小菜蛾对Bt Cry1Ac杀虫蛋白抗性的遗传与信号调控机制

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摘要：十字花科蔬菜是我国最重要的蔬菜类群之一，不仅是“菜篮子”工程的核心品类，更是种业振兴、乡村振兴和功能农业的重要抓手。小菜蛾*Plutella xylostella*是十字花科蔬菜的重大害虫之一，每年给农业造成巨额经济损失。苏云金芽胞杆菌*Bacillus thuringiensis*（Bt）能产生多种杀虫蛋白（如Cry1Ac），因其杀虫特性高效特异和环境友好等特点，在小菜蛾防治中发挥着重要作用。然而，小菜蛾已对Bt Cry1Ac杀虫蛋白产生抗性，这严重阻碍了Bt的实际应用效果。该文综述了小菜蛾对Bt Cry1Ac杀虫蛋白的抗性机制，重点阐述了中肠受体变异及信号通路改变为主导的抗性进化途径。此外，展望了未来研究方向，提出应综合运用现代遗传学、分子生物学及多组学技术进一步揭示其抗性分子机制。

关键词：小菜蛾；苏云金芽胞杆菌；Cry杀虫蛋白；抗性机制；信号途径

Genetic and signaling regulatory mechanisms underlying resistance to the Bt Cry1Ac toxin in the diamondback moth *Plutella xylostella*

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Abstract: Cruciferous vegetables are among the most important vegetable crops in China. They are not only a core component of the national vegetable supply system but also play a crucial role in seed industry revitalization, rural development, and functional agriculture. The diamondback moth *Plutella xylostella* is a major pest of cruciferous vegetables and causes substantial economic losses to agricultural production each year. *Bacillus thuringiensis* (Bt) produces a variety of insecticidal proteins, including Cry1Ac, which have been widely used for the control of *P. xylostella* because of their high efficacy, target specificity, and environmental safety. However, the evolution of resistance to the Bt Cry1Ac toxin in *P. xylostella* has greatly reduced the effectiveness of Bt-based pest control. This review summarizes the resistance mechanisms of *P. xylostella* to Bt Cry1Ac toxin, with particular emphasis on resistance evolution mediated by alterations in midgut receptors and signaling pathways. Future research direc-

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tions are also discussed, highlighting the need to integrate modern genetics, molecular biology, and multi-omics approaches to further elucidate the molecular mechanisms underlying Bt resistance.

Key words: *Plutella xylostella*; *Bacillus thuringiensis*; Cry toxin; resistance mechanism; signaling pathway

大白菜 *Brassica rapa* subsp. *pekinensis*、甘蓝 *Brassica oleracea* var. *capitata*、萝卜 *Raphanus sativus*、芥菜 *Brassica juncea*、青花菜 *Brassica oleracea* var. *italica* 和油菜 *Brassica napus* 等十字花科蔬菜不仅种类多样，而且含有丰富的营养物质，是我国常见的蔬菜种类。中国是全球十字花科蔬菜的重要生产国和消费国，十字花科蔬菜栽培面积约占国内蔬菜总栽培面积的1/3（史应仙等，2025）。小菜蛾 *Plutella xylostella* 是严重为害十字花科蔬菜的重要害虫，因其分布广、繁殖快和适应性强，对蔬菜产业构成持续威胁（张友军等，2013；郭兆将等，2015），每年在全球范围内造成约40亿~50亿美元的经济损失（Furlong et al.，2013），其中在中国造成的经济损失就达到7.7亿美元（Li et al.，2016）。该害虫导致十字花科蔬菜产出减少、商品品质降低以及防治投入增加，这严重影响十字花科蔬菜农产品安全（吴青君和张友军，2025）。更严峻的是，小菜蛾对药剂的抗性发展迅速，导致化学防治效果不断下降，进一步增加了防控难度（杨蕊弘等，2025）。近年来，结合生物防治、物理防治、化学防治和基因编辑遗传技术等手段的综合防控策略逐渐成为小菜蛾治理的核心方向，多学科防控技术的融合为其可持续治理提供了新的可能（陆宴辉等，2023；吴青君和张友军，2025）。

