

Supporting Information

Classification and secondary metabolite-biosynthetic gene clusters of marine *Streptomyces* strains including a lobophorin- and divergolide-producer

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Table S1. Most similar known cluster searched by antiSMASH for the gene clusters in *S. olivaceus* N11-26.

Gene cluster	Most similar known cluster		Similarity
<i>t1pks-1</i>	SF2487	Polyketide	17 %
<i>nrps-1</i>	coelichelin	NRP*	100 %
<i>t1pks-2</i> ^a <i>nrps-3</i> ^a	divergolides A, B, C & D	Polyketide: Modular type I polyketide	100 %
<i>nrps-4</i> ^b	hopene	Terpene	92 %
<i>nrps-5</i>	nogalamycin	Polyketide	40 %
<i>nrps-6</i>	diisonitrile antibiotic SF2768	NRP	55 %
<i>pks/nrps-1</i>	xiamycin A	Terpene ^c	72 %
<i>nrps-7</i>	telomycin	NRP	29 %
<i>pks/nrps-2</i>	auroramycin	Polyketide ^d	8 %
<i>t2pks-2</i>	spore pigment	Polyketide	85 %
<i>t1pks-4</i>	butyrolactol A	Polyketide	86 %
<i>pks/nrps-3</i>	detoxins P1, P2 & P3	NRP+Polyketide	75 %
<i>t3pks-1</i>	flaviolin & 1,3,6,8-tetrahydroxynaphthalene	Polyketide	100 %
<i>t3pks-2</i>	germicidin	Other ^e	100 %
<i>pks/nrps-4</i> ^f <i>t1pks-5</i> ^f	lobophorin A	Polyketide	96 %

* NRP, nonribosomal peptide

a. Although two gene clusters are encoded, they were considered as a hybrid PKS/NRPS gene cluster. Consequently, the presence of mirubactin-biosynthetic gene cluster will not be noticed.

b. As hopene-biosynthetic gene cluster is encoded near *nrps-4*, hopene/Terpen was indicated as the Most similar known cluster although an NRPS gene cluster is present.

c. Although *pks/nrps-1* is a hybrid PKS/NRPS gene cluster, the biosynthetic gene cluster of xiamycin A, which is a terpene compound, was shown with a high similarity.

d. Even though *pks/nrps-2* is a hybrid PKS/NRPS gene cluster, the biosynthetic gene cluster of auroramycin, which is not a hybrid polyketide/nonribosomal peptide but a polyketide compound, was searched.

e. Germicidin is not 'Other' but 'Polyketide'.

f. Two independent gene cluster are at least encoded in this region although they are considered as a hybrid gene cluster by antiSMASH.

Table S2. Most similar known cluster searched by antiSMASH for the gene clusters in *S. olivaceus* DC10-5.

Gene cluster	Most similar known cluster		Similarity
<i>t1pks-1</i>	linfuranones B & C	Polyketide	46 %
<i>nrps-1</i>	coelichelin	NRP	100 %
<i>nrps-2</i>	cyclomarin D	NRP	8 %
<i>t1pks-2</i> ^a <i>nrps-3</i> ^a	divergolides A, B, C & D	Polyketide: Modular type I	96 %
<i>nrps-4</i> ^b	hopene	Terpene	92 %
<i>nrps-5</i>	nogalamycin	Polyketide	40 %
<i>nrps-6</i>	diisonitrile antibiotic SF2768	NRP	55 %
<i>t1pks-3</i>	arsono-polyketide	Polyketide	100%
<i>pks/nrps-1</i>	xiamycin A	Terpene ^c	72 %
<i>t2pks-1</i> ^g <i>nrps-7</i> ^g	olimycins A & B	Polyketide	100 %
<i>t2pks-2</i>	spore pigment	Polyketide	85 %
<i>nrps-8</i>	ishigamide	NRP + Polyketide ^h	27 %
<i>pks/nrps-3</i>	rimosamide	NRP	21 %
<i>t3pks-1</i>	herboxidiene	Polyketide	8 %
<i>t3pks-2</i>	germicidin	Other ^e	100 %
<i>pks/nrps-4</i> ^f <i>t1pks-5</i> ^f	lobophorin A	Polyketide	91 %

Footnotes are the same in Table S1.

g. Although this region was considered as a hybrid PKS/NRPS gene cluster by antiSMASH, two independent gene cluster are present.

h. Although ishigamide- biosynthetic gene cluster encodes NRPSs and PKSs, *nrps-8* does not encode any PKSs.

