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Review 综 述

糖丝菌属放线菌研究进展

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摘　要：1984 年美国著名放线菌分类学家 Labeda 建立的糖丝菌属(*Saccharothrix*)，是典型的丝状稀有放线菌重要类群之一。糖丝菌的气生菌丝在孢子形成过程中通常呈现锯齿状形态，细胞壁含 *meso*-二氨基庚二酸，磷酸类脂主要包括磷脂酰乙醇胺，优势甲基萘醌是 MK-9(H_4)和 MK-10(H_4)，基因组中 16S rRNA 基因的特异性诊断核苷酸序列为 CAC(607–609)和 GTG(617–619)。近年来基因组学研究证实，糖丝菌基因组中存在丰富的聚酮合成酶、非核糖体多肽合成酶等基因簇，具有生物合成化学结构新颖、生物活性多样的次生代谢物与酶产物的潜能，且研究证实糖丝菌能够代谢产生已知抗生素的衍生物或新骨架结构的抗生素，如二硫吡咯酮类、内酰胺类、蒽环类和氯霉素等新抗生素，在抗病毒、抑菌和抗肿瘤等方面具有巨大的医药价值。同时，糖丝菌也是工业酶制剂生产菌种资源的新成员，在酶制剂应用方面具有较强的开发潜力，其代谢产生的几丁质酶、纤维素酶等新型活性酶在现代农业以及轻工业等领域有着广泛应用。另外，糖丝菌凭借自身独特的遗传代谢多样性在土壤有机污染物降解和重金属污染修复中扮演着重要角色。结合近期本实验室发表的一株糖丝菌新种，查阅相关文献资料，本文从糖丝菌属的分类学典型特征、基因组学、次级代谢产物生物合成以及产酶应用开发进行了综述，以期为进一步挖掘糖丝菌的应用潜力提供理论基础。

关键词：糖丝菌属；基因组挖掘；次级代谢产物；酶活性

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Recent advance on the genus *Saccharothrix*

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Abstract: The genus *Saccharothrix* was established in 1984 by Labeda, a famous American taxonomist of actinobacteria. This genus is an important group of rare actinomycetes with filamentous hyphae, and most species have zigzag aerial hyphae during sporulation. They contained *meso*-diaminopimelic acid in cell wall, abundant phosphatidylethanolamine in phospholipids, MK-9(H_4) and MK-10(H_4) as the principal menaquinones, and the genus-specific motifs CAC (607–609) and GTG (617–619) in the 16S rRNA gene. Recent studies of genome mining have confirmed the existence of non-ribosomal peptide synthetase genes with high frequency in the genomes of *Saccharothrix* spp., which have the potential to produce structurally-novel secondary metabolites and enzyme products with diverse activities. Further, *Saccharothrix* can produce derivatives of known antibiotics or antibiotics with new structures, such as dithiopyrrolones, lactams, anthracyclines, and chloramphenicol, which have a great value in antiviral, antibacterial and antitumor treatment. Moreover, *Saccharothrix* serves as a new microbial resource for the production of industrial enzyme preparations, which has strong development potential in the application of enzyme preparations. New active enzymes such as chitinase and cellulase generated by the metabolism of *Saccharothrix* are widely used in modern agriculture, light industry and other fields. Owing to the unique genetic and metabolic diversity, *Saccharothrix* plays a key role in the degradation of organic pollutants and remediation of heavy metal pollution in soil. On the basis a novel species of *Saccharothrix* discovered by our laboratory and relevant literature, we reviewed the typical taxonomic characteristics, genomics, secondary metabolites, and enzyme development of *Saccharothrix*, aiming to provide a scientific basis for further mining the *Saccharothrix* strains with application potential.

Keywords: *Saccharothrix*; genome mining; secondary metabolites; enzymatic activity

糖丝菌属(*Saccharothrix*)隶属于放线菌门(*Actinobacteria*)，放线菌纲(*Actinobacteria*)，假诺卡氏菌目(*Pseudonocardiales*)，假诺卡氏菌科(*Pseudonocardiaceae*)。目前该属共有 21 个有效描述种和 3 个亚种，该属模式种是分离自澳大利亚土壤的 *Saccharothrix australiensis*[1]。基于不依赖纯培养的宏基因组学[2]、宏转录组学、宏蛋白质组学和 DNA 稳定同位素探针(DNA-SIP)[3]等现代前沿技术，研究发现糖丝菌广泛分布在土壤、植物组织或根际中，甚至在诸如沙漠、盐碱地、洞穴、金属矿床以及湖泊或海洋沉积物等极端环境中也有糖丝菌的踪迹。

