斯氏线虫–致病杆菌共生体侵染昆虫的生物标志物

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摘要：昆虫病原线虫是一类专性侵染和寄生昆虫的病原线虫，是非常重要的生防资源。斯氏线虫属*Steinernema*和致病杆菌属*Xenorhabdus*通过形成共生体在侵染昆虫过程中共同完成生活史，其中致病杆菌释放效应物质引发昆虫败血症是其重要机制。该文对斯氏线虫–致病杆菌共生体的侵染策略和在侵染过程中产生的免疫调节因子、释放的毒素蛋白和活性代谢物进行概述，其中，苯乙酰胺作为免疫抑制因子促进自身定殖，脂多糖作为内毒素引起寄主血细胞裂解，Tc毒素蛋白作为外毒素导致寄主中肠上皮细胞溶解，活性代谢产物如xenematides、fabclavine和PAX肽等具有抑菌、诱导细胞凋亡等活性。而斯氏线虫本身也能够产生表皮/分泌蛋白来抑制寄主免疫，与共生菌协同致死寄主。因此，通过对斯氏线虫–致病杆菌共生体产生的致病物质进行汇总分析，为研究昆虫病原线虫致病机制提供理论参考，同时也为新型绿色杀虫剂的开发和应用提供证据支持。

关键词：昆虫病原线虫；斯氏线虫；致病杆菌；侵染策略；生物标志物

Biomarkers of insect septicemia caused by *Steinernema-Xenorhabdus* symbionts

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Abstract: Entomopathogenic nematodes (EPNs), which are obligate parasitic nematodes that infect a wide range of insects, are a valuable resource for biocontrol. During the process of infecting a host insect, the *Steinernema-Xenorhabdus* symbionts releases various pathogenic factors to complete their life cycle. In this paper, the pathogenic strategies employed by *Steinernema* spp. and *Xenorhabdus* spp. were reviewed. This includes utilizing phenylethylamides as immunosuppressive factors to facilitate colonization, lipopolysaccharide (LPS) as an endotoxin to cause host blood cell lysis, Tc proteins as exotoxins to kill host insects, and the production of special metabolites (e.g. fabclavine, PAX peptides, and other antibiotics) that have bacteriostatic and apoptosis-inducing activities. Additionally, some epidermal/secretory proteins can inhibit the host's immune system, work together with the symbiotic bacteria to kill the host, and cause a series of changes in the host insect's physiology and metabolism. Therefore, this review of the biochemical metabolism caused by *Steinernema-Xenorhabdus* symbionts can serve as both a theoretical guide for exploring the septicemia mechanism of EPN infestations and as evidence to support the creation of novel, environmentally friendly insecticides.

Key words: entomopathogenic nematodes; *Steinernema*; *Xenorhabdus*; infestation strategies; biomarker

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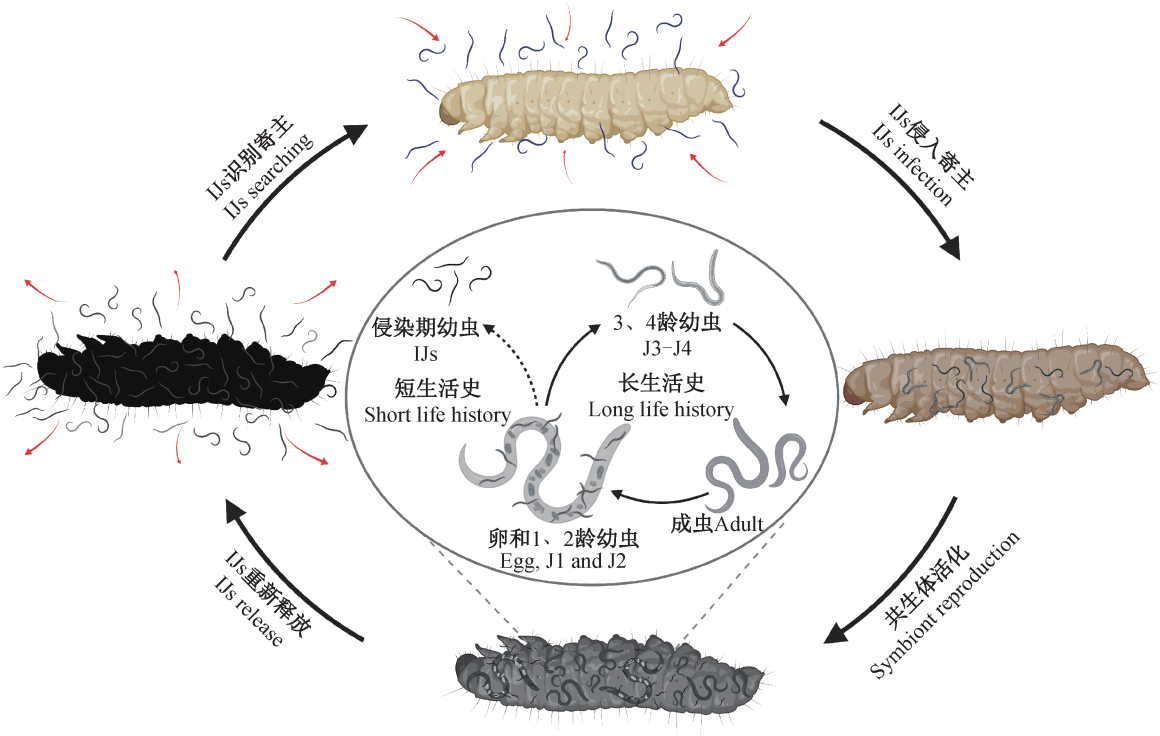
昆虫病原线虫是一类专性侵染和寄生昆虫的病原线虫，斯氏科斯氏线虫属 *Steinernema* 线虫（简称斯氏线虫）是其中重要的一类，能够与体内细菌致病杆菌属 *Xenorhabdus* 细菌（简称致病杆菌）共生进而对昆虫形成复合侵染（武海斌等，2015；李而涛等，2022），但斯氏线虫和致病杆菌之间具有不完全的营养专化性，一种斯氏线虫只携带一种共生菌，但一种共生菌可以和多种斯氏线虫形成共生关系（Kämpfer et al.，2017）。侵染期斯氏线虫是侵染昆虫并造成寄主死亡的唯一虫态，其自由生活在土壤中并搜寻寄主，通过寄主体表的自然孔口，如口、肛门和气孔等或节间膜穿透体壁进入昆虫体内，并将致病杆菌释放到昆虫的血腔中（Strauch & Ehlers，1998；刘奇志等，2023），致病杆菌在血腔中繁殖并产生多种毒素分子，使寄主在24~48 h内患败血症而死亡。同时，致病杆菌通过产生胞外酶将昆虫组织分解，当寄主体内营养消耗殆尽，侵染期斯氏线虫从寄主体内爬出，并进入土壤中寻找新的寄主昆虫（Akhurst，1980；1983）。随着研究的不断深入，近年来有大量关于斯氏线虫和致病杆菌复合侵染昆虫过程中释放的生化代谢物的研究报道，如Tc毒素（Roderer et al.，2020）、xenoamicin（Zhou et al.，2013）、fabclavine（Wenski et al.，2020）和PAX（peptide-antimicrobial-*Xenorhabdus*）肽（Fuchs et al.，2011）。因此，本文主要对斯氏线虫与致病杆菌复合侵染寄主昆虫过程中导致其死亡的致病生化物质进行综述，以期为深入挖掘昆虫病原线虫的生防潜力和分析致病机理提供参考，并为昆虫病原线虫杀虫因子的开发提供重要依据。