Table S3. Closest biosynthetic enzymes to PKSs and/or NRPSs in the gene clusters of *S. olivaceus* N11-26.

Gene cluster	ORF encoding PKS or NRPS (Domain organization) ^a	Closest biosynthetic enzyme (Domain organization) ^b	Product ^c	Similarity (I/P, %) ^d
<i>t1pks-1</i>	TPA0906_11330 (KS AT _m ACP KS AT _m DH KR ACP KS AT _{mm} KR ACP)	ORF 3 ^e (KS AT _m ACP KS AT _{mm} DH KR ACP KS AT _{mm} KR ACP)	E-837	47/57
	TPA0906_11340 (KS AT _m ACP KS AT _{mm} DH KR ACP KS AT _m DH KR ACP KS AT _{mm} KR ACP)	ORF 4 ^f (KS AT _m DH KR ACP KS AT _{mm} DH KR ACP)		47/58
	TPA0906_11310 (KS AT _m DH ER KR ACP KS AT _{mm} DH KR ACP)	ORF 6 ^g (KS AT _m DH KR ACP KS AT _{mm} KR ACP)		53/64
	TPA0906_11300 (KS AT _m ACP TE)	ORF 7 ^h (KS AT _{mm} KR ACP TE)		53/62
<i>nrps-1</i>	TPA0906_09680 (A PCP E C A _{thr} PCP E C A PCP)	SCO0492 (A _{orn} PCP E C A _{thr} PCP E C A _{orn} PCP)	coelichelin	82/87
<i>t1pks-2</i>	TPA0906_04350 (CoL KR ACP KS AT _{mm} DH KR ACP KS AT _m ACP KS AT _m KR ACP)	DivK (CoL KR ACP KS AT _{mm} DH KR ACP KS AT _m ACP KS AT _m KR ACP)	divergolides A to D	99/99
	TPA0906_04360 (KS AT _{em} DH ER KR ACP)	DivL1 (KS AT _{em} DH ER KR ACP)		99/99
	TPA0906_04370 (KS AT _m DH KR ACP)	DivL2 (KS AT _m DH KR ACP)		99/99
	TPA0906_04380 (KS AT DH ER KR ACP)	DivL3 (KS AT DH ER KR ACP)		98/98
	TPA0906_04390 (KS AT _{mm} ACP KS AT _m DH KR ACP)	DivM (KS AT _{mm} ACP KS AT _m DH KR ACP)		99/99
<i>nrps-3</i>	TPA0906_04020 (C A PCP E C A PCP E C)	Amir_2719 (C A PCP E C A PCP E C)	mirubactin	60/68
<i>nrps-4</i>	TPA0906_03310 (PCP C A PCP C A _{cys} PCP)	SCO7682 (PCP C A _{arg} PCP C A _{cys} PCP)	coelibactin	82/85
	TPA0906_03320 (C A _{cys} MT PCP TE)	SCO7683 (C A _{cys} MT PCP TE)		87/91
<i>nrps-5</i>	TPA0906_13190 (C A _{val} PCP TE)	- ⁱ	-	-
<i>nrps-6</i>	TPA0906_14110 (A)	SfaB (A)	SF2768	75/83
	TPA0906_14100 (PCP)	SfaC (PCP)		62/77
	TPA0906_14090 (C A PCP TD)	SfaD (C A PCP TD)		65/74
<i>pks/nrps-1</i>	TPA0906_17130 (KS AT DH KR ACP C A _{orn} PCP TE)	PtmA (KS AT DH KR ACP C A _{orn} PCP TE)	pactamides	98/98
<i>nrps-7</i>	TPA0906_17860 (C A _{orn} PCP C A _{orn} PCP)	-	-	-