糖丝菌是典型的丝状稀有放线菌，能够产生多种新型生物活性代谢物，对人类肿瘤细胞、植物病原性和产毒素真菌以及包括耐甲氧西林金黄色葡萄球菌(methicillin-resistant *Staphylococcus aureus*)在内的多种耐药病原体及病毒具有抑制活性[4]，是新型抗生素的重要来源。此外，一

些糖丝菌还能产生几丁质酶、纤维素酶等活性酶用来治疗各种真菌类感染疾病、降解纤维素和有机污染物等，在生物医药、现代农业和环境治理等方面有着广泛的应用潜力。近年来基因组学技术突飞猛进，研究表明糖丝菌基因组中含有丰富的与次生代谢产物相关的功能基因簇，新骨架、新功能活性代谢产物通过基因簇克隆、改造，以及菌株共培养等方法而被发现[5]，为新药研发、农业发展和环境污染治理提供了新的解决方案。

1 糖丝菌属系统分类

1.1 糖丝菌属典型特征

1984 年，Labeda 等首次从土壤中分离出一株能产生新型氨基糖苷类抗生素的菌株，结合其形态特征和系统发育特性，以 *S. australiensis* 为模式种建立放线菌新属——糖丝菌属[6]。随后分别经过 Labeda 等[7]和 Zhi 等[8]两次修正，将邻近菌属的放线菌陆续重新分类纳入到糖丝菌属中，包括来自拟诺卡氏菌属的 *Nocardiopsis coeruleofusca* 和 *Nocardiopsis mutabilis*、马杜拉放线菌属的 *Actinomadura longispora* 以及指孢囊菌属的 *Dactylosporangium variisporea* 等[9]。相反，根据 16S rRNA 特征核苷酸分析结果，一些糖丝菌被重新归属到邻近属，如 *Lechevalieria aerocolonigenes*、*Lentzea albidocapillata*、*Lentzea flava*、*Lentzea violacea*、*Lentzea waywayandensis*、*Crossiella cryophilis*、*Goodfellowia coeruleoviolacea*、*Umezawaea tangerinus*[10–11]。当然，也有近年来加入糖丝菌属的新成员，如 2020 年本课题组从新疆荒漠中分离出的 *S. deserti*[12]、2017 年 Bouznada 等从撒哈拉沙漠分离出的 *S. ghardaiensis*[13]等。

糖丝菌的营养菌丝(直径约 0.5–0.7 μm)和气生菌丝通常断裂成球形或杆状，无运动。营养菌丝呈黄色至棕黄色，少数菌株呈现其他颜色，如 *S. deserti* 和 *S. tamanrassetensis* 在 ISP 2 培养基上为深红棕色，气生菌丝在孢子形成过程中通常呈“之”字形，部分菌株产生黄色至棕色的可溶性色素[12,14]。糖丝菌为革兰氏阳性，需氧，对溶菌酶敏感，过氧化氢酶阳性，生长温度为 10–45 °C，其中 *S. mutabilis* 耐 80 °C 高温[15]。除 *S. carnea*[16]和 *S. espanaensis*[7]等部分菌株外，大部分糖丝菌能水解明胶，利用酪蛋白和淀粉。细胞壁含 *meso*-二氨基庚二酸，无甘氨酸。全细胞水解物以半乳糖、鼠李糖和甘露糖为特征性糖。磷脂模式为 PII 型或 PIV 型，包含磷脂酰乙醇胺(phosphatidylethanolamine，PE)、羟基磷脂酰乙醇胺(hydroxy-phosphatidylethanolamine，OH-PE)，*S. australiensis* 和 *S. stipae*[17]的磷脂为典型的 PII 型。MK-9(H_4)和 MK-10(H_4)是主要的甲基萘醌。脂肪酸主要含有 *iso*-$C_{16:0}$，$C_{17:1}\omega 8c$，*iso*-$C_{15:0}$。无分枝菌酸。DNA 的(G+C)含量为 67.0–76.0 mol%，16S rRNA 基因特异性诊断核苷酸序列为 CAC (607–609)和 GTG (617–619)，糖丝菌属及其近缘菌属分类学特征见表 1。

基于 16S rRNA 基因序列的系统发育进化分析(图 1)，糖丝菌属 21 株有效发表种聚集为一个大分支，其中本实验室报道的新物种 *S. deserti* BMP8144^T 与 *S. lopnurensis* YIM LPA2h^T 的 16S rRNA 基因序列相似性达到 98.9%，位于一个亚分支内[12]。此外，糖丝菌属与梅泽宾夫氏菌属(*Umezawaea*)的进化距离最近，其次是束丝放线菌属(*Actinosynnema*)、涅什瓦列属(*Lechevalieria*)、伦茨菌属(*Lentzea*)和放线动孢菌属(*Actinokineospora*)[19–20]聚类在一起，亲缘关系密切。