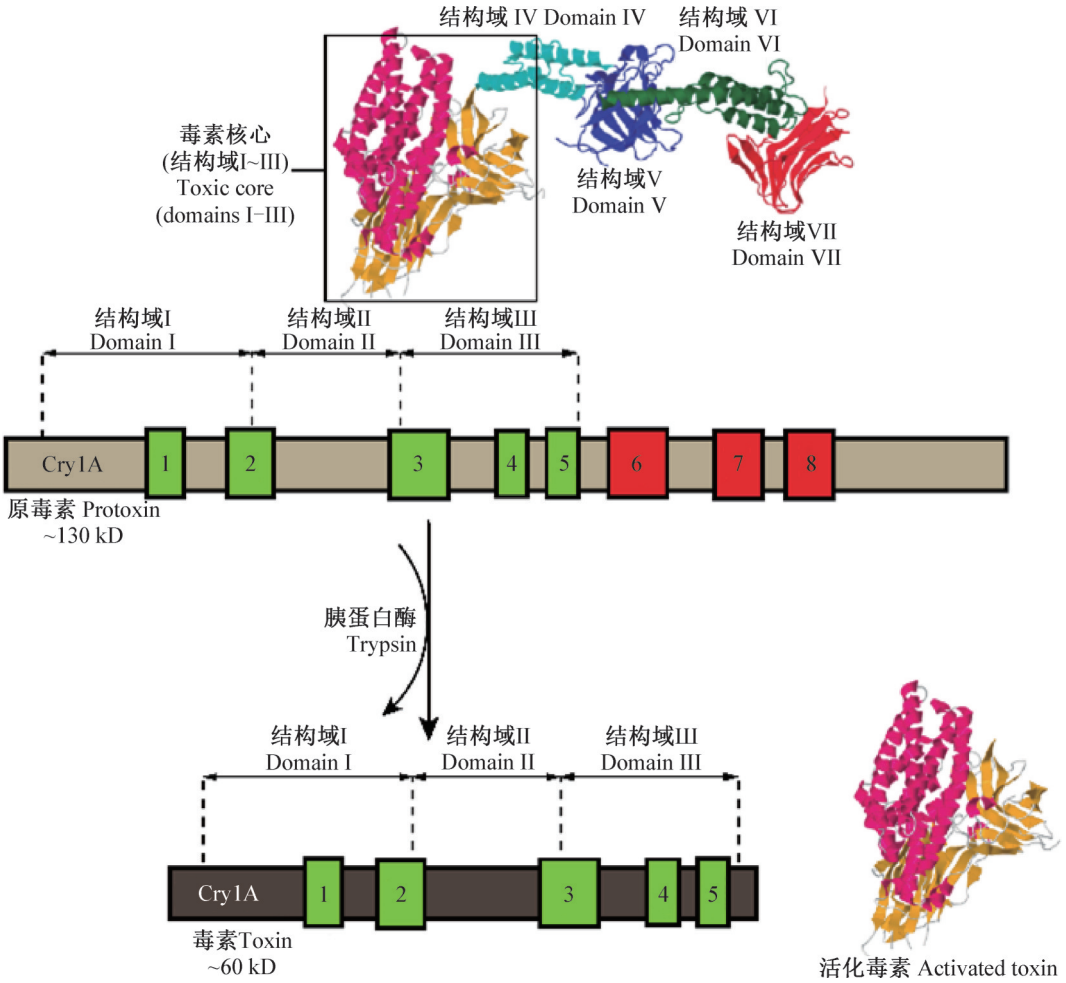
苏云金芽胞杆菌 *Bacillus thuringiensis*（Bt）是一种好氧型的革兰氏阳性细菌，是目前应用最广、机理研究最系统的微生物杀虫剂（Usta，2013）。其在生长过程中主要合成两类杀虫蛋白：一类为芽孢形成期产生的杀虫晶体蛋白，包括Cry和Cyt蛋白（Höfte & Whiteley，1989；Schnepf et al.，1998）；另一类为分泌型蛋白，如营养期杀虫蛋白（vegetative insecticidal protein，VIP）和分泌期杀虫蛋白（secretory insecticidal protein，SIP）（Estruch et al.，1996；Donovan et al.，2006）。

Bt杀虫蛋白因对靶标害虫具有高效杀虫活性、对非靶标生物相对安全等特点而被广泛推广（Mendelsohn et al.，2003；Bravo et al.，2011；Comas et al.，2014；Krogh et al.，2020）。在1996—2019年，全球转Bt基因作物的种植规模由100万 hm^2 扩展至1.09亿 hm^2，种植规模增长了109倍（ISAAA，2019）。转Bt作物的广泛应用显著提升了对害虫的防控效果，同时降低了化学农药的使用量（Dively et al.，2018；Hutchison et al.，2010；National Academies of Sciences & Medicine，2016；Tabashnik et al.，2021）。然而，随着害虫对转Bt基因作物/Bt微生物杀虫剂抗性的不断发展，Bt杀虫蛋白的应用效果正逐渐被削弱（Tabashnik & Carrière，2019）。至今已有13种害虫（包括11种鳞翅目昆虫和两种鞘翅目昆虫）对一种或更多种Bt作物产生抗性（Tabashnik et al.，2023）。尤其是小菜蛾，早在1990年就对Bt微生物杀虫剂表现出高抗性（Tabashnik et al.，1990）。目前用于小菜蛾防治的Bt菌株以Bt库斯塔克亚种 *B. thuringiensis* subsp. *kurstaki*（Btk）菌株为主，Btk菌株所含的Cry1Aa、Cry1Ab和Cry1Ac蛋白对鳞翅目害虫具有特异性毒杀作用，以Cry1Ac的毒力最高（Jallouli et al.，2020）。由此可见，小菜蛾对Cry1Ac蛋白的抗性演化已成为当前Bt技术应用中最为严峻的挑战之一，深入解析Cry杀虫蛋白的作用模式及小菜蛾对其的抗性分子机制，是延缓Bt抗性发展、保障Bt技术可持续应用的核心科学问题。本文系统阐述了Cry杀虫蛋白的孔洞形成、信号转导及Jurat-Fuentes三类核心作用模型，重点综述了近年来小菜蛾对Bt Cry1Ac抗性的分子机制，包括Bt受体改变及其他关键因子的调控作用，并对未来研究方向进行了展望，旨在为Bt的广泛应用与抗性治理提供理论参考。