	C A _{om} PCP)			
<i>pks/nrps-2</i>	TPA0906_18230 (PCP C A PCP)	-	-	-
	TPA0906_18220 (ACP KS AT _m)	-		-
	TPA0906_18200 (A _{pro} PCP)	-		-
<i>t2pks-2</i>	TPA0906_23390 (KS α)	AAG26879.1 (KS α)	spore pigment	78/84
	TPA0906_23390 (KS β)	AAG26880.1 (KS β)		75/83
	TPA0906_23390 (ACP)	AAG26884.1 (ACP)		55/69
<i>t1pks-4</i>	TPA0906_62330 (KS AT _{mm} ACP KS AT _{mm} DH ER KR ACP)	APK71_RS29920 (AT _{mm} ACP KS AT _{mm} DH ER KR ACP KS AT _m KR ACP KS AT _m DH KR ACP)	butyrolactol A	50/58
	TPA0906_62340 (KS AT _{mm} DH KR ACP)	APK71_RS29940 (KS AT _m DH KR ACP KS AT _m DH KR ACP)		47/57
	TPA0906_62350 (KS AT _{mm} DH ER KR APC KS KR ACP)	APK71_RS29945 (KS AT DH ER KR ACP KS KR ACP)		57/66
	TPA0906_62360 (KS AT _m KR ACP KS AT _m KR ACP)	APK71_RS29950 (KS AT _m KR ACP KS AT _m KR ACP)		65/74
	TPA0906_62370 (KS DH KR ACP)	APK71_RS29955 (KS DH KR ACP)		63/72
<i>pks/nrps-3</i>	TPA0906_63450 (C A _{val} PCP TE)	RmoH ^j (C A _{val} PCP TE)	rimosamide	58/69
	TPA0906_63440 (A PCP C A _{pro} PCP KS KR ACP TE)	RmoI ^k (A _{ile} PCP C A _{pro} PCP KS KR ACP TE)		61/69
<i>t3pks-1</i>	TPA0906_64630 (KS)	SCO1206 (KS)	flaviolin <i>etc.</i> ¹	90/95
<i>t3pks-2</i>	TPA0906_72820 (KS)	germicidins A and B synthase ^m (KS)	germicidins A & B	100/100
<i>pks/nrps-4</i>	TPA0906_73770 (KS AT _m ACP KS AT _{mm} DH KR ACP KS AT _{mm} KR ACP KS AT _{mm} DH ER KR ACP)	TotA1 (KS AT _m ACP KS AT _{mm} DH KR ACP KS AT _{mm} KR ACP KS AT _{mm} DH ER KR ACP)	totopotensamides A & B	98/98
	TPA0906_73780 (KS AT _{mm} DH ER KR ACP KS AT _m KR ACP)	TotA2 (KS AT _{mm} DH ER KR ACP KS AT _m KR ACP)		98/98
	TPA0906_73810 (C A _{thr} PCP C A _{ala} PCP C PCP C A _{dhb} PCP C A PCP C A PCP TE)	TotA3 (C A _{thr} PCP C A _{ala} PCP C PCP C A _{dhb} PCP C A PCP C A PCP TE)		98/98
<i>t1pks-5</i>	TPA0906_74290 (KS AT ACP)	LobS1 (KS AT ACP)	lobophorin A	99/99

KS AT _{mm} DH KR ACP	KS AT _{mm} DH KR ACP	
KS AT DH KR ACP	KS AT DH KR ACP	
KS AT _{mm} DH KR ACP)	KS AT _{mm} DH KR ACP)	
TPA0906_74280	LobS2	97/97
(KS AT _m DH KR ACP	(KS AT _{mm} DH KR ACP	
KS AT _{mm} DH KR ACP	KS AT _m DH KR ACP	
KS AT _m DH KR ACP	KS AT _m DH KR ACP	
KS AT _m DH KR ACP)	KS AT _m DH KR ACP)	
TPA0906_74270	LobS3	87/89
(KS AT _{mm} DH KR ACP)	(KS AT _{mm} DH KR ACP)	
TPA0906_74260	LobS5	97/97
(KS AT _m ACP)	(KS AT _m ACP)	
TPA0906_74140	LobS4	96/96
(KS AT DH ER KR ACP	(KS AT DH ER KR ACP	
KS AT _{mm} DH KR ACP)	KS AT _{mm} DH KR ACP)	

Abbreviations of domains are as follows: A, adenylation; A_{xxx}, adenylation domain incorporating the amino acid shown in subscript three code letter; ACP, acyl carrier protein; AT, acyltransferase; AT_{em}, AT incorporating ethylmalonyl-CoA; AT_m, AT incorporating malonyl-CoA; AT_{mm}, AT incorporating methylmalonyl-CoA; C, condensation; CoL, CoA ligase; DH, dehydratase; E, epimerase; ER, enoyl reductase; KS, ketoacylsynthase; KR, ketoreductase; MT, methyltransferase; PCP, peptidyl carrier protein; TD, termination; TE, thioesterase.