表 1　糖丝菌属及其近缘菌属的分类学特征

Table 1　Taxonomy characteristics of the genus *Saccharothrix* and closely related genera

Characteristics	*Saccharothrix*[6]	*Lentzea*[18]	*Lechevalieria*[11]	*Actinosynnema*[19]	*Umezawaea*[20]
Cell	Cocci/ rod-shaped	Rod-shaped	Cocci/ rod-shaped	Rod-shaped	Cocci/ rod-shaped
pH	6.0–9.0	5.0–11.0	5.0–11.0	6.0–8.5	6.0–8.0
T/°C	10–45	10–37	28–30	28–30	20–30
NaCl tolerance (%, *W/V*)	0–3	0–4	0–4	0–2	0–4
Polar lipidsd	PE, OH-PE, PI, PIM, DPG, PG	PE, DPG, PG, PI	PE	PE, OH-PE, PI, PIM, DPG	PE
Whole-cell sugar	Gal, Rha, Man	Gal, Man, Rib	Gal, Rha, Man	Gal, Man	Gal, Rha
Major cellular fatty acids	*iso*-$C_{16:0}$ $C_{17:1}\omega8c$ *iso*-$C_{15:0}$	*iso*-$C_{14:0}$ *iso*-$C_{15:0}$ *iso*-$C_{16:0}$ *anteiso*-$C_{15:0}$	*iso*-$C_{16:0}$ *anteiso*-$C_{15:0}$ $C_{16:1}\omega7c$ *anteiso*-$C_{17:0}$	$C_{17:0}$ *anteiso*-$C_{17:0}$ *iso*-$C_{16:0}$	*iso*-$C_{14:0}$ *iso*-$C_{15:0}$ *iso*-$C_{16:0}$ *iso*-$C_{16:1}$
DNA G+C content (mol%)	67.0–76.0	68.6–79.6	68.0–71.4	71.0–73.0	74.0

Gal: galactose; Man: mannose; Rib: ribose; Rha: rhamnose. PE: phosphatidylethanolamine; PG: phosphatidylglycerol; PI: phosphatidylinositol; DPG: diphosphatidylglycerol; PIM: phosphatidylinositolmannoside; OH-PE: hydroxy-phosphatidylethanolamine.