1 Cry杀虫蛋白的作用模式

目前有新旧2套体系用于Cry杀虫蛋白的分类。旧的分类体系根据Cry杀虫晶体蛋白氨基酸序列的相似性将其划分为4个层级：第1层级序列一致性低于45%，以阿拉伯数字标识，例如Cry1与Cry2；第2层级序列一致性介于45%~78%之间，用大写英文字母区分，如Cry1A和Cry1B；第3层级序列一致性大于78%且≤95%，以小写字母表示，例如Cry1Ab与Cry1Ac；第4层级序列一致性高于95%，仍以阿拉伯数字编号，比如Cry1Ac1和Cry1Ac2（Crickmore et al.，1998）。截至2021年，根据另一套新的分类体系，Cry毒素可分为78大类（Cry1~Cry78）和312小

类（Cry1Aa~Cry78Aa）（Crickmore et al., 2021），如图1所示，Cry1A原毒素由两大部分组成：第1部分为毒素核心活性区域（结构域I~III），共有5个序列保守区；第2部分为C端的原毒素区域（结构域IV~VII），共有3个序列保守区，其中，结构域IV和结构域VI由多个α螺旋组成，它们类似于结构上相互作用的结构域；而结构域V和结构域VII主要由β链组成（Palma et al.，2014）。



1~8代表3个不同结构域Cry蛋白中保守的氨基酸片段，其中绿色方框所示为Höfte & Whiteley（1989）首次描述的位于Cry蛋白毒性核心区域的5个保守氨基酸片段，红色方框所示为Schnepf et al.（1998）发现的另外3个保守氨基酸片段。1–8 indicate conserved amino acid blocks shared among three-domain Cry proteins. The green boxes represent the five conserved amino acid blocks within the toxic core of the Cry protein first described by Höfte & Whiteley (1989), whereas the red boxes indicate the three additional conserved amino acid blocks identified by Schnepf et al. (1998).

图1　Cry1A原毒素的序列和结构特征（Palma et al.，2014）

Fig. 1　Sequence and structural features of the Cry1A protoxin (Palma et al., 2014)

通常情况下，全长（~130 kD）原毒素经过中肠蛋白酶的切割后形成小片段（~60 kD）的活化毒素（图1）。活化的毒素与中肠上皮细胞刷状缘膜囊（brush border membrane vesicle，BBMV）上锚定的受体发生特异性结合，进而嵌入细胞膜形成穿孔，最终因离子渗透压失调引发细胞裂解，这是Cry毒素第一种作用机制，即孔洞形成模型。另一种作用机制是信号转导模型，即Cry活化的毒素–受体复合物激活下游信号传导通路，诱发细胞凋亡（Vachon et al., 2012; Pardo-López et al., 2013; Adang et al., 2014; Wu, 2014）。此外，也有学者整合了上述两种机制提出第3种模型，即Jurat-Fuentes模型。

1.1　孔洞形成模型

该模型源于对Cry1Ab与烟草天蛾 *Manduca sexta* 中肠BBMV结合的研究（Gómez et al.，2002；Zhuang et al.，2002；Bravo et al.，2004）。其过程包括多个步骤：伴孢晶体在碱性肠液中溶解，原毒素经蛋白酶水解转化为活性形态；活化后的毒素与中肠上

皮细胞膜上的特定受体如氨肽酶N(aminopeptidase N,APN)和碱性磷酸酶(alkaline phosphatase,ALP)结合(Xu et al.,2020),从而富集于BBMV区域,并与钙黏蛋白(cadherin,CAD)发生高亲和力相互作用(Gómez et al.,2006;Pacheco et al.,2009;Arenas et al.,2010)。CAD胞外结构域CR7、CR11和CR12与毒素结构域II中的loop2、loop3及α8结合,触发蛋白酶切并暴露毒素N端结构域I的疏水区域,促使毒素寡聚化。形成的寡聚体对ALP和APN的亲和力显著提高,进一步引导其插入膜中形成阳离子通道,最终引起细胞裂解(Pardo-López et al.,2013)。该过程中任一阶段受阻均可能引起昆虫对Cry毒素的抗性。由于鳞翅目昆虫间受体组成存在差异,其抗性机制亦呈现多样性。