1 斯氏线虫–致病杆菌共生体侵染策略

斯氏线虫分为长生活史型线虫和短生活史型线虫，长生活史型线虫会经历卵、幼虫及成虫的完整发育阶段，当线虫密度过高和寄主食物供应不足时，转化为短生活史型线虫；短生活史型线虫的卵直接发育成侵染期线虫（丛斌等，1999；Gaugler，2002）。斯氏线虫–致病杆菌共生体的侵染分为4个阶段：侵染期线虫首先识别并定位昆虫；穿透寄主体壁并侵入寄主体内；释放共生菌，引发寄主败血症并开始发育；食物耗尽后侵染期线虫重新形成并释放寻找新的寄主。线虫–共生菌共生体侵染是一种始于侵染期线虫侵染并以侵染期线虫形成为结束的周期性循环（图1）。



IJs：侵染期线虫。IJs: Infective juveniles; J1, J2, J3, J4: indicate the 1st, 2nd, 3rd and 4th instar juveniles, respectively.

图1 斯氏线虫和致病杆菌共生体的生活史和侵染策略

Fig. 1 Life history and infestation strategies of symbionts of *Steinernema* and *Xenorhabdus*

1.1 侵染期斯氏线虫识别和定位寄主

侵染期斯氏线虫通过对昆虫分泌物、表皮或肠道内容物进行识别，如CO_2、精氨酸和尿酸，并向寄主昆虫所在方向移动（杨秀芬和杨怀文，1998），如小

卷蛾斯氏线虫*S. carpocapsae*对红棕象甲*Rhynchophorus ferrugineus*的搜寻与嗅觉识别通路基因的表达相关(Santhi et al.,2021)。此外,侵染期线虫还可以回避已被侵染的寄主,避免资源的过度分配,利于线虫种群的繁衍(Baiocchi et al.,2017;王杰等,2021)。除生物因素外,温湿度和渗透压等非生物因素也会影响线虫对寄主的识别(王杰等,2021)。线虫能够通过主动传播和被动传播进行扩散(Epsky et al.,1988),主动传播是借助水膜进行水平和垂直方向的短距离移动,被动传播则依靠风、雨、人类或昆虫活动进行长达数千米的长距离传播(Epsky et al.,1988;Timper et al.,1988)。

1.2　侵染期斯氏线虫穿透和侵入寄主

侵染期斯氏线虫能够通过昆虫的自然孔口直接侵入,也可以通过昆虫的伤口直接分泌蛋白酶破坏寄主的原表皮形成开口,进入寄主体内(AbuHatab et al.,1995)。线虫对不同寄主的侵入方式不同,其中昆虫的气门和肛门是重要的侵染途径,如夜蛾斯氏线虫*S. feltiae*通过气门侵入大蜡螟*Galleria mellonella*,并在钻入后会将鞘及头部附器留在寄主昆虫体外,而侵入家蝇*Musca domestica*幼虫时则是通过肛门(Parkman et al.,1993;Renn,1998)。

1.3　侵染期斯氏线虫共生体活化并致死寄主

侵染期斯氏线虫进入寄主昆虫血腔中恢复取食,并通过反刍将存在于肠道前端特殊囊泡中的致病杆菌释放到昆虫体内(Bird & Akhurst,1983;Martens & Goodrich-Blair,2005),致病杆菌繁殖并分泌一系列毒素因子和免疫抑制因子,在短时间内杀死寄主(Brivio & Mastore,2018)。此外,致病杆菌还可以产生胞外酶,将昆虫的尸体转化成供自身和线虫利用的营养物质,同时线虫也可以通过取食共生菌完成自身生长、发育和繁殖(王立霞等,2000;Mucci et al.,2022)。

1.4　侵染期斯氏线虫重新形成并离开寄主

当斯氏线虫接收到营养资源匮乏的信号时,2龄幼虫重新将一个或几个致病杆菌储存在菌囊中,并繁殖形成50~100 CFU/侵染期斯氏线虫的稳定种群,进而形成侵染前期斯氏线虫和侵染期斯氏线虫(Martens et al.,2003;王立婷等,2013)。新生成的侵染期斯氏线虫从昆虫尸体中钻出并向周围环境扩散,潜伏在土壤中进入半休眠状态,等待下一轮侵染。

2　斯氏线虫–致病杆菌共生体产生的致病生化物

斯氏线虫–致病杆菌共生体通过逃避或抑制免疫在昆虫体内定殖,逃避免疫是通过合成或获得某些与寄主本身相关的物质附在线虫或细菌的表面,避免被寄主免疫系统识别(Brivio & Mastore,2018);抑制免疫则是通过分泌一些物质来减弱寄主免疫系统对自身的攻击(Burman,1982;刘劲等,2012)。致病杆菌可以通过鞭毛附着在昆虫血腔中某些组织的表面,产生多种免疫抑制因子、毒素蛋白和特殊代谢物,使寄主迅速死亡(Moureaux et al.,1995)。

2.1　线虫表皮/分泌蛋白

斯氏线虫在复合侵染中除了起到载体作用外,还能利用自身表皮复合物逃避寄主免疫攻击,并产生一些物质来抑制昆虫的免疫反应,甚至合成毒素相关蛋白破坏寄主的中肠上皮细胞,导致昆虫停止进食,随后破坏寄主脂肪体、马氏管或消化道等组织(Wang et al.,1995;常豆豆等,2022)。斯氏线虫的外层表皮会直接与寄主免疫系统接触,但由于其幼虫蜕皮并且在生长发育过程中受多种因素的影响,其表皮成分存在一定差异,因此不同线虫在寄主昆虫中发挥作用的方式也不同(Shamseldean et al.,2007)。夜蛾斯氏线虫表皮中的脂类物质可以与大蜡螟血淋巴因子结合,在自身周围形成一层非特异性薄膜,逃避寄主免疫系统的识别,也可以通过抑制酚氧化酶活性、血细胞包埋反应和抗菌肽合成来抑制寄主的免疫攻击(Brivio et al.,2006;Mastore & Brivio,2008)。格氏斯氏线虫*S. glaseri*的表皮蛋白不仅可以逃避日本金龟子*Popillia japonica*血细胞的识别,甚至还可以引起血细胞凋亡(Li et al.,2009),并且通过验证无菌线虫和携菌线虫对日本金龟子血细胞的包埋和黑化作用,发现这种烯醇化酶家族的免疫活性蛋白Sg-ENOL(*S. glaseri* enolase)是由线虫自身产生的(刘华,2012;常豆豆等,2022)。除表皮蛋白外,侵染期斯氏线虫还可以产生分泌蛋白,分泌蛋白对寄主免疫系统的抑制能力更强,毒性也更高(刘劲等,2012)。将小卷蛾斯氏线虫产生的分泌蛋白注射到大蜡螟体内,发现来自于线虫的分泌蛋白对大蜡螟具有相当高的细胞毒性(Lu et al.,2017),目前已鉴定了包括Sc-CHYM(*S. carpocapsae* chymotrypsin)(Hao et al.,2009)、Trypsin-like protease(Balasubramanian et al.,2010)、Sc-AST(*S. carpocapsae* astacin metalloprotease)(Jing et al.,2010)和Sc-KU-4(*S. carpocapsae* BPTI-Kunitz family inhibitor)(Toubarro et al.,2009)等在内的蛋白酶,这些成分通过降解寄主组织、促进线虫发育、抑制血细胞扩散、诱导血细胞凋亡、溶解纤维蛋白、抑制寄