- ORFs are indicated by locus tags. Domain organizations were predicted by antiSMASH.
- Not orphan but biosynthetic enzyme whose products were elucidated are shown by the name, locus tag or accession number. Domain organizations predicted by antiSMASH are indicated.
- product of the closest biosynthetic gene cluster
- I/P, identities/positives in amino acid sequences.
- ABB88519
- ABB88520
- ABB88522
- ABB88523
- , N/A (no close enzyme with high sequence similarity)
- SRIM_RS28565
- SRIM_RS28570
- flaviolin and 1,3,6,8-tetrahydroxynaphthalene
- CCA62437

Table S4. Closest biosynthetic enzymes to PKSs and/or NRPSs in the gene clusters of *S. olivaceus* DC10-5.

Gene cluster	ORF encoding PKS or NRPS (Domain organization) ^a	Closest biosynthetic enzyme (Domain organization) ^b	Product ^c	Similarity (I/P, %) ^d
<i>t1pks-1</i>	TPA0905_20000 (AT _m ACP KS AT _m DH KR ACP KS AT _{mm} KR ACP)	ORF 3 ^e (KS AT _m ACP KS AT _{mm} DH KR ACP KS AT _{mm} KR ACP)	E-837	46/56
	TPA0905_19990 (KS AT _m ACP KS AT _{mm} DH KR ACP KS AT _m DH KR ACP KS AT _{mm} KR ACP)	ORF 4 ^f (KS AT _m DH KR ACP KS AT _{mm} DH KR ACP)		47/58
	TPA0905_20030 (KS AT _m DH ER KR ACP KS AT _{mm} DH KR ACP)	ORF 6 ^g (KS AT _m DH KR ACP KS AT _{mm} KR ACP)		53/64
	TPA0905_20040 (KS AT _m ACP TE)	ORF 7 ^h (KS AT _{mm} KR ACP TE)		53/62
<i>nrps-1</i>	TPA0905_21720 (A _{orn} PCP E C A _{thr} PCP E C A _{orn} PCP)	SCO0492 (A _{orn} PCP E C A _{thr} PCP E C A _{orn} PCP)	coelichelin	83/87
<i>nrps-2</i>	TPA0905_26970 (C A _{thr} PCP C A PCP C A _{pro} PCP C A _{phe} PCP C A _{tyr} MT PCP C A _{val} PCP TE)	SpnA ⁿ (C A PCP C A _{thr} PCP C A PCP C A _{pro} PCP C A _{phe} PCP C A _{tyr} MT PCP C A _{val} PCP TE)	streptopectolin	87/91
<i>t1pks-2</i>	TPA0905_27620 (CoL KR ACP KS AT _{mm} DH KR ACP KS AT _m ACP KS AT _m KR ACP)	DivK (CoL KR ACP KS AT _{mm} DH KR ACP KS AT _m ACP KS AT _m KR ACP)	divergolides A to D	98/98
	TPA0905_27610 (KS AT _{em} DH ER KR ACP)	DivL1 (KS AT _{em} DH ER KR ACP)		97/98
	TPA0905_27600 (KS AT _m DH KR ACP)	DivL2 (KS AT _m DH KR ACP)		97/97
	TPA0905_27590 (KS AT DH ER KR ACP)	DivL3 (KS AT DH ER KR ACP)		96/97
	TPA0905_27580 (KS AT _{mm} ACP KS AT _m DH KR ACP)	DivM (KS AT _{mm} ACP KS AT _m DH KR ACP)		98/99
<i>nrps-3</i>	TPA0905_27950 (C A PCP E C A PCP E C)	Amir_2719 (C A PCP E C A PCP E C)	mirubactin	61/68
<i>nrps-4</i>	TPA0905_28750 (PCP C A PCP C A _{cys} PCP)	SCO7682 (PCP C A _{arg} PCP C A _{cys} PCP)	coelibactin	81/85
	TPA0905_28740 (C A _{cys} MT PCP TE)	SCO7683 (C A _{cys} MT PCP TE)		87/91
<i>nrps-5</i>	TPA0905_31870 (C A _{val} PCP TE)	-	-	-
<i>nrps-6</i>	TPA0905_32610 (A)	SfaB (A)	SF2768	75/84