1.2 信号转导模型

孔洞形成模型强调毒素寡聚化后插入膜结构,但有研究显示膜结合态寡聚体并未形成有效孔洞且不具备毒性(Zhang et al.,2005)。因此,Zhang et al.(2005;2006)提出了信号转导模型。在该模型中,活化的毒素单体与CAD结合后激活一条依赖Mg^{2+}的信号通路,从而诱发程序性细胞死亡。具体而言,毒素与CAD结合后促使G蛋白与腺苷酸环化酶(adenylyl cyclase,AC)活化,大幅提升环磷酸腺苷(cyclic adenosine monophosphate,cAMP)水平。cAMP进一步激活蛋白激酶A(protein kinase A,PKA),引起细胞骨架重组与离子流动等变化。同时,胞内CAD会向膜表面迁移,增强毒素结合(Zhang et al.,2005;2008)。该信号级联放大最终导致细胞凋亡。

然而,也有研究指出Cry毒素虽可诱发细胞凋亡,但并未依赖AC/PKA通路。Portugal et al.(2016)研究结果表明在Cry1Ab和Cry1Ac作用下,PKA、AC与cAMP通路并未被激活。

1.3 Jurat-Fuentes模型

通过比较烟芽夜蛾*Heliothis virescens*对Cry1Ac的抗性与敏感种群中CAD的作用差异,并结合前述两种机制,Jurat-Fuentes & Adang(2006)提出了新的作用模型——Jurat-Fuentes模型。该模型认为活化毒素与CAD结合后激活磷酸酶调控的信号通路。部分毒素可能与肌动蛋白及细胞内磷酸酶互作引起细胞凋亡;另一部分则形成寡聚体,与糖基磷脂酰肌醇(glycosylphosphatidylinositol,GPI)锚定蛋白如ALP和APN结合并插入膜中。因此,细胞死亡可能同时来自于信号通路触发的凋亡和孔洞导致的渗透压失衡。