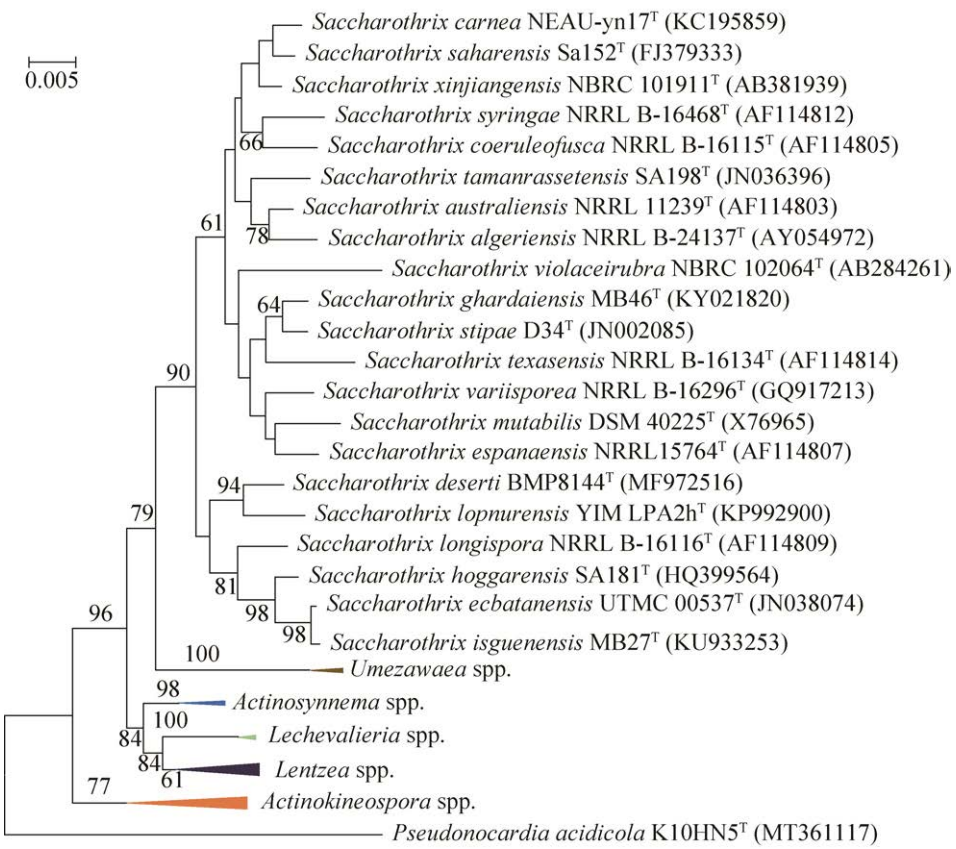

图 1　基于 16S rRNA 基因序列邻近法构建的糖丝菌属有效发表种的系统发育树

Figure 1　Neighbor-joining phylogenetic tree based on 16S rRNA gene sequences of the validly published species of the *Saccharothrix*. Numbers at nodes indicate levels of bootstrap support based on a neighbor-joining analysis of 1 000 resampled datasets, only values >50% were given. Bar, 5 substitutions per 1 000 nucleotide positions.

1.2 基因组及基因资源发掘

放线菌产生的许多抗生素都是通过非核糖体多肽合成酶(nonribosomal peptide synthetases，NRPSs)或聚酮合酶(polyketide synthases，PKSs)的途径进行生物合成的[21]。糖丝菌基因组中NRPSs 基因的高频率存在是其产生大量生物活性次级代谢产物的有力证据[22]。截至 2021 年 9 月，GenBank、JGI 和 GTDB 的数据库中共收录了 17 株糖丝菌的基因组序列，基于 Type Strain Genome Server (https://tygs. dsmz.de/)服务器的系统发育分析如图 2。antiSMASH (V5.2.0)基因组注释预测显示糖丝菌属菌株的 NRPSs 和 PKSs 基因簇相当丰富(表 2)，推测糖丝菌产生的次生代谢产物与酶在治疗细菌、真菌和病毒类感染疾病，抗肿瘤和抗结核等方面有重要作用。如最近 Feng 等报道了 *S. texasensis* 6-C 的完整基因组大小为 9.04 Mb，有 9 个 NRPSs、5 个 I 型 PKSs 基因簇，能编码大量抗菌活性物质，该基因组信息有助于阐明 *S. texasensis* 6-C 生物防治马铃薯晚疫病的分子机制[23]；本实验室通过多相分类获得的 *S. deserti* BMP B8144^T 基因组大小为 10.80 Mb，其中 1 213 个基因包含 43 个与次级代谢产物相关的推定基因簇，包括 14 个 NRPSs、9 个 I 型 PKSs、2 个 II 型 PKSs，推测该菌株产生的次生代谢产物具有广泛的生物活性，如抗肿瘤、抗结核等[12]。