主酚/原酚氧化酶活性和水解细胞外基质蛋白等方式抑制寄主的免疫系统，发挥毒性作用（常豆豆等，2022）。

2.2 致病杆菌的代谢产物

致病杆菌到达昆虫血腔后识别L-脯氨酸，从与线虫的共生型转换成对昆虫的致病型，调节多种毒力蛋白和代谢产物的合成（Herbert & Goodrich-Blair，2007；Crawford et al.，2010）。致病杆菌在复合侵染过程中对寄主昆虫表现出强烈的致病力（杨秀芬和杨怀文，1998），其致病性主要体现在生成免疫因子逃逸或抑制寄主免疫系统的攻击，产生毒素蛋白使寄主昆虫患败血病迅速死亡，通过分泌具抑菌活性和细胞毒性的特殊代谢物质来抑制其他杂菌的生长并为线虫创造良好的生长发育环境，最终对寄主昆虫产生强烈的致病作用（Seryczyńska & Bajan，1975；王立霞等，2000）。

2.2.1 免疫抑制因子

致病杆菌会被寄主的免疫系统识别并清除，但致病杆菌可以通过逃避或者抵抗寄主免疫系统的攻击在昆虫体内定殖（王立霞等，2000）。致病杆菌细胞壁中的脂多糖（lipopolysaccharide，LPS）类物质通过破坏酚氧化酶级联反应抑制血细胞免疫（Tang，2009）；也可以通过产生苯乙酰胺来抑制血清素受体介导的免疫反应，从而抑制寄主昆虫的免疫（Hasan et al.，2019）；*X. hominickii*还可以通过抑制斜纹夜蛾*Spodoptera litura*体内类花生酸的合成来破坏昆虫免疫系统（Mollah et al.，2021）。

2.2.2 毒素蛋白

除了能够产生免疫因子逃避和抑制寄主的免疫外，致病杆菌产生的毒素才是导致寄主死亡的关键。致病杆菌对多种原生动物和昆虫表现出较高的毒性，但物种特异性很强，根据毒素存在的位置可分为内毒素和外毒素（王立霞等，2000）。

内毒素是致病杆菌细胞壁中的LPS类物质，由类脂A、核心多糖和O-抗原构成，毒性部分是类脂A，细菌裂解后将类脂A释放到寄主体内发挥毒性（Dunphy & Webster，1988）。将LPS注射到家蚕幼虫体内后能诱导其中肠*BmToll9-2*基因的转录，激活昆虫的免疫相关Toll信号（廖文丽等，2017）。嗜线虫致病杆菌*X. nematophilus*将LPS释放到昆虫体内后通过D-氨基葡萄糖苷残基结合外源凝集素包围血细胞引起裂解，并导致脂肪体解离（Dunphy & Webster，1988）。

外毒素是由致病杆菌产生并分泌到体外的一类毒素，包括外毒素蛋白和一些胞外酶，其中外毒素蛋白可以直接杀死寄主（王立霞等，2000）。致病杆菌能产生具有极高杀虫活性的蛋白毒素复合物Xpts（*Xenorhabdus* protein toxins），每个活性蛋白复合体由A、B和C三个成分组成（Morgan et al.，2001；崔龙等，2005），A作为毒素的核心元件促进毒素和受体相互作用，导致中肠上皮细胞顶端膨胀并加速生长、溶解，甚至穿越中肠到血腔中引发酚氧化酶反应（Roderer et al.，2020）。XhlA（*Xenorhabdus* haemolysin）是一种细胞表面相关的溶血素，可以溶解最常见的2种昆虫免疫细胞，在线虫逃避昆虫免疫过程中发挥了重要作用（Cowles & Goodrich-Blair，2004）。Txp40（40 kD toxin from *Xenorhabdus*）是一种普遍存在于致病杆菌中的杀虫毒素蛋白，可导致中肠肠壁细胞间排列紊乱，降解周围的营养基质和脂肪体核（Brown et al.，2006）。Xax（*Xenorhabdus* alpha-xenorhabdolysin）二元毒素引起细胞凋亡并具有溶血活性，XaxA和XaxB对于Xax毒素发挥作用是必需的，每个单独表达时均不会产生溶血活性（Vigneux et al.，2007）。近几年，已从致病杆菌中分离鉴定到的SrfABC（Yang et al.，2019）、Tp40（杨君等，2008）、HipBA（Yadav & Rathore，2020）和几丁质酶（Mahmood et al.，2020）等均具有不同程度的血腔毒性或口服毒性，甚至可以抑制抗菌肽活性（Vo et al.，2021）。除毒素蛋白外，致病杆菌还可以产生酯酶和蛋白酶等胞外酶，它们几乎没有杀虫活性，而是通过参与抑制寄主免疫反应和分解转化昆虫尸体为线虫生长发育提供营养，对致病起辅助作用（Caldas et al.，2002）。

2.2.3 具有抑菌活性和细胞毒性的特殊代谢物质

致病杆菌可以产生多种具有抗细菌、真菌、昆虫、线虫、原生生物和癌细胞的活性物质，防止寄主尸体被感染，从而维持自身特殊的环境生态位（McInerney et al.，1991a）。不同致病杆菌之间产生的代谢物存在较大差异，主要包括由聚酮合成酶（polyketide synthetase，PKS）和非核糖体肽合成酶（non-ribosomal peptide synthetase，NRPS）编码合成的多种肽，包括缩肽类、xenocoumacins、fabclavine、普那霉素（pristinamycin）、rhabdopeptides、bicornitun、PAX肽、cabanillasin和nemaucin；除此之外还可以产生由核糖体编码的细菌素、吲哚及其衍生物、氨基酸衍生物、亚苄基丙酮类、呋喃酮类和二硫吡咯类等具有抗菌和杀虫活性的代谢物质（表1）（Dreyer et al.，2018）。

表1 致病杆菌产生的特殊代谢物功能

Table 1 Functions of specialized metabolites produced by *Xenorhabdus* spp.