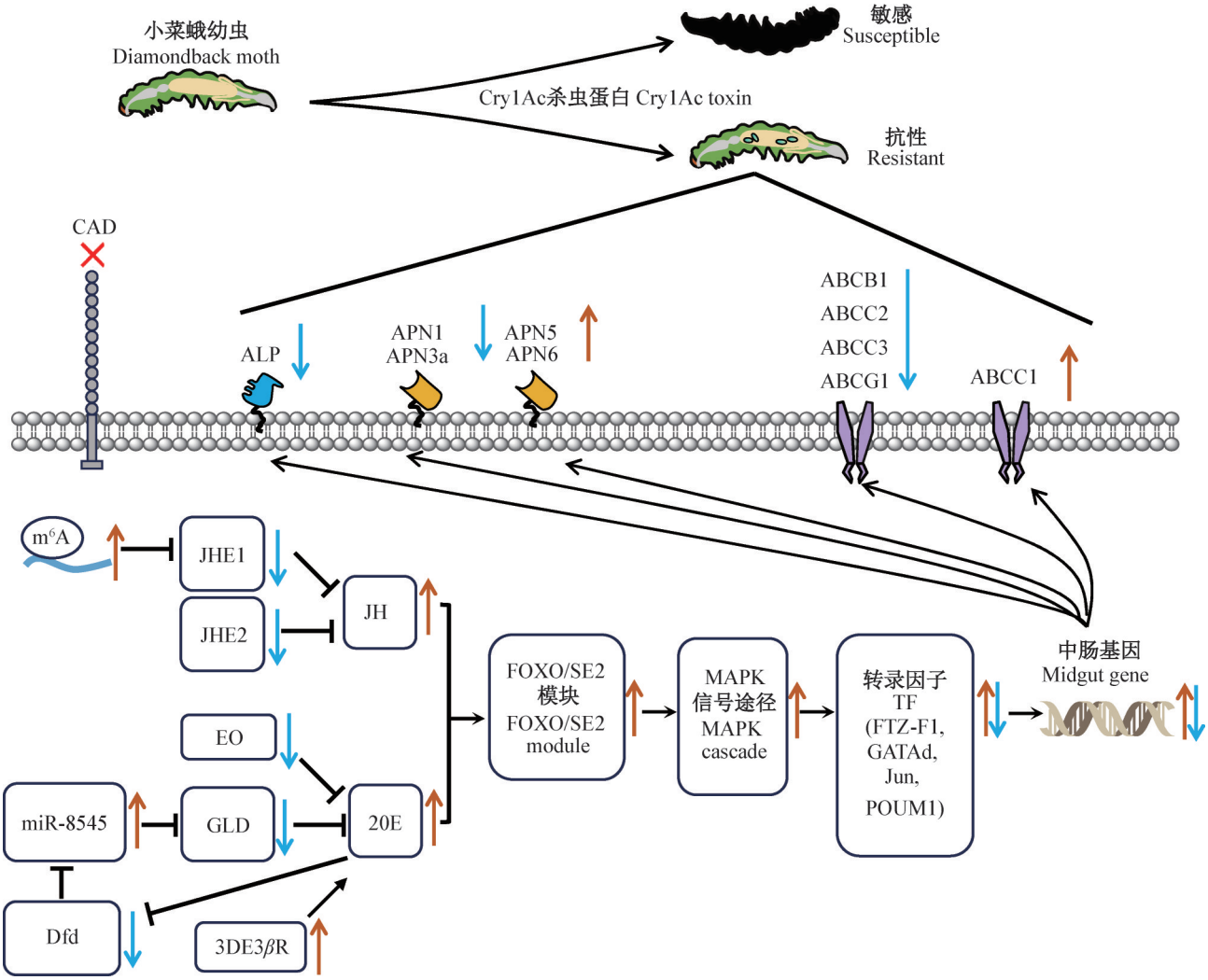
2 小菜蛾对Bt Cry1Ac的抗性机制

小菜蛾是首个被报道在田间环境下对Bt生物农药产生耐受性的昆虫(Tabashnik et al.,1990),因此深入解析其抗性机制,不仅有助于揭示鳞翅目昆虫对Bt的耐药规律,也对制订田间抗性治理策略具有重要的应用价值。

在鳞翅目昆虫中,常见的Bt抗性表型为对一种或多种Cry1A毒素产生不低于500倍的抗性水平,且通常不与Cry1C类毒素发生交叉抗性(Tabashnik et al.,1998)。全球多个地区的小菜蛾抗性种群均符合这一模式。例如,最早发现的小菜蛾夏威夷NO-QA种群,在采用含Cry1Aa、Cry1Ab、Cry1Ac、Cry2A及Cry2B的复配制剂Dipel进行室内多代筛选后,其对Dipel的耐受性提高超过3 000倍,同时对Cry1F和Cry1J表现出交叉抗性,但对Cry1B、Cry1C、Cry1E和Cry1I未显示交互抗性(Tabashnik et al.,1993;1994;1996)。遗传研究表明,该种群的抗性为常染色体隐性遗传,并与中肠上皮细胞上毒素结合能力的下降相关(Tabashnik et al.,1992;1997)。后续来自宾夕法尼亚的小菜蛾PEN种群以及来自菲律宾的小菜蛾PHI种群通过遗传互补试验被证实与NO-QA种群享有同一抗性位点(Tabashnik et al.,1997)。更多针对小菜蛾的研究结果显示,马来西亚的SERD4、Kluang和Karak种群,夏威夷的SC1以及佛罗里达的DBM1Ac-R种群,也均具有与NO-QA种群相同的抗性遗传位点;中国深圳的SZBT种群和美国的Cry1Ac-R种群亦被推测可能存在同一抗性机制(Gong et al.,2010;Crickmore,2016)。Heckel et al.(1999)通过遗传作图和基因定位,发现该抗性位点位于一段约2.1 cM的常染色体区域BtR-1内。值得注意的是,腺苷三磷酸结合盒(ATP-binding cassette,ABC)转运蛋白C亚家族基因*ABCC2*与该抗性表现完全连锁,且在NO-QA种群中该基因发生了10个氨基酸的缺失突变(Baxter et al.,2011)。除上述常见的Bt抗性表型外,还存在其他抗性表型。如源自美国南卡罗来纳州的一个小菜蛾田间种群,其对Cry1C原毒素的初始抗性约为31倍,经实验室持续筛选后抗性水平可增至300倍以上(Zhao et al.,2000)。

自NO-QA种群被发现以来,科研人员在遗传、生理与生化机制方面开展了小菜蛾Bt抗性机制的系统性研究工作。Bt Cry杀虫蛋白的毒理机制是一

个多步骤顺序作用的过程，理论上任何一个步骤的改变都有可能导致小菜蛾产生抗性。鉴于Bt Cry杀虫蛋白与中肠受体结合是毒理过程中最重要的步骤，中肠受体与杀虫蛋白结合能力的减弱是小菜蛾产生Bt Cry抗性的重要原因。但不同的田间抗性种群也暗示Bt的抗性机制可能是多样的。



