸酶,其可能行使水解寄主磷酸酯而为寄生蜂幼虫提供营养物质的功能 (Zhu *et al.*, 2008; Liu *et al.*, 2017b, 2018)。

寄生蜂毒液对寄主体内营养物质含量的调控已有很多研究,不同寄生蜂对寄主的营养调控有其特异性。寄生蜂毒液中普遍存在丝氨酸蛋白酶、脂肪酶、磷酸酯酶 A1、葡萄糖苷酶、烯醇酶等多种具有消化或分解代谢重要物质的酶类,

它们也可能具有调控寄主营养代谢的功能 (Yan *et al.*, 2016; Zhu, 2016; Teng *et al.*, 2017; Xin *et al.*, 2017; Zhao *et al.*, 2017; Liu *et al.*, 2017a, 2018; Lin *et al.*, 2019)。其中,以模式寄生蜂丽蝇蛹集金小蜂为对象,已开展了系列研究,以揭示其毒液对其寄主体内代谢的调控作用。结果表明,其毒液并非简单的抑制寄主代谢水平,而是特异性的针对寄主某些重要的代谢过程 (Mrinalini *et al.*, 2015)。丽蝇蛹集金小蜂毒液能激活寄主山梨糖醇的生物合成,且该毒液亦可改变人肾脏细胞山梨醇代谢相关基因的表达水平,这也预示着其具有良好药用前景 (Siebert *et al.*, 2019)。同时,毒液能保持寄主稳定的血糖水平;通过切换无氧呼吸和阻止三羧酸循环,进而改变中间产物转变;阻止几丁质合成可能影响成虫结构形成进而延缓寄主发育;提升寄主体内大部分自由氨基酸水平并增加其磷脂降解 (Mrinalini *et al.*, 2015)。该蜂毒液中的高丰度蛋白组分毒液 Y 蛋白可参与寄主麻蝇的解毒代谢过程 (Martinson *et al.*, 2019)。此外,黑胸茧蜂 *Bracon nigricans* 毒液可为寄主组织提供所需的营养支持,改变寄主血淋巴蛋白、糖类和酰基甘油滴度 (Becchimanzi *et al.*, 2017)。姬小蜂 *Euplectrus separatae* 寄生或注射毒液至寄主粘虫后,粘虫血淋巴中蛋白和脂类含量均显著升高,而脂肪体中蛋白和脂类含量在后期显著降低 (Nakamatsu and Tanaka, 2004)。蝶蛹金小蜂寄生可下调菜粉蝶蛹脂肪体内贮藏蛋白基因转录水平 (Zhu *et al.*, 2009)。阿尔蚜茧蜂 *A. ervi* 寄生豌豆长管豆蚜 *Acyrtosiphon pisum* 后,能导致寄主血淋巴内氨基酸含量发生变化 (Rahbé *et al.*, 2002)。螟黄足绒茧蜂 *C. flavipes* 寄生可减少寄主对食物的消耗,降低其生长速率,而提升寄主淀粉酶和海藻糖酶活性水平 (Rossi *et al.*, 2014)。另,寄生蜂毒液蛋白中的酸性磷酸酶和海藻糖酶组分可能降低寄主血淋巴中的碳水化合物,毒液中的脂酶或酯酶推测其可能与和寄主脂肪体降解相关 (Richards, 2012; Heavner *et al.*, 2013)。

除 PDV 与毒液外,寄生蜂胚胎所释放的畸形细胞亦可影响寄主的生长与发育。例如,阿尔

蚜茧蜂畸形细胞可在寄主体内大量分泌脂肪酸结合蛋白,其能与寄主脂肪体中的脂肪酸结合并将它们运送给发育中的幼蜂取食 (Caccia *et al.*, 2005)。菜蛾盘绒茧蜂畸形细胞分泌蛋白可通过抑制寄主小菜蛾的保幼激素酯酶活性,下调其蜕皮激素受体基因的表达水平,以调控寄主体内内分泌信号,最终延缓寄主的发育与变态 (Ali *et al.*, 2013)。红足侧沟茧蜂 *M. croceipes* 胚胎所释放的畸形细胞中含有一种蛋白 TSP14,它能显著抑制寄主烟芽夜蛾幼虫生长与发育,并能抑制其蛋白质合成 (Dahlman *et al.*, 2003)。此外,畸形细胞不仅可以调控寄主代谢,而且可以直接作为营养物质被寄生蜂幼虫取食,还能分泌如卵黄蛋白、储藏蛋白等与寄主血淋巴中营养物质相似的蛋白作为寄生蜂子代的营养来源 (Dahlman *et al.*, 2003)。另,菜蛾盘绒茧蜂 PDV 及其畸形细胞,均可表达特异的 microRNA,靶向寄主蜕皮激素受体,从而延缓寄主发育 (Wang *et al.*, 2018),这也是首次在昆虫体内发现 microRNA 的跨物种传递。