类别 Class	致病杆菌 *Xenorhabdus* spp.	特殊代谢物 Specialized metabolite	功能 Function	参考文献 Reference
聚酮合成酶和非核糖体肽合成酶编码的抗菌肽 Antimicrobial peptides encoded by polyketide synthetase/non-ribosomal peptide synthetase	*X. doucetiae*, *X. mauleonii*	Xenoamicins	抗细菌、真菌、原生动物和弱细胞毒性 Antibacterial, antifungal, antiprotozoal activities and weakly cytotoxic	Zhou et al., 2013
	X. indica	Lipodepsipeptides	抗原生动物和癌细胞 Antiprotozoal and anticancer cells activities	Kronenwerth et al., 2014
	X. nematophila	Xenematides	抗细菌，弱杀虫性 Antibacterial and weak insecticidal activities	Lang et al., 2008; Crawford et al., 2011
	Xenorhabdus sp.	Xenobactin	抗细菌 Antibacterial activity	Nollmann et al., 2012
	X. szentirmaii	Szentiamide	抗原生动物 Antiprotozoal activity	Nollmann et al., 2012; Grundmann et al., 2013
	嗜线虫致病杆菌 *X. nematophilus*	Xenocoumacins	抗细菌、真菌和溃疡 Antibacterial, antifungal and antiulcer activities	McInerney et al., 1991a
	X. budapestensis, *X. szentirmaii*	Fabclavines	抗细菌、真菌和原生动物 Antibacterial, antifungal and antiprotozoal activities	Fuchs et al., 2014; Wenski et al., 2020
	X. nematophila	普那霉素 Pristinamycin	抗细菌 Antibacterial activity	Brachmann et al., 2012
	嗜线虫致病杆菌 *X. nematophilus*	Xenortides	抗细菌和原生动物 Antibacterial and antiprotozoal activities	Reimer et al., 2014
	X. nematophila	Rhabdopeptides	抗细菌、原生动物、弱细胞和血腔毒性 Antibacterial and antiprotozoal activities, weakly cytotoxicity and haemotoxic	Bi et al., 2018
	X. budapestensis	Bicornitun	抗细菌和真菌 Antibacterial and antifungal activities	Fuchs et al., 2012
	嗜线虫致病杆菌 *X. nematophilus*	PAX肽 PAX peptides	抗细菌和真菌 Antibacterial and antifungal activities	Fuchs et al., 2011
	X. cabanillasii	Cabanillasin, nemaucin	抗细菌和真菌 Antibacterial and antifungal activities	Houard et al., 2013
核糖体编码的细菌素 Bacteriocins encoded by ribosomes	嗜线虫致病杆菌 *X. nematophilus*	Xenorhabdicin	抗细菌 Antibacterial activity	Morales-Soto et al., 2012
	X. nematophila	Xenocin	抗细菌 Antibacterial activity	Singh & Banerjee, 2008
吲哚及其衍生物 Indole and its derivatives	伯氏致病杆菌、嗜线虫致病杆菌 *X. bovienii*, *X. nematophilus*	吲哚 Indole	抗细菌、真菌、溃疡和杀虫 Antibacterial, antifungal, and antiulcer insecticidal activities	McInerney et al., 1991b; Sundar & Chang, 1993; Zhang et al., 2019
	X. nematophila	羟吲哚 Oxindole	抑制磷脂酶A_2 Inhibition of phospholipase A_2 activity	Shrestha & Kim, 2007
	伯氏致病杆菌 *X. bovienii*	Xenocycloins	血腔毒性 Haemotoxic	Proschak et al., 2014
	嗜线虫致病杆菌 *X. nematophilus*	Nematophin	抗细菌 Antibacterial activity	Li et al., 1997
氨基酸衍生物 Amino acid derivatives	*X. nematophila*	Rhabduscin	抑制酚氧化酶，具杀虫活性 Inhibition of phenoloxidase and insecticidal activities	Crawford et al., 2012
亚苄基丙酮类 Benzylideneacetones	*X. nematophila*	苯亚甲基丙酮 Benzylideneacetonee	抗细菌，抑制磷脂酶A_2 Antibacterial and inhibition of phospholipase A_2 activities	Spogliarich et al., 1989; Ji et al., 2004
呋喃酮类 Furanones	*X. szentirmaii*	Xenofuranones	弱细胞毒性 Weak cytotoxicity	Brachmann et al., 2006
二硫吡咯类 Dithiopyrroles	伯氏致病杆菌 *X. bovienii*	Xenorhabdins, Xenorxides	抗细菌、真菌、癌细胞和杀虫 Antibacterial, antifungal, anticancer cells and insecticidal activities	Olivaetal.,2001; Challinor & Bode, 2015

由PKS/NRPS编码的缩肽类物质是指多肽中的一个或多个酰胺基被羟基取代形成酯键，包括xenoamicins、lipodepsipeptides、xenematides、xenobactin和szentiamide共5类，其中szentiamide对恶性疟原虫*Plasmodium falciparum*有较大的毒性，并对布氏锥虫*Trypanosoma brucei*和克氏锥虫*T. cruzi*均有一定的致死效果（Nollmann et al.，2012）。其他由PKS/NRPS合成的物质中，fabclavines和一些阳离子抗菌肽结构非常相似，可以抑制革兰氏阳性和阴性细菌、酿酒酵母*Saccharomyces cerevisiae*、恶性疟原虫、布氏锥虫和克氏锥虫的生长（Fuchs et al.，2014；Wenski et al.，2020）。在致病杆菌中共分离得到8种rhabdopeptide，不同rhabdopeptide的活性不同，rhabdopeptide 2对成肌细胞的毒性较弱，rhabdopeptide 2、7和8对原生动物有抗性，rhabdopeptide 7和8有微弱的血腔毒性，并在昆虫的生物转化和线虫繁殖阶段发挥着重要作用（Bi et al.，2018）。

除上述由PKS/NRPS基因簇控制编码合成的毒素物质外，致病杆菌还能产生由核糖体编码的细菌素、二硫吡咯类和吲哚类等特殊代谢物。核糖体编码的细菌素中xenocin的产生由低浓度铁离子触发，铁的消耗与一种铁抑制蛋白有关，该蛋白可能作为敏感菌株的毒素受体，因此这种细菌素在营养浓度较低且竞争加剧时在寄主幼虫中产生，进而发挥毒素作用（Singh & Banerjee，2008）。在致病杆菌中分离的吲哚及其衍生物中，能发挥杀虫活性的有吲哚、羟吲哚和xenocycloins，其中吲哚是一种芳香族杂环化合物，通过增加核苷酸鸟苷四磷酸（guanosine-3′，5′-（his）pyrophosphate，ppGpp）的合成来抑制细菌RNA的合成，表现出强烈的抑制细菌、真菌及溃疡活性和杀虫活性（McInerney et al.，1991b；Zhang et al.，2019）；羟吲哚具有较弱的磷脂酶A_2抑制作用，可以抑制昆虫的免疫反应，使其更易受到微生物侵染（Shrestha & Kim，2007）；xenocycloins对大蜡螟血细胞有血腔活性，有助于斯氏线虫–致病杆菌共生体发挥杀虫活性（Proschak et al.，2014）。rhabduscin是一种酪氨酸衍生物，通过将昆虫体内的酚氧化酶浓度控制在低纳摩尔水平实现其杀虫活性（Crawford et al.，2012）。苯亚甲基丙酮作为磷脂酶A_2的抑制剂调控类花生酸的合成，减弱寄主血细胞的吞噬作用，抑制昆虫免疫反应，间接参与线虫–共生菌共生体的毒力效应（Spogliarich et al.，1989）。二硫吡咯类物质具有典型的异双环吡咯酮二硫唑核，通过抑制RNA的合成发挥细胞毒性（Oliva et al.，2001；Challinor & Bode，2015）。Xiao et al.（2012）从*X. budapestensis*中分离到2种未命名的抗菌肽GP-19和EP-20，其对真菌和细菌均表现出广谱抗菌活性，但具体的作用模式尚未阐明。