	TPA0905_32600 (PCP)	SfaC (PCP)		64/77
	TPA0905_32590 (C A PCP TD)	SfaD (C A PCP TD)		65/73
<i>t1pks-3</i>	TPA0905_36560 (KS AT _{mm} DH ER KR ACP ACP)	SLI_1088 (KS AT _{mm} DH ER KR ACP ACP)	arsono-polyketide	83/88
<i>pks/nrps-1</i>	TPA0905_37460 (KS AT DH KR ACP C A _{orn} PCP TE)	PtmA (KS AT DH KR ACP C A _{orn} PCP TE)	pactamides	99/99
<i>t2pks-1</i>	TPA0905_38360 (KS α)	RslK3 (KS α)	rishirilide B	93/94
	TPA0905_38350 (KS β)	RslK2 (KS β)		89/92
	TPA0905_38340 (ACP)	RslK1 (ACP)		85/94
<i>nrps-7</i>	TPA0905_38170 (C A PCP C A PCP C A PCP)	-	-	-
<i>t2pks-2</i>	TPA0905_44220 (KS α)	AAG26879.1 (KS α)	spore pigment	81/87
	TPA0905_44220 (KS β)	AAG26880.1 (KS β)		75/83
	TPA0905_44220 (ACP)	AAG26884.1 (ACP)		55/70
<i>nrps-8</i>	TPA0905_46660 (C A PCP E C PCP)	-	-	-
	TPA0905_46650 (C A _{phe} PCP C A _{gly} PCP TE)	-		-
<i>pks/nrps-3</i>	TPA0905_63960 (C A PCP TE)	RmoH ^j (C A _{val} PCP TE)	rimosamide	58/69
	TPA0905_63950 (A PCP C A _{pro} PCP KS KR ACP TE)	RmoI ^k (A _{ile} PCP C A _{pro} PCP KS KR ACP TE)		61/69
<i>t3pks-1</i>	TPA0905_65120 (KS)	SCO1206 (KS)	flaviolin <i>etc.</i> ¹	90/94
<i>t3pks-2</i>	TPA0905_72620 (KS)	germicidins A and B synthase ^m (KS)	germicidins A & B	99/100
<i>pks/nrps-4</i>	TPA0905_73570 (KS AT _m ACP KS AT _{mm} DH KR ACP KS AT _{mm} KR ACP KS AT _{mm} DH ER KR ACP)	TotA1 (KS AT _m ACP KS AT _{mm} DH KR ACP KS AT _{mm} KR ACP KS AT _{mm} DH ER KR ACP)	totopotensamides A & B	99/99
	TPA0905_73580 (KS AT _{mm} DH ER KR ACP KS AT _m KR ACP)	TotA2 (KS AT _{mm} DH ER KR ACP KS AT _m KR ACP)		99/98
	TPA0905_73610 (C A _{thr} PCP C A PCP C PCP C A PCP C A PCP C A _{ser} PCP TE)	TotA3 (C A _{thr} PCP C A _{ala} PCP C PCP C A _{dhb} PCP C A PCP C A PCP TE)		99/99

<i>t1pks-5</i>	TPA0905_74080 (KS AT ACP KS AT _{mm} DH KR ACP KS AT DH KR ACP KS AT _{mm} DH KR ACP)	LobS1 (KS AT ACP KS AT _{mm} DH KR ACP KS AT DH KR ACP KS AT _{mm} DH KR ACP)	lobophorin A	97/97
	TPA0905_74070 (KS AT _m DH KR ACP KS AT _{mm} DH KR ACP KS AT _m DH KR ACP KS AT _m DH KR ACP)	LobS2 (KS AT _{mm} DH KR ACP KS AT _m DH KR ACP KS AT _m DH KR ACP KS AT _m DH KR ACP)		94/95
	TPA0905_74060 (KS AT _{mm} DH KR ACP)	LobS3 (KS AT _{mm} DH KR ACP)		84/87
	TPA0905_74050 (KS AT _m KR ACP)	LobS5 (KS AT _m ACP)		95/95
	TPA0905_74930 (KS AT DH ER KR ACP KS AT _{mm} DH KR ACP)	LobS4 (KS AT DH ER KR ACP KS AT _{mm} DH KR ACP)		93/94

Footnotes are the same in Table S3.

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