此外,某些寄生蜂还能通过抑制寄主内生殖系统的发育,造成寄生性去势 (Parasitic castration)。如阿尔蚜茧蜂毒液中的 γ -谷氨酰转肽酶能诱导寄主豌豆长管蚜卵巢组织凋亡,对寄主构成寄生性去势 (Falabella *et al.*, 2007)。而对于蚜虫、飞虱、果蝇等寄主昆虫,内共生菌除在它们的物质利用以及抵御寄生蜂寄生中具有重要作用,也发现寄生蜂可与内共生菌竞争摄取寄主体内物质,提示寄生蜂可通过内共生菌影响寄主物质代谢,但寄生蜂-内共生菌-寄主内在物质互作机制尚不清楚 (Paredes *et al.*, 2016; Vorburger and Rouchee, 2016)。

4 结论与展望

寄生蜂所携带的寄生因子种类繁多且组分多样,随着现代基因组测序技术与生物大分子质谱鉴定技术的迅猛发展,鉴定并解析不同种类寄生因子的组分组成已变得相对容易。但是,寄生蜂毒液不同于同为寄生因子的 PDV (较易对不

同基因进行体外异源表达)和畸形细胞(体外培养即可自行分泌有效组分),也不同于蝎子等节肢动物毒液(可通过外界刺激使毒液直接分泌至体外且便于收集),其中有效组分鉴定往往建立在毒器官差异转录组分析结合毒液(量极少且非自行分泌)蛋白质组分析之基础上,因而毒液蛋白候选组分的筛选过程存在一定不足。同时,目前有关寄生蜂毒液组分的鉴定与解析主要集中于蛋白或多肽,而几乎未涉及其中结构简单的小分子化合物。因此,寄生因子毒液组分鉴定与解析仍有很大提升空间,颇值得深究。

另方面,寄生蜂对寄主害虫的调控机理复杂且多元,目前有关该领域的研究结果主要集中于寄生蜂对寄主免疫的调控机理方面,而有关其调控寄主发育、代谢及行为等方面相对稍显薄弱,亟待加强。此外,针对寄生蜂寄生因子及其调控寄主的机理两大块的系统研究,不仅可以提升昆虫寄生学与生理学研究领域的认知水平,具有深远的科学意义。同时,由于寄生蜂所携带的部分寄生因子,具有成为绿色、安全有效的杀虫活性物质候选资源的潜在可能,可将其编码基因通过一定遗传操作手段导入昆虫病原微生物或植物中,以提高微生物及植物的抗虫活性。同时,部分寄生因子组分亦具有潜在的医用或药用价值,前景十分广阔。但是,与寄生因子广阔的应用前景相比,目前其已成形并已成功的应用实例则十分稀少。仅有, Rodriguez-Andres 等 (2012) 将毁侧沟茧蜂寄生因子 PDV 中的 Egfl.0 蛋白编码基因转入塞姆利基森林病毒 (Semliki forest virus) 中,进而有效提高了该病毒对埃及伊蚊的致死效果。Maiti 等 (2003) 将红足侧沟茧蜂 *M. croceipes* 畸形细胞分泌蛋白 TSP14 转入了烟草,使烟草增强了对靶标害虫烟芽夜蛾和烟草天蛾的抗性。此外, Di Lelio 等 (2014) 将黑头折脉茧蜂 PDV 上的 TnBVANK1 基因转入烟草,使其获得了对夜蛾科埃及棉叶蛾 *Spodoptera littoralis* 的抗性。虽然,截止目前有关寄生因子应用的成功案例较少,但其为靶标害虫生物防治,非靶标生物保护及新型生物杀虫剂研发提供了全新思路及可能性。

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