CAD：钙黏蛋白；ALP：碱性磷酸酶；APN：氨基肽酶N；ABC：腺苷三磷酸结合盒；JHE：保幼激素酯酶；JH：保幼激素；EO：蜕皮激素氧化酶；miR-8545：小RNA；GLD：葡萄糖脱氢酶；20E：20-羟基蜕皮酮；Dfd：deformed转录因子；3DE3βR：3-脱氢蜕皮酮-3β还原酶；FOXO：叉头框O；SE2：SINE转座子元件2；MAPK：丝裂原活化蛋白激酶；FTZ-F1：fushi tarazu因子1；GATAd：GATA基序结合蛋白d；Jun：bZIP家族转录因子；POUM1：Pit-Oct-Unc结构域M类转录因子1。CAD: Cadherin; ALP: alkaline phosphatase; APN: aminopeptidase N; ABC: ATP-binding cassette; JHE: juvenile hormone esterase; JH: juvenile hormone; EO: ecdysone oxidase; miR-8545: microRNA; GLD: glucose dehydrogenase; 20E: 20-hydroxyecdysone; Dfd: deformed transcription factor; 3DE3βR: 3-dehydroecdysone-3β reductase; FOXO: Forkhead box O; SE2: SINE-element 2; MAPK: mitogen-activated protein kinase; FTZ-F1: fushi tarazu factor 1; GATAd: GATA motif-binding protein d; Jun: bZIP-family transcription factor; POUM1: Pit-Oct-Unc domain class M transcription factor 1.

图2　小菜蛾对Bt Cry1Ac的抗性机制总结

Fig. 2　Summary of the resistance mechanisms of *Plutella xylostella* to the Bt Cry1Ac toxin

2.1　Bt受体改变介导的小菜蛾抗性机制

CAD、APN、ALP（Xu et al.，2020）和ABC转运蛋白家族是小菜蛾中研究最多的Bt Cry1Ac受体。这些受体基因发生突变或其表达水平下降均可导致Bt杀虫蛋白与中肠结合能力减弱，这是小菜蛾产生Bt抗性的关键机制之一。

尽管CAD在其他鳞翅目昆虫中已被广泛证实是Bt Cry杀虫蛋白的重要受体，但其在小菜蛾抗性

形成中的作用仍缺乏充分证据。Park et al.(2014)研究发现,抑制小菜蛾*PxCad*表达不仅轻微降低了其对Cry1Ac的敏感性(约2倍),还减弱了中肠与杀虫蛋白的结合能力。然而Baxter et al.(2005)通过遗传定位分析发现NO-QA种群的抗性位点与*PxCad*无关。后续有研究表明,小菜蛾对Cry1Ac或Btk的抗性并非由*CAD*基因改变而引起;同时,敏感种群与抗性种群之间*CAD*基因的转录水平无显著差异,且利用RNA干扰技术抑制该基因表达后,幼虫对Cry1Ac杀虫蛋白的敏感性并未发生明显改变(Guo et al.,2015a)。这表明小菜蛾对Cry1Ac的抗性在很大程度上并不依赖于*CAD*基因。

就ALP而言,异源表达试验证实PxmALP是小菜蛾中Bt Cry1Ac杀虫蛋白的功能性受体;同时,抗性种群的中肠BBMV内ALP活性及其编码基因*mALP*的表达水平均显著下降,且抑制该基因表达可降低幼虫对Cry1Ac的敏感性,这进一步表明ALP受体表达下调介导了小菜蛾对Bt Cry1Ac的抗性(Sun et al.,2025a)。单基因敲除可诱导小菜蛾对Cry1Ac/Cry1Ab产生极高水平抗性,而*PxmALP*与*ABCC2*/*ABCC3*联合敲除会引发极端抗性,证明中肠受体蛋白之间存在功能互补效应(Sun et al.,2025a)。

小菜蛾的APN基因家族包含15个成员。异源表达与CRISPR/Cas9基因编辑试验证实,该家族中的PxAPN1和PxAPN3a为Cry1Ac的功能性受体(Guo et al.,2020a;Sun et al.,2022)。尽管早期研究显示,与敏感种群相比,抗性种群BBMV的APN整体活性未见显著变化(Guo et al.,2015b),但后续定量分析发现,抗性种群中肠内功能性受体基因*PxAPN1*和*PxAPN3a*的表达量显著下调,而同家族非受体基因*PxAPN5*与*PxAPN6*的表达量则呈上调趋势(Guo et al.,2020a;Kang et al.,2022a)。这种家族成员间的差异表达模式,可能在维持APN正常生理活性的同时,减少了Bt Cry1Ac与中肠的结合。进一步的功能验证表明,敲低*PxAPN1*或*PxAPN3a*会降低幼虫对Cry1Ac的敏感性,且这两个基因的表达水平与Cry1Ac抗性呈遗传连锁关系(Guo et al.,2020a)。另有研究发现,通过RNA干扰技术沉默*PxAPN2*虽可显著提高小菜蛾对Cry1Ac的抗性,但会导致幼虫死亡率上升,并显著降低蛹化率、蛹重、羽化率、产卵量、孵化率及雌虫寿命(Lv et al.,2024),表明通过下调*PxAPN2*表达获取抗性需付出明显的适合度代价。综上,APN基因表达水平的改变参与了小菜蛾对Bt Cry1Ac的抗性形成。