致病杆菌产生的特殊代谢物不仅在保证线虫繁殖方面发挥着关键作用，还可以抑制昆虫免疫反应，发挥杀虫活性，在防治农业病害和人类疾病方面具有潜在价值。随着生物学技术的飞速发展与相关研究的不断深入，越来越多的新型抗生素被发现，例如siderophores、khoicin和xenopep（Booysen et al.，2021）。并且已有研究证明抗菌物质和具杀虫活性物质的运输与致病杆菌的VI型分泌系统密切相关，它们通过分泌系统将毒素分子运输到寄主细胞内并引发弥散性败血症的级联效应，但目前对其发挥毒力的作用机制研究还相对较浅，仍有巨大的研究空间（Kochanowsky et al.，2020；Pei et al.，2020）。

3 展望

昆虫病原线虫–共生菌复合侵染具有致病力高、持效期长和绿色安全等特点，已成为国际上生物防治研究领域的热点，致病杆菌也逐渐成为开发新型抗菌剂和杀虫剂的极佳资源。本文总结了斯氏线虫和致病杆菌共生体在复合侵染寄主昆虫过程中的生理变化和代谢变化，包括免疫抑制因子、表皮/分泌蛋白、毒素蛋白和活性次生代谢物的产生和作用机制。Dreyer et al.（2018）研究结果表明，*X. nematophila*的DSM 3370^{T}基因组包含多种编码生物合成的基因簇，据统计这种细菌产生的潜在毒力因子数量远远超过已知的所有抗生素代谢物的数量。此外，不同致病杆菌产生的代谢活性物质不同，因此致病杆菌不同种以及不同菌株几乎可以产生无限的新型生物活性化合物。但由于多数活性代谢产物是由非核糖体编码产生，并非单一基因的产物，因此需要开发新的研究方法和技术进行深入挖掘。另外，昆虫病原线虫–共生菌–昆虫构成了一个可以用于研究寄生虫和寄主互作分子机制的独特系统，并且黑腹果蝇*Drosophila melanogaster*–致病杆菌模型已被广泛用于昆虫和共生细菌之间致病机制的研究。值得注意的是，黑腹果蝇的基因组和人类有60%的同源性，并且有75%的致病基因在黑腹果蝇中具有同源性。因此，深入研究昆虫病原线虫–共生菌的关键信号分子和生物标志物，不仅有助于推进新型生物农药的开发，而且还有助于推进对人类寄生虫病的理解和研究。

参 考 文 献（References）

AbuHatab M, Selvan S, Gaugler R. 1995. Role of proteases in penetration of insect gut by the entomopathogenic nematode *Steinernema glaseri* (Nematoda: Steinernematidae). Journal of Invertebrate Pathology, 66(2): 125−130

Akhurst RJ. 1980. Morphological and functional dimorphism in *Xenorhabdus* spp., bacteria symbiotically associated with the insect pathogenic nematodes *Neoaplectana* and *Heterorhabditis*. Microbiology, 121(2): 303−309

Akhurst RJ. 1983. *Neoaplectana* species: specificity of association with bacteria of the genus *Xenorhabdus*. Experimental Parasitology, 55(2): 258−263

Baiocchi T, Lee G, Choe DH, Dillman AR. 2017. Host seeking parasitic nematodes use specific odors to assess host resources. Scientific Reports, 7(1): 6270

Balasubramanian N, Toubarro D, Simões N. 2010. Biochemical study and *in vitro* insect immune suppression by a trypsin-like secreted protease from the nematode *Steinernema carpocapsae*. Parasite Immunology, 32(3): 165−175

Bi YH, Gao CZ, Yu ZG. 2018. Rhabdopeptides from *Xenorhabdus budapestensis* SN84 and their nematicidal activities against *Meloidogyne incognita*. Journal of Agricultural and Food Chemistry, 66(15): 3833−3839

Bird AF, Akhurst RJ. 1983. The nature of the intestinal vesicle in nematodes of the family Steinernematidae. International Journal for Parasitology, 13(6): 599−606

Booysen E, Rautenbach M, Stander MA, Dicks LMT. 2021. Profiling the production of antimicrobial secondary metabolites by *Xenorhabdus khoisanae* J194 under different culturing conditions. Frontiers in Chemistry, 9: 626653

Brachmann AO, Forst S, Furgani GM, Fodor A, Bode HB. 2006. Xenofuranones A and B: phenylpyruvate dimers from *Xenorhabdus szentirmaii*. Journal of Natural Products, 69(12): 1830−1832

Brachmann AO, Reimer D, Lorenzen W, Alonso EA, Kopp Y, Piel J, Bode HB. 2012. Reciprocal cross talk between fatty acid and antibiotic biosynthesis in a nematode symbiont. Angewandte Chemie, 51(48): 12086−12089

Brivio MF, Mastore M. 2018. Nematobacterial complexes and insect hosts: different weapons for the same war. Insects, 9(3): 117

Brivio MF, Moro M, Mastore M. 2006. Down-regulation of antibacterial peptide synthesis in an insect model induced by the body-surface of an entomoparasite (*Steinernema feltiae*). Developmental & Comparative Immunology, 30(7): 627−638

Brown SE, Cao AT, Dobson P, Hines ER, Akhurst RJ, East PD. 2006. Txp40, a ubiquitous insecticidal toxin protein from *Xenorhabdus* and *Photorhabdus* bacteria. Applied and Environmental Microbiology, 72(2): 1653−1662

Burman M. 1982. *Neoaplectana carpocapsae*: toxin production by axenic insect parasitic nematodes. Nematologica, 28(1): 62−70

Caldas C, Cherqui A, Pereira A, Simões N. 2002. Purification and characterization of an extracellular protease from *Xenorhabdus nematophila* involved in insect immunosuppression. Applied and Environmental Microbiology, 68(3): 1297−1304

Challinor VL, Bode HB. 2015. Bioactive natural products from novel microbial sources. Annals of the New York Academy of Sciences, 1354(1): 82−97

Chang DD, Wang CL, Li CJ. 2022. Advances on the pathogenic mechanism of entompathogenic nematodes. Chinese Journal of Biological Control, 38(5): 1325−1333 (in Chinese) [常豆豆, 王从丽, 李春杰. 2022. 昆虫病原线虫致病机制研究进展. 中国生物防治学报, 38(5): 1325−1333]

Cong B, Wang QS, Jian H.. 1999. Comparison on the variation of dispersal and host-searching ability of five species of entomopathogenic nematode. Journal of Shenyang Agricultural University, 30(3): 263−266 (in Chinese) [丛斌, 王秋实, 简恒. 1999. 昆虫病原线虫扩散能力与寄主搜索能力的研究. 沈阳农业大学学报, 30(3): 263−266]

Cowles KN, Goodrich-Blair H. 2004. Expression and activity of a *Xenorhabdus nematophila* haemolysin required for full virulence towards *Manduca sexta* insects. Cellular Microbiology, 7(2): 209−219

Crawford JM, Kontnik R, Clardy J. 2010. Regulating alternative lifestyles in entomopathogenic bacteria. Current Biology, 20(1): 69−74

Crawford JM, Portmann C, Kontnik R, Walsh CT, Clardy J. 2011. NRPS substrate promiscuity diversifies the xenematides. Organic Letters, 13(19): 5144−5147