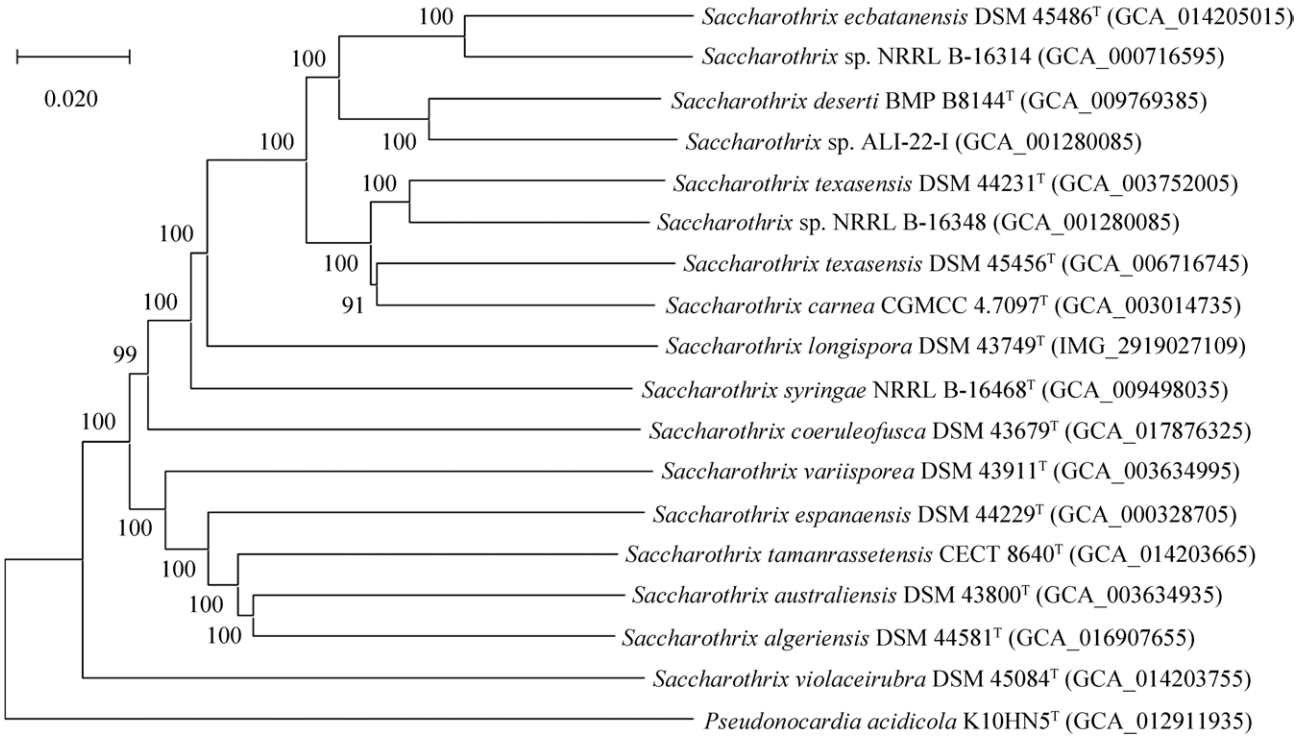

图 2 基于 TYGS 服务器中糖丝菌基因组序列的系统发育树

Figure 2 Phylogenomic tree based on genome sequences of the genus *Saccharothrix* in the TYGS server. Tree inferred with FastME 2.1.6.1 from GBDP distances calculated from genome sequences. The branch lengths are scaled in terms of GBDP distance formula d5. The numbers above branches are GBDP pseudo-bootstrap support values>60% from 100 replications, with an average branch support of 94.6%. Bar, 2 nucleotide substitution per 100 nucleotides.

表 2 糖丝菌属基因组特征

Table 2 Features of *Saccharothrix* genomes

Species	Genome size/bp	CDSs	rRNAs	tRNAs	BGCs	PKS	NRPS
S. algeriensis DSM 44581^T	6 878 582	6 066	12	49	29	5	5
S. australiensis DSM 43800^T	7 861 373	6 694	12	52	33	10	8
S. carnea CGMCC 4.7097^T	8 918 169	7 939	7	59	38	11	10
S. coeruleofusca DSM 43679^T	7 721 092	7 222	15	57	24	8	8
S. deserti BMP B8144^T	10 832 261	9 959	5	71	49	19	14
S. ecbatanensis DSM 45486^T	9 689 237	8 599	12	58	39	9	13
S. espanaensis DSM 44229^T	9 360 653	8 436	12	56	33	6	11
S. longispora DSM 43749^T	8 375 440	7 529	12	57	29	9	10
S. saharensis DSM 45456^T	8 924 967	7 995	12	52	34	8	9
S. syringae NRRL B-16468^T	10 929 570	9 301	12	53	48	16	14
S. tamanrassetensis CECT 8640^T	8 053 586	7 177	6	50	33	6	10
S. texasensis DSM 44231^T	9 178 199	8 137	12	52	36	10	9
S variisporea DSM 43911^T	9 408 895	8 387	12	53	29	10	10
S. violaceirubra DSM 45084^T	7 354 386	6 781	12	52	31	7	10
Saccharothrix sp. ALI-22-I	10 300 059	9 372	3	59	41	13	16
Saccharothrix sp. CB00851	9 304 003	8 377	4	53	43	11	15
Saccharothrix sp. NRRL B-16314	8 934 493	8 023	9	58	41	14	9
Saccharothrix sp. NRRL B-16348	10 896 489	9 728	20	67	43	15	10

随着后基因组时代的到来，挖掘发现新型活性天然产物已成为近年来国内外研究的热点，实验证明挖掘放线菌基因组是寻求新天然化合物的有效途径。从海量的基因序列中筛选鉴定出有价值的基因簇，是基因组挖掘(genome mining)的关键步骤。如 Lin 等筛选鉴定了 *Saccharothrix* sp. ST-888 中与磷霉素有关的生物合成基因簇，为阐明天然磷酸盐的生物合成机制奠定了基础[24]。由于实验条件及自然因素等制约，放线菌基因组中与活性代谢产物相关的基因簇常处于低表达量或沉默状态[25]，激活放线菌次级代谢产物合成基因簇的表达具有十分重要的意义。如 Gorniaková 等通过遗传操作激活 *S. espanaensis* DSM 44229 的一个隐秘生物合成基因簇，获得了新型手霉素(manumycins)[5]。通过放线菌的培养条件优化或在培养过程中添加诱导物以及与其他微生物联合培养等手段都有可能激活放线菌基因簇的成功表达，如 Bakour 等发现优化 *S. tamanrassetensis* DSM 45947 的碳氮源可促进产生新型抗生素[26]。