ABC转运蛋白家族同样有多个成员被证实可作为小菜蛾Bt Cry1Ac的功能性受体。其中,ABCC2作为最早在昆虫中被鉴定为Bt受体的成员,其基因缺失突变与小菜蛾NO-QA种群对Cry1Ac的抗性显著相关(Baxter et al.,2011)。在根据小菜蛾田间抗性种群建立的近等基因系抗性种群中(Zhu et al.,2015;2016a),虽然ABC转运蛋白的序列多样性与Cry1Ac抗性无直接连锁,但多个家族成员在抗性与敏感种群间的表达水平存在显著差异(Xia et al.,2016;Zhu et al.,2016b)。与APN家族类似,受体基因*PxABCC2*和*PxABCC3*在抗性种群中下调表达,而非受体同源基因*PxABCC1*则上调表达(Guo et al.,2015b)。功能验证试验进一步证实ABCC2和ABCC3为Cry1Ac的功能性受体,干扰任一基因均会降低小菜蛾对Cry1Ac的敏感性(Guo et al.,2015b;2019;Sun et al.,2022)。此外,除ABC转运蛋白C亚家族外,ABC转运蛋白B亚家族的*ABCB1*以及ABC转运蛋白G亚家族的*White*基因表达下调也与小菜蛾对Cry1Ac的抗性密切相关(Guo et al.,2015c;Zhou et al.,2020;Ouyang et al.,2023)。以上结果表明,ABC转运蛋白家族中多个成员的表达变化共同介导了小菜蛾对Bt毒素的抗性。

在小菜蛾中,Bt Cry1Ac抗性的产生主要涉及多个中肠受体基因及其非受体同源基因的差异化表达。这种差异表达受位于BtR-1抗性基因座内的丝裂原活化蛋白激酶(mitogen-activated protein kinase,MAPK)信号通路转录激活的上游基因*MAP4K4*的反式调控(Guo L et al.,2020;Ouyang et al.,2023;Kang et al.,2026)。MAP4K4通过依次磷酸化MAP3K、MAP2K和MAPK,激活p38、c-Jun氨基末端激酶(c-Jun N-terminal kinase,JNK)和细胞外信号调节激酶(extracellular signal-regulated kinase,ERK)3条信号通路,进而通过转录因子fushi tarazu因子1(fushi tarazu factor 1,FTZ-F1)、Jun、Pit-Oct-Unc结构域M类转录因子1(Pit-Oct-Unc domain class M transcription factor 1,POUM1)和GATA基序结合蛋白d(GATA motif binding protein d,GATAd),最终导致中肠受体基因与非受体同源基因的差异表达(Guo L et al.,2022)。该机制在减少Bt Cry1Ac毒素结合的同时,维持了小菜蛾正常的生长发育,从而避免了明显的适合度代价(Guo et al.,2021;Qin et al.,2021a;Guo ZJ et al.,2022;Xu et al.,2022)。进一步研究发现,抗性种群中*MAP4K4*表达的上调受到两种主要昆虫激素——保幼激素(juvenile hor-

mone，JH）和20-羟基蜕皮酮（20-hydroxyecdysone，20E）的协同调控（Callier & Nijhout，2013；Guo et al.，2020a）。这两种激素通过降低转录因子叉头框蛋白O（Forkhead box O，FOXO）的磷酸化水平增强其活性；同时，小菜蛾抗性种群中反转录转座子SE2在*MAP4K4*启动子区的插入进一步增强了FOXO与启动子的结合能力，这两方面作用共同促进了*MAP4K4*的表达升高（郭乐等，2018；Guo et al.，2023；Sun et al.，2025b）。此外，近期研究揭示，小菜蛾抗性种群中JH和20E含量的上升分别受保幼激素酯酶（JH esterase，JHE）、葡萄糖脱氢酶（glucose dehydrogenase，GLD）及蜕皮激素氧化酶（ecdysone oxidase，EO）等酶的调控，而这些酶基因的表达又受到RNA修饰与microRNA等表观遗传机制的调控（Guo et al.，2024a，b；Dong et al.，2025；Cheng et al.，2026）。而且，Bai et al.（2026）证实小菜蛾3-脱氢蜕皮酮-3β还原酶（3-dehydroecdysone-3β reductase，3DE3βR）基因*Px3DE3βR*可促进20E合成，激活MAPK通路，正向调控小菜蛾对Bt Cry1Ac的抗性，这为该害虫的抗性治理提供了新靶点。