Crawford JM, Portmann C, Zhang X, Roeffaers MBJ, Clardy J. 2012. Small molecule perimeter defense in entomopathogenic bacteria. Proceedings of the National Academy of Sciences of the United States of America, 109(27): 10821−10826

Cui L, Wang QY, Qiu LH, Pang Y. 2005. Insecticidal activity of insecticidal toxin gene *xptA2* in *Xenorhabdus nematophila* BP. Journal of Plant Protection, 32(4): 407−410 (in Chinese) [崔龙, 王勤英, 邱礼鸿, 庞义. 2005. 昆虫病原线虫共生菌BP品系杀虫毒素基因*xptA2*的杀虫活性分析. 植物保护学报, 32(4): 407−410]

Dreyer J, Malan AP, Dicks LMT. 2018. Bacteria of the genus *Xenorhabdus*, a novel source of bioactive compounds. Frontiers in Microbiology, 9: 3177

Dunphy GB, Webster JM. 1988. Virulence mechanisms of *Heterorhabditis heliothidis* and its bacterial associate, *Xenorhabdus luminescens*, in non-immune larvae of the greater wax moth, *Galleria mellonella*. International Journal for Parasitology, 18(6): 729−737

Epsky ND, Walter DE, Capinera JL. 1988. Potential role of nematophagous microarthropods as biotic mortality factors of entomogenous nematodes (Rhabditida: Steinernematidae, Heterorhabditidae). Journal of Economic Entomology, 81(3): 821−825

Fuchs SW, Grundmann F, Kurz M, Kaiser M, Bode HB. 2014. Fabclavines: bioactive peptide-polyketide-polyamino hybrids from *Xenorhabdus*. ChemBioChem, 15(4): 512−516

Fuchs SW, Proschak A, Jaskolla TW, Karas M, Bode HB. 2011. Structure elucidation and biosynthesis of lysine-rich cyclic peptides in

Xenorhabdus nematophila. Organic & Biomolecular Chemistry, 9(9): 3130−3132

Fuchs SW, Sachs CC, Kegler C, Nollmann FI, Karas M, Bode HB. 2012. Neutral loss fragmentation pattern based screening for arginine-rich natural products in *Xenorhabdus* and *Photorhabdus*. Analytical Chemistry, 84(16): 6948−6955

Gaugler R. 2002. Entomopathogenic nematology. UK: CABI Publishing, pp. 57−78

Grundmann F, Kaiser M, Kurz M, Schiell M, Batzer A, Bode HB. 2013. Structure determination of the bioactive depsipeptide xenobactin from *Xenorhabdus* sp. PB30.3. RSC Advances, 3(44): 22072−22077

Hao YJ, Montiel R, Nascimento G, Toubarro D, Simoes N. 2009. Identification and expression analysis of the *Steinernema carpocapsae* elastase-like serine protease gene during the parasitic stage. Experimental Parasitology, 122(1): 51−60

Hasan A, Yeom HS, Ryu J, Bode HB, Kim Y. 2019. Phenylethylamides derived from bacterial secondary metabolites specifically inhibit an insect serotonin receptor. Scientific Reports, 9: 20358

Herbert EE, Goodrich-Blair H. 2007. Friend and foe: the two faces of *Xenorhabdus nematophila*. Nature Reviews Microbiology, 5(8): 634−646

Houard J, Aumelas A, Noël T, Pages S, Givaudan A, Fitton-Ouhabi V, Villain-Guillot P, Gualtieri M. 2013. Cabanillasin, a new antifungal metabolite, produced by entomopathogenic *Xenorhabdus cabanillasii* JM26. Journal of Antibiotics, 66(10): 617−620

Ji DJ, Yi Y, Kang GH, Choi YH, Kim P, Baek NI, Kim Y. 2004. Identification of an antibacterial compound, benzylideneacetone, from *Xenorhabdus nematophila* against major plant-pathogenic bacteria. FEMS Microbiology Letters, 239(2): 241−248

Jing YJ, Toubarro D, Hao YJ, Simoes N. 2010. Cloning, characterisation and heterologous expression of an astacin metalloprotease, *Sc*-AST, from the entomoparasitic nematode *Steinernema carpocapsae*. Molecular and Biochemical Parasitology, 174(2): 101−108

Kämpfer P, Tobias NJ, Ke LP, Bode HB, Glaeser SP. 2017. *Xenorhabdus thuongxuanensis* sp. nov. and *Xenorhabdus eapokensis* sp. nov., isolated from *Steinernema* species. International Journal of Systematic and Evolutionary Microbiology, 67(5): 1107−1114

Kochanowsky RM, Bradshaw C, Forlastro I, Stock SP. 2020. *Xenorhabdus bovienii* strain jolietti uses a type 6 secretion system to kill closely related *Xenorhabdus* strains. FEMS Microbiology Ecology, 96(8): fiaa073

Kronenwerth M, Bozhüyük KAJ, Kahnt AS, Steinhilber D, Gaudriault S, Kaiser M, Bode HB. 2014. Characterisation of taxlllaids A-G: natural products from *Xenorhabdus indica*. Chemistry, 20(52): 17478−17487

Lang G, Kalvelage T, Peters A, Wiese J, Imhoff JF. 2008. Linear and cyclic peptides from the entomopathogenic bacterium *Xenorhabdus nematophilus*. Journal of Natural Products, 71(6): 1074−1077

Li ET, Lu QH, Zhang DF, Kong WJ, An CJ. 2022. Effects of entomopathogenic nematodes on the physiobiochemistry and histopathology of fall armyworm *Spodoptera frugiperda*. Journal of Plant Protection, 49(6): 1731−1741 (in Chinese) [李而涛, 鲁祺晗, 张丹凤, 孔维捷, 安春菊. 2022. 昆虫病原线虫对草地贪夜蛾生理生化和组织病理学的影响. 植物保护学报, 49(6): 1731−1741]

Li JX, Chen GH, Webster JM. 1997. Nematophin, a novel antimicrobial substance produced by *Xenorhabdus nematophilus* (Enterobactereaceae). Canadian Journal of Microbiology, 43(8): 770−773

Li XY, Cowles EA, Cowles RS, Gaugler R, Cox-Foster DL. 2009. Characterization of immunosuppressive surface coat proteins from *Steinernema glaseri* that selectively kill blood cells in susceptible hosts. Molecular and Biochemical Parasitology, 165(2): 162−169

Liao WL, Bu XL, Jiang WY, Liu JS. 2017. Influence of lipopolysaccharide on the expression of the Toll-like receptor gene *BmToll9-2* in larval *Bombyx mori*. Acta Entomologica Sinica, 60(4): 372−378 (in Chinese) [廖文丽, 卜晓玲, 江婉仪, 刘吉升. 2017. 脂多糖对家蚕幼虫Toll样受体基因*BmToll9-2*表达的影响. 昆虫学报, 60(4): 372−378]

Liu H. 2012. Research on immune suppressive protein on the surface coat of *Steinernema glaseri*. PhD thesis. Beijing: Chinese Academy of Agricultural Sciences (in Chinese) [刘华. 2012. 格氏线虫表皮免疫抑制蛋白的研究. 博士学位论文. 北京: 中国农业科学院]