2 糖丝菌属应用潜力研究

2.1 次生代谢产物研究

抗生素在临床上的广泛使用使得许多病原菌和病毒耐药能力增强，因此继续寻找结构新颖、高效低毒的新型抗生素成为当下天然活性产物研究的热点。研究表明，糖丝菌能够产生已知抗生素的衍生物或新骨架结构的抗生素，如二硫吡咯酮类、内酰胺类、蒽环类和氯霉素[27−28]等抑菌或抗癌类抗生素(表 3)。2013 年 Wang 等从 *S. xinjiangensis* NRRL B-24321 中分离获得两种新的 16 元大环内酯类聚酮化合物 tianchimycin A 和 B[29]，2020 年 Babadi 等也从同种不同菌株 Act24Zk 中分离纯化出化

合物 saccharopyrone，对人宫颈癌 HeLa 细胞 KB3.1 具有较好的细胞毒性，IC_{50} 值达到 5.4 μmol/L[30]。

近年来，国内研究者对于 *S. syringae* NRRL B-16468 代谢产物的研究相对较深。诺卡霉素是特特拉姆酸家族的天然产物，具广泛的抗菌活性及抗肿瘤作用，确切抑菌作用还未证实，但与之紧密相关的化合物 tirandamycin 和 streptolydigin 已被证实是细菌 RNA 聚合酶(ribonucleic acid polymerase，RNAP)的抑制剂[41]，因此诺卡霉素可能是 RNAP 的抑制剂。随着高通量技术的快速发展，基因组挖掘方法不断精进，诺卡霉素的生物合成途径也不断被完善。2017 年 Mo 等鉴定出诺卡霉素合成相关基因簇并提出假定生物合成途径：诺卡霉素骨架由 5 种I型聚酮合酶(NcmA I，NcmA II，NcmA III，NcmA IV，NcmA V)和一种非核糖体多肽合成酶(NcmB)组成，一种环化酶(NcmC)催化，5 种酶(NcmEDGOP)剪裁以及 5 种酶(NcmNJKIM)起调节作用[33]。随后证实，NcmP 是一种甲基转移酶[42]，短链脱氢酶 NcmD 与一种未知酶负责诺卡霉素 F 的 C-10 氧化[43]，但由于诺卡霉素生物合成路线长，诺卡霉素 F 之前的合成步骤还未完全明确(图 3)，仍需继续深入研究。

表 3　糖丝菌产生的天然活性产物

Table 3　Natural active products of *Saccharothrix* strains

Species	Compounds	Biological activities
S. algeriensis[31]	Dithiolopyrrolone antibiotics	Broad-spectrum antibacterial
S. australiensis DSM 43800[6]	Antibiotic LL-BM-782-E	Antibacterial
S. espanaensis[5,32]	Saccharothrixins (A, B, C)	Antibacterial
	Saccharomicins (A, B)	Antitumor and immunosuppressive
	Manumycins	Farnesyltransferase inhibitor
	Antibiotic LL-C19004-D	Antibacterial
S. mutabilis[7]	Capreomycin	Antibacterial
	Polynitoxin	Antibacterial
S. syringae NRRL B-16468[33]	Nocamycin	Antibacterial and antitumor
S. xinjiangensis[29–30]	Caerulomycin M	Antitumor
	Accharopyrone	Antitumor
	Saccharonoic acid	Antitumor
	Tianchimycin (A, B)	Antibacterial
	Swalpamycin B	Antibacterial
Saccharothrix sp. ABH26[34]	Cyanogrisides (I, J)	Antibacterial
	Caerulomycins (A, B, C, D, E, F)	Antifungal, antiparasitic and antitumor
Saccharothrix sp. A1506[35]	Saccharothriolide (A, B, C, D, E, F, C2)	Antibacterial, antifungal and antitumor
Saccharothrix sp. MI-293-N4[36]	Kinamycins 1 and 2	Antibacterial
	Saccharothrixones (D, E, F, G, H, I)	Anticancer and antibacterial
Saccharothrix sp. DSM12931[37]	Pluraflavins	Antitumor
Saccharothrix sp. 10-10[38]	Saccharothrixone D	Antibacterial
	Tetracenomycin X	Antitumor
Saccharothrix sp. PAL54[28]	Chloramphenicol	Antibacterial
Saccharothrix sp. AJ9571[39]	Ammocidin (A, B, C, D)	Apoptosis inducer
Saccharothrix sp. SA 103[40]	Mutactimycin PR	Antibacterial