总之，受体突变或表达水平改变所介导的抗性机制是小菜蛾产生Bt抗性的关键途径。受体表达的调控在Bt杀虫蛋白抗性机制中极为复杂，涉及激素、信号通路及转录因子等多层面的相互作用（图2）。探索Bt受体介导的小菜蛾抗性机制，也为防治小菜蛾以及控制Bt抗性提供了靶标（Guo et al.，2015d；Kang et al.，2022b）。未来仍需进一步揭示不同调控因子之间的内在联系，从而系统阐明小菜蛾对Bt杀虫蛋白的抗性形成机制，同时探索更多抗性治理的靶标。

2.2　其他因子改变介导的抗性机制

此外，中肠蛋白酶（Sayyed et al.，2001；2005；Talaei-Hassanloui et al.，2014）、酯酶（Sayyed et al.，2008）及中性鞘糖脂（Kumaraswami et al.，2001）的变化可能与小菜蛾对Cry1Ab/Cry1Ac的抗性有关，但相关机制尚未得到系统验证，仍缺乏关键试验证据支持。有一些研究排除了一部分与Bt抗性相关的因素（Liu et al.，2019；Guo et al.，2020b；Liao et al.，2021）。

相比之下，近年来一些具体调控机制逐渐被揭示。如Hox转录因子Antp（Antennapedia）的调控机制：由于Antp结合位点发生顺式突变，降低了*PxABCG1*启动子活性，抑制该Cry1Ac毒素受体基因表达，从而在小菜蛾对Cry1Ac毒素的抗性形成中发挥了关键作用（Qin et al.，2021b）。microRNA−蛋白酶调控机制：miR-108/miR-234通过靶向幼虫激素酯酶基因（如*PxJHE*）进而调控发育及Cry1Ac耐受性（Yang et al.，2023）；miR-2b-3p通过抑制胰蛋白酶基因*PxTrypsin-9*的表达，阻碍Cry1Ac原毒素激活，从而产生抗性（Zhang et al.，2024）；miR-8510a-3p可靶向结合*PxABCG3*编码区并抑制其表达，进而直接改变小菜蛾对Cry1Ac的耐受能力（Yang et al.，2024）。新型蛋白酶基因作用机制：小菜蛾中肠特异性胰蛋白酶基因*PxTryp_SPc1*的表达水平下降直接参与抗性的形成（Gong et al.，2020）。肠道菌群介导抗性机制：在Bt胞外多糖与Cry1Ac联合作用下，小菜蛾肠道菌群丰度发生显著变化，且肠道微生物能增强Cry1Ac杀虫活性，表明肠道菌群是Bt毒素杀虫协同作用的关键因子，直接影响Cry1Ac毒素的杀虫效果，是影响虫害敏感性的重要生态因素（Wang et al.，2024）。囊泡型ATP酶（vacuolar-type ATPase，V-ATPase）基因家族调控机制：Xie et al.（2022）首次在小菜蛾基因组中鉴定出35个V-ATPase基因，在Cry1Ac抗性种群中*PxVHA-G1*基因显著上调，而且沉默该基因后小菜蛾对Cry1Ac毒素的敏感性显著提升，证实V-ATPase家族基因参与调控小菜蛾Bt抗性，为其抗性机制研究提供了新靶点。

3　总结与展望

小菜蛾是十字花科蔬菜生产中的重大害虫，常造成巨大的经济损失。此外，小菜蛾对化学农药及Bt生物农药迅速产生了抗药性，进一步增加了其防治难度。Bt及其产生的杀虫蛋白（如Cry1Ac）因杀虫高效、对环境安全，已成为全球广泛使用的生物杀虫剂及抗虫转基因作物的主要基因来源，在经济和生态方面具有显著效益。

小菜蛾对Bt毒素（尤其是Cry1A类）已发展出复杂多样的抗性机制，主要涉及中肠上皮细胞表面受体蛋白的表达下调、突变或功能异常，从而导致毒素结合能力下降。更为重要的是激素的相互串扰影响MAPK信号途径进而调控中肠受体基因的表达，进行介导小菜蛾对Bt的抗性。

为进一步应对小菜蛾的抗性问题，未来需深入揭示其对Bt毒素抗性的精确分子机制，尤其要厘清不同受体蛋白的具体功能、分工及彼此间的调控关系，并探索除典型“mode 1”类型以外的其他抗性形式。基于对抗性机制的理解，还应开发新型防控策略以延缓或克服抗性，例如利用CRISPR/Cas9等基

因编辑技术进行关键基因功能验证、设计可规避现有抗性机制的新型修饰毒素(如Cry1AcMod),以及实施不同作用机理药剂的轮用与混用策略。

同时,应推进多学科融合的害虫综合治理体系,将生物防治、农业管理、物理防治、化学防治及转基因技术等措施有机结合,构建可持续的治理模式,并推动这些技术成果在生产实践中有效集成与应用,统筹经济、生态与社会效益。在Bt作物及生物农药推广应用过程中,还需持续关注其生态安全性(如基因漂移风险),监测靶标害虫抗性动态,实施科学的抗性管理策略,以维持防治效果并延长其使用寿命。

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