Liu J, Liu H, Yuan JJ, Liu Z, Yang XF, Zhang LL, Qiu DW, Zeng HM. 2012. Comparison of the immunosuppressive activity between cuticle coat proteins and secrete proteins from *Steinernema glaseri*. Chinese Journal of Biological Control, 28(3): 400−407 (in Chinese) [刘劲, 刘华, 袁京京, 刘峥, 杨秀芬, 张利莉, 邱德文, 曾洪梅. 2012. 格氏线虫表皮蛋白和分泌蛋白抑制昆虫免疫活性的比较. 中国生物防治学报, 28(3): 400−407]

Liu QZ, Cai JY, Zhang XH. 2023. Entomopathogenic nematodes for biocontrol of fall armyworm *Spodoptera frugiperda* and their indoor/field control efficiency and influencing factors. Journal of Plant Protection, 50(1): 50−58 (in Chinese) [刘奇志, 蔡佳仪, 张小涵. 2023. 昆虫病原线虫生物防控草地贪夜蛾的室内及田间效果和影响因素. 植物保护学报, 50(1): 50−58]

Lu DH, Macchietto M, Chang D, Barros MM, Baldwin J, Mortazavi A, Dillman AR. 2017. Activated entomopathogenic nematode infective juveniles release lethal venom proteins. PLoS Pathogens, 13 (4): e1006302

Mahmood S, Kumar M, Kumari P, Mahapatro GK, Banerjee N, Sarin NB. 2020. Novel insecticidal chitinase from the insect pathogen *Xenorhabdus nematophila*. International Journal of Biological Macromolecules, 159: 394−401

Martens EC, Goodrich-Blair H. 2005. The *Steinernema carpocapsae* intestinal vesicle contains a subcellular structure with which *Xenorhabdus nematophila* associates during colonization initiation. Cellular Microbiology, 7(12): 1723−1735

Martens EC, Heungens K, Goodrich-Blair H. 2003. Early colonization

events in the mutualistic association between *Steinernema carpocapsae* nematodes and *Xenorhabdus nematophila* bacteria. Journal of Bacteriology, 185(10): 3147−3154

Mastore M, Brivio MF. 2008. Cuticular surface lipids are responsible for disguise properties of an entomoparasite against host cellular responses. Developmental & Comparative Immunology, 32(9): 1050−1062

McInerney BV, Gregson RP, Lacey MJ, Akhurst RJ, Lyons GR, Rhodes SH, Smith DRJ, Engelhardt LM, White AH. 1991a. Biologically active metabolites from *Xenorhabdus* spp., Part 1: dithiolopyrrolone derivatives with antibiotic activity. Journal of Natural Products, 54(3): 774−784

McInerney BV, Taylor WC, Lacey MJ, Akhurst RJ, Gregson RP. 1991b. Biologically active metabolites from *Xenorhabdus* spp., Part 2: benzopyran-1-one derivatives with gastroprotective activity. Journal of Natural Products, 54(3): 785−795

Mollah MMI, Ahmed S, Kim Y. 2021. Immune mediation of HMG-like DSP1 via Toll-Spätzle pathway and its specific inhibition by salicylic acid analogs. PLoS Pathogens, 17(3): e1009467

Morales-Soto N, Gaudriault S, Ogier JC, Thappeta KRV, Forst S. 2012. Comparative analysis of P2-type remnant prophage loci in *Xenorhabdus bovienii* and *Xenorhabdus nematophila* required for xenorhabdicin production. FEMS Microbiology Letters, 333(1): 69−76

Morgan JAW, Sergeant M, Ellis D, Ousley M, Jarrett P. 2001. Sequence analysis of insecticidal genes from *Xenorhabdus nematophilus* PMFI296. Applied and Environmental Microbiology, 67 (5): 2062−2069

Moureaux N, Karjalainen T, Givaudan A, Bourlioux P, Boemare N. 1995. Biochemical characterization and agglutinating properties of *Xenorhabdus nematophilus* F_1 fimbriae. Applied and Environmental Microbiology, 61(7): 2707−2712

Mucci NC, Jones KA, Cao MY, Wyatt MR II, Foye SN, Kauffman SJ, Richards GR, Taufer M, Chikaraishi Y, Steffan SA, et al. 2022. Apex predator nematodes and meso-predator bacteria consume their basal insect prey through discrete stages of chemical transformations. mSystems, 7(3): e0031222

Nollmann FI, Dowling A, Kaiser M, Deckmann K, Grösch S, Ffrench-Constant R, Bode HB. 2012. Synthesis of szentiamide, a depsipeptide from entomopathogenic *Xenorhabdus szentirmaii* with activity against *Plasmodium falciparum*. Beilstein Journal of Organic Chemistry, 8: 528−533

Oliva B, O'Neill A, Wilson JM, O'Hanlon PJ, Chopra I. 2001. Antimicrobial properties and mode of action of the pyrrothine holomycin. Antimicrobial Agents and Chemotherapy, 45(2): 532−539

Parkman JP, Frank JH, Nguyen KB, Smart GC. 1993. Dispersal of *Steinernema scapterisci* (Rhabditida: Steinernematidae) after inoculative applications for mole cricket (Orthoptera: Gryllotalpidae) control in pastures. Biological Control, 3(3): 226−232

Pei TT, Li H, Liang XY, Wang ZH, Liu GF, Wu LL, Kim H, Xie ZP, Yu M, Lin SJ, et al. 2020. Intramolecular chaperone-mediated secretion of an Rhs effector toxin by a type VI secretion system. Nature Communications, 11: 1865

Proschak A, Zhou QQ, Schöner T, Thanwisai A, Kresovic D, Dowling A, Ffrench-Constant R, Proschak E, Bode HB. 2014. Biosynthesis of the insecticidal xenocyloins in *Xenorhabdus bovienii*. ChemBioChem, 15(3): 369−372

Reimer D, Nollmann FI, Schultz K, Kaiser M, Bode HB. 2014. Xenortide biosynthesis by entomopathogenic *Xenorhabdus nematophila*. Journal of Natural Products, 77(8): 1976−1980

Renn N. 1998. Routes of penetration of the entomopathogenic nematode *Steinernema feltiae* attacking larval and adult houseflies (*Musca domestica*). Journal of Invertebrate Pathology, 72(3): 281−287

Roderer D, Bröcker F, Sitsel O, Kaplonek P, Leidreiter F, Seeberger PH, Raunser S. 2020. Glycan-dependent cell adhesion mechanism of Tc toxins. Nature Communications, 11: 2694

Santhi VS, Ment D, Faigenboim A, Salame L, Soroker V, Hetzroni A, Glazer I. 2021. Behavioral and molecular response of the insect parasitic nematode *Steinernema carpocapsae* to cues emitted by a host, the red palm weevil, *Rhynchophorus ferrugineus*. Molecular and Biochemical Parasitology, 241: 111345

Seryczyńska H, Bajan C. 1975. Defensive reactions of L3, L4 larvae of the Colorado beetle to the insecticidal fungi *Paecilomyces farinosus* (Dicks) Brown et Smith, *Paecilomyces fumoso-roseus* (Wize), *Beauveria bassiana* (Bols/Vuill.) (Fungi Imperfecti: Moniliales). Bulletin de L'Academie Polonaise des Sciences: Serie Des Sciences Biologiques, 23(4): 267−271

Shamseldean MM, Platzer EG, Gaugler R. 2007. Role of the surface coat of *Romanomermis culicivorax* in immune evasion. Nematology, 9(1): 17−24