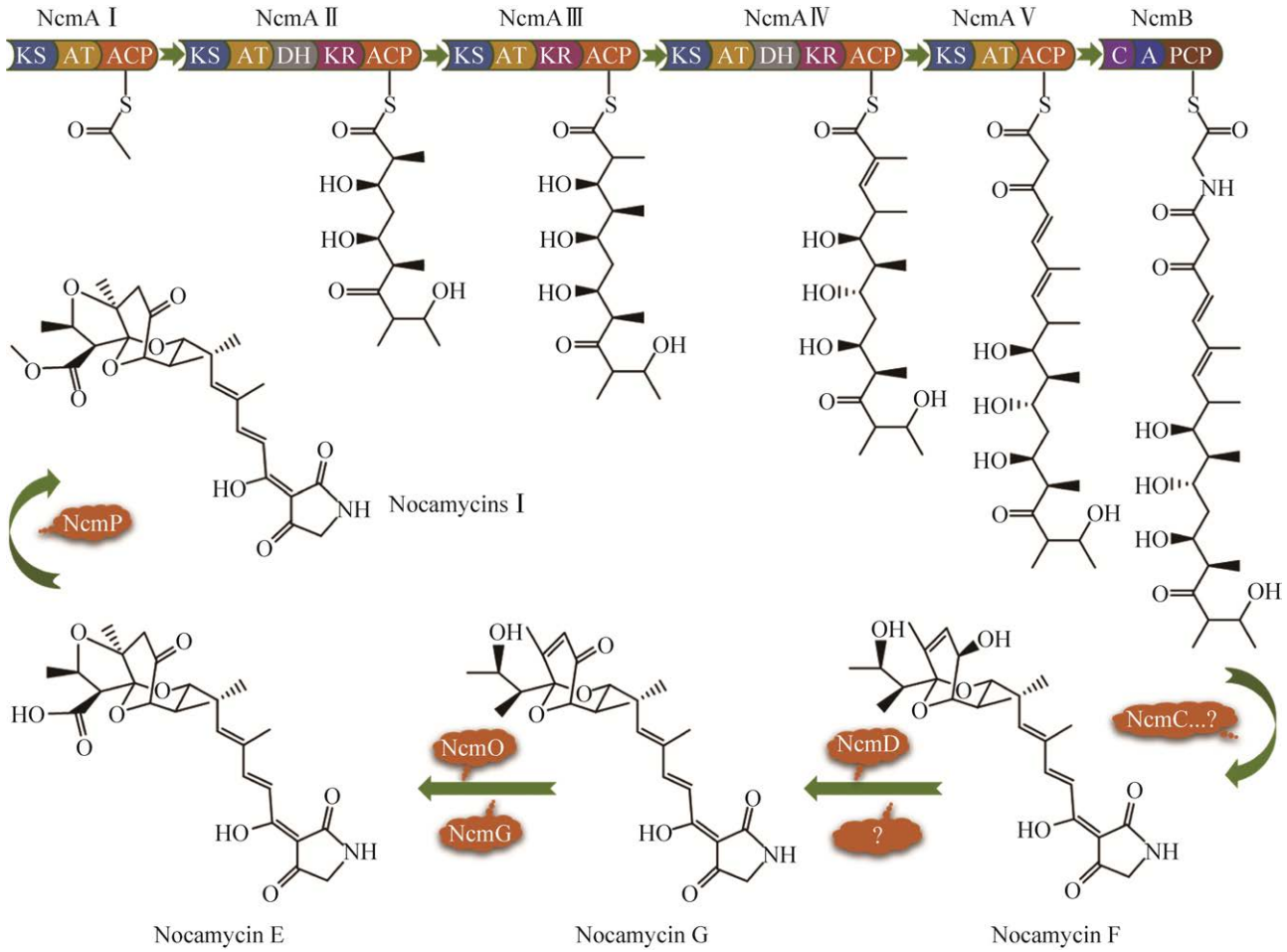

图 3　诺卡霉素的假定生物合成途径[33,41–42]

Figure 3　The putative biosynthetic pathway of nokamycin[33,41–42].

2.2　产酶应用研究

放线菌一直以来都是工业生产酶制剂的重要来源。国内学者研究发现 *S. yanglingensis* Hhs.015 能产生一种新型几丁质酶[44]，具有广阔的应用前景。在生态农业领域，几丁质酶能降解害虫和植物病原真菌的不同结构，作为应用开发潜力巨大的生防微生物菌剂，近年受到广泛关注。在医药领域，几丁质酶是抗真菌药物设计研究的理想靶酶，可用来治疗各种真菌类感染疾病。另一个重要的医学应用是几丁质酶可催化几丁质和壳聚糖反应生成无毒、较好生物相容性的衍生物，这些衍生物往往具有抗菌、抗肿瘤和调节人体免疫等生理活性[45]。