Shrestha S, Kim Y. 2007. An entomopathogenic bacterium, *Xenorhabdus nematophila*, inhibits hemocyte phagocytosis of *Spodoptera exigua* by inhibiting phospholipase A_2. Journal of Invertebrate Pathology, 96(1): 64−70

Singh J, Banerjee N. 2008. Transcriptional analysis and functional characterization of a gene pair encoding iron-regulated xenocin and immunity proteins of *Xenorhabdus nematophila*. Journal of Bacteriology, 190(11): 3877−3885

Spogliarich R, Farnetti E, Kašpar J, Graziani M, Cesarotti E. 1989. Selective hydrogenation of benzylideneacetone catalyzed by iridium diphosphine complexes. Journal of Molecular Catalysis, 50(1): 19−29

Strauch O, Ehlers RU. 1998. Food signal production of *Photorhabdus luminescens* inducing the recovery of entomopathogenic nematodes *Heterorhabditis* spp. in liquid culture. Applied Microbiology and Biotechnology, 50(3): 369−374

Sundar L, Chang FN. 1993. Antimicrobial activity and biosynthesis of indole antibiotics produced by *Xenorhabdus nematophilus*. Journal of General Microbiology, 139(12): 3139−3148

Tang HP. 2009. Regulation and function of the melanization reaction in *Drosophila*. Fly, 3(1): 105−111

Timper P, Kaya HK, Gaugler R. 1988. Dispersal of the entomogenous nematode *Steinernema feltiae* (Rhabditida: Steinernematidae) by

infected adult insects. Environmental Entomology, 17(3): 546−550

Toubarro D, Lucena-Robles M, Nascimento G, Costa G, Montiel R, Coelho AV, Simões N. 2009. An apoptosis-inducing serine protease secreted by the entomopathogenic nematode *Steinernema carpocapsae*. International Journal for Parasitology, 39(12): 1319−1330

Vigneux F, Zumbihl R, Jubelin G, Ribeiro C, Poncet J, Baghdiguian S, Givaudan A, Brehélin M. 2007. The *xaxAB* genes encoding a new apoptotic toxin from the insect pathogen *Xenorhabdus nematophila* are present in plant and human pathogens. Journal of Biological Chemistry, 282(13): 9571−9580

Vo TD, Spahn C, Heilemann M, Bode HB. 2021. Microbial cationic peptides as a natural defense mechanism against insect antimicrobial peptides. ACS Chemical Biology, 16(3): 447−451

Wang J, Dai K, Kong XX, Cao L, Qu L, Jin YL, Li YL, Gu XH, Li JZ, Xu CT, et al. 2021. Research progress and perspective on entomopathogenic nematodes. Journal of Environmental Entomology, 43(4): 811−839 (in Chinese) [王杰, 戴康, 孔祥鑫, 曹莉, 屈玲, 金永玲, 李玉玲, 谷星慧, 李江舟, 徐成体, 等. 2021. 昆虫病原线虫与环境生物、非生物因素关系的研究进展. 环境昆虫学报, 43(4): 811−839]

Wang LT, Qiu XH, Wu CY, Chen JH, Han RC. 2013. Advances in the species-specific colonization of entomopathogenic nematodes by their symbiotic bacteria. Journal of Environmental Entomology, 35(2): 232−241 (in Chinese) [王立婷, 丘雪红, 吴春艳, 陈镜华, 韩日畴. 2013. 昆虫病原线虫和共生细菌定殖关系的研究进展. 环境昆虫学报, 35(2): 232−241]

Wang LX, Yang HW, Huang DF. 2000. Pathogenic mechanism of entomopathogenic bacteria: *Xenorabdus* and *Photorhabdus*. Acta Microbiologica Sinica, 40(4): 448−451 (in Chinese) [王立霞, 杨怀文, 黄大昉. 2000. 昆虫病原线虫共生细菌致病机理的研究进展. 微生物学报, 40(4): 448−451]

Wang Y, Campbell JF, Gaugler R. 1995. Infection of entomopathogenic nematodes *Steinernema glaseri* and *Heterorhabditis bacteriophora* against *Popillia japonica* (Coleoptera: Scarabaeidae) larvae. Journal of Invertebrate Pathology, 66(2): 178−184

Wu HB, Gong QT, Zhang KP, Zhang XP, Sun RH. 2015. The efficacy of synergism of entomopathogenic nematodes and black sticky cards to *Bradysia odoriphaga*. Journal of Plant Protection, 42(4): 632−638 (in Chinese) [武海斌, 宫庆涛, 张坤鹏, 张学萍, 孙瑞红. 2015. 昆虫病原线虫与黑色粘板配合使用对韭菜迟眼蕈蚊的防治. 植物保护学报, 42(4): 632−638]

Wenski SL, Cimen HR, Berghaus N, Fuchs SW, Hazir S, Bode HB. 2020. Fabclavine diversity in *Xenorhabdus* bacteria. Beilstein Journal of Organic Chemistry, 16: 956−965

Xiao Y, Meng FL, Qiu DW, Yang XF. 2012. Two novel antimicrobial peptides purified from the symbiotic bacteria *Xenorhabdus budapestensis* NMC-10. Peptides, 35(2): 253−260

Yadav M, Rathore JS. 2020. The $hipBA^{Xn}$ operon from *Xenorhabdus nematophila* functions as a bonafide toxin-antitoxin module. Applied Microbiology and Biotechnology, 104(7): 3081−3095

Yang J, Wang QY, Song P, Nangong ZY, Cui L, Kong FF, Feng SS 2008. Purification and characterization of the haemocoel insecticide Tp40 from *Xenorhabdus nematophila*. Acta Microbiologica Sinica, 48(5): 677−683 (in Chinese) [杨君, 王勤英, 宋萍, 南宫自艳, 崔龙, 孔繁芳, 冯姗姗. 2008. 嗜线虫致病杆菌血腔毒素Tp40的纯化和特性分析. 微生物学报, 48(5): 677−683]

Yang X, Hou XQ, Sun YW, Zhang GY, Hu XF, Xie YL, Mo XT, Ding XZ, Xia LQ, Hu SB. 2019. Screening a fosmid library of *Xenorhabdus stockiae* HN_xs01 reveals SrfABC toxin that exhibits both cytotoxicity and injectable insecticidal activity. Journal of Invertebrate Pathology, 167: 107247

Yang XF, Yang HW. 1998. The pathogenic mechanism of entomopathogenic nematodes. Chinese Journal of Biological Control, 14(4): 181−185 (in Chinese) [杨秀芬, 杨怀文. 1998. 昆虫病原线虫的致病机理. 中国生物防治, 14(4): 181−185]

Zhang SJ, Liu Q, Han YF, Han JH, Yan ZQ, Wang YH, Zhang X. 2019. Nematophin, an antimicrobial dipeptide compound from *Xenorhabdus nematophila* YL001 as a potent biopesticide for *Rhizoctonia solani* control. Frontiers in Microbiology, 10: 1765

Zhou QQ, Grundmann F, Kaiser M, Schiell M, Gaudriault S, Batzer A, Kurz M, Bode HB. 2013. Structure and biosynthesis of xenoamicins from entomopathogenic *Xenorhabdus*. Chemistry, 19(49): 16772−16779

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