糖丝菌能产生内切 β-1,4-葡聚糖酶，该酶是纤维素酶系中研究最为广泛深入的一种酶，随机水解 β-1,4-葡聚糖苷键，将长链的纤维素截断，从而形成纤维低聚糖，被广泛应用于纺织、啤酒、饲料和造纸等领域[46]。由 *S. australiensis* IFO 14444，S. *texasensis* NRRL B-16134，*S. coeruleofusca* ATCC 35108，*S. mutabilis* ATCC 23892，*S. syringae* DSM 43886，*S. longispora* ATCC 31109 等数种优选糖丝菌产生的内切葡聚糖酶制剂可应用于洗涤剂或织物柔软组合物中，或在纺织工业中用于改善纤维素或织物的

特性[47]。*S. mutabilis* NM-6-5 能在高温下分解纤维素，在工、农业废弃物处理中具有较高的应用价值[48]，具体代谢途径和功能机制值得进一步研究。

2.3 污染修复研究

值得一提的是，在有机物污染降解和重金属污染修复方面糖丝菌也有不俗的表现。*Saccharothrix* sp. PYX-6 以蒽、菲、芘为唯一碳源，能降解含 4 个苯环的稠环芳烃化合物芘，中间代谢产物是邻苯二甲酸[49]，这与以前报道的 *Mycobacterium* sp. PYR-1 的降解途径不同。*Saccharothrix* sp. BG 以邻苯二甲酸二(2-乙基己基)酯为唯一碳源，在 48 h 内可将其浓度从 20 mg/L 降解到 2 mg/L，在污水处理系统中能发挥较好的作用[50]。*Saccharothrix* sp. APL5 能降解聚琥珀酸丁二烯(polybutadiene-styrene)[51]。糖丝菌也是生物修复重金属污染过程中的重要参与者。从韩国[52]、德国[53]、伊朗[54]的不同重金属污染土壤中分离出的 *S. violacea* LM 036、*S. albidocapillata* DSM 44073、*S. waywayandensis* Tosca4 、*Saccharothrix* sp. UTMC 2163 和 *Saccharothrix* sp. UTMC 2185 显示出对镉、镍等重金属有良好的耐受性，可修复重金属污染土壤，可能的修复机制是通过产生酶和次级代谢产物以及生物吸附作用抵抗重金属胁迫。但由于微生物降解有机物、抵抗重金属反应机制复杂，具体降解途径并未完全研究清楚，有待继续深入。

3 展望

生活在如沙漠、海洋沉积物等极端环境中的糖丝菌类群表现出多样化的生理遗传性和独特的代谢特征，具有丰富的次级代谢产物基因簇，产生的活性产物表现出了新颖的化学结构和高效低毒的特性。诚然，自然环境中的糖丝菌远不止目前的 21 个有效描述种，新物种资源的挖掘任重道远。注重加强极端环境中的糖丝菌类群的研究，尤其是难培养的菌株，要尝试从纯培养技术上有所突破，在技术优化和创新方面下足功夫，如基于膜扩散的培养方法、微流控培养方法和基于细胞分选的培养方法[55]。同时，随着各种高通量组学技术的快速发展，使用高通量测序分析和靶向方法分离培养新型微生物是研究糖丝菌的重要手段之一。利用反向基因组学对未经培养的微生物进行定向分离和靶向培养，有可能解决尚未培养微生物生命树分支中物种的分离、培养和表征问题[56]。或者采用非靶向培养方法：通过高通量技术深度测序，结合文献确定培养基等条件进行大规模培养分离纯化，对最终纯化的菌株进行菌种鉴定，从基因水平上再次确认菌株的分类学属性[57]。

研究证实，一些稀有放线菌的代谢产物表现出特异的酶抑制剂活性，能够阻断病毒的复制途径，在临床上对病毒引起的疾病起到一定治疗作用。邻近糖丝菌属的 *Lentzea chajnantorensis* H45^T 代谢合成的二烯和单烯糖苷化合物 lentzeaosides A–F 对人体免疫缺陷病毒I型(human immunodeficiency virus type I)整合酶显示出不同水平的抑制活性，并已应用于临床治疗[58]。早在 1991 年学者就发现 *S. mutabilis* R869-90 代谢合成的化合物 fluvirucin 对 A 型流感病毒株具有抑制活性[59]，这提示糖丝菌在抗病毒药物研发道路上也有潜在的应用前景。正值当下，新型冠状病毒肺炎(corona virus disease 2019)在全世界范围内肆虐横行，迅速变异的病毒株的传染性和致死率不断提高，而临床仍缺乏效果明显的靶向治疗药物，这一严峻形势向天然活性化合物的药物研发提出了新的挑战。

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