

A-domain*	substrate †	236	239	278	299	301	322	330	331	organism	Natural Product
		202	205	244	272	274	298	306	307		
		204	207	246	274	276	300	308	309		
WP_052174032.1 (2)	Apd1,2,4,5,6	V	W	C	G	G	L	L	V	<i>Streptomyces scabrisporus</i>	unknown
WP_050486890.1 (2)	Apd1,2,4,5,6	V	W	C	S	G	L	L	V	<i>Streptomyces</i> sp. CNS654	unknown
WP_051836849.1 (2)	Apd1,2,4,5,6	V	W	C	G	G	L	L	V	<i>Streptomyces</i> sp. NRRL WC-3742	unknown
WP_037678228.1 (2)	Apd1,2,4,6	V	M	T	G	G	C	M	A	<i>Streptomyces catenulae</i>	unknown
WP_040888422.1 (2)	Apd1,2,4,6	V	M	T	G	G	C	M	A	<i>Streptomyces mobaraensis</i>	unknown
KUN18767.1 (2)	Apd1,2,3,4,6	V	M	T	G	G	C	M	A	<i>Streptomyces antibioticus</i> DSM 40234	unknown
EHM24066.1	Apd1,2,6	T	F	N	A	G	Y	L	A	<i>Streptomyces</i> sp.W007	unknown
WP_051187885.1 (1)	Apd1,2,6	A	Y	S	T	G	T	L	C	<i>Nocardia tenerifensis</i> II	unknown
WP_036391166.1	Apd1,2,4,6	V	Q	F	A	A	E	I	I	<i>Micromonospora chokoriensis</i>	unknown
WP_030677493.1	Apd1,2,6	V	Q	F	N	A	H	M	V	<i>Streptomyces</i> sp. NRRL B-1347	unknown
HrmP (3)	DH-PPL <sub>h</sub>	V	Q	F	S	A	H	G	A	<i>Streptomyces griseoflavus</i>	Hormaomycin
GrsB (1)	Pro	V	Q	S	I	A	H	V	V	<i>Bacillus brevis</i>	Gramicidin-S
TycB1 (1)	Pro	V	Q	S	I	A	H	V	V	<i>Bacillus brevis</i>	Tyrocidine
FenA (1)	Pro	V	Q	V	I	A	H	V	V	<i>Bacillus subtilis</i>	Fengycin
MycB (4)	Pro	V	Q	F	I	A	H	V	V	<i>Bacillus subtilis</i>	Mycosubtilin
ItuB (4)	Pro	V	Q	F	I	A	H	V	V	<i>Bacillus subtilis</i>	Iturin A
Pps4 (1)	Pro	V	Q	F	I	A	H	V	V	<i>Bacillus subtilis</i>	Plipastatin
SypA (2)	Pro	V	Q	Y	I	A	H	V	V	<i>Pseudomonas syringae</i>	Syringopeptin
PuwA (2)	Pro	V	Q	F	M	A	Q	V	V	<i>Cylindrospermum alatosporum</i>	Puwanaphycins
MchC (2)	Pro	A	Q	F	I	A	Q	V	A	<i>Stigmatella aurantiaca</i>	Myxochromides S1-3
NosD (2)	Pro	V	Q	F	I	A	H	V	I	<i>Nostoc</i> sp. GSV224	Nostopeptolide A
NcpB (3)	mePro	V	Q	F	I	A	H	V	A	<i>Nostoc</i> sp. ATCC 53789	Nostocyclopeptide A
NosA (3)	mePro	V	Q	F	I	A	H	L	A	<i>Nostoc</i> sp. GSV224	Nostopeptolide A
CipA (2)	Pro	V	Q	Y	V	A	H	V	T	<i>Pseudomonas cichorii</i> SF1-54	Cichoheptins
PstD (2)	Pro	V	Q	Y	V	A	H	V	V	<i>Actinoplanes friuliensis</i>	Friulimycin
LpmD (2)	Pro	V	Q	Y	I	A	H	V	V	<i>Streptomyces viridochromogenes</i>	Laspartomycin
ACMSIII (1)	Pro	V	Q	F	A	A	H	V	L	<i>Streptomyces iakyrus</i>	Actinomycins
AcmC (1)	Pro	V	Q	F	A	A	H	V	V	<i>Streptomyces chrysomallus</i>	Actinomycins
Sky30 (2)	Pro	V	Q	Y	A	A	H	V	V	<i>Streptomyces</i> sp.	Skyllamycin
SnbDE (1)	Pro	V	Q	Y	A	A	H	V	M	<i>Streptomyces pristinaespiralis</i>	pristinamycin I(A)
WP_037773348.1	DH-EPL?	V	M	Y	A	V	M	L	A	<i>Streptomyces sclerotialis</i>	LIM
Lim2	DH-EPL	V	M	Y	A	V	M	L	A	<i>Streptomyces</i> sp. ICBB 8177	Limazepines
TomB	DH-EPL	V	M	Y	T	V	M	L	A	<i>Streptomyces achromogenes</i>	Tomaymycin
WP_019884141.1	DH-EPL	V	M	Y	T	V	M	L	A	<i>Streptomyces purpureus</i>	TOM
WP_061926494.1	DH-EPL?	V	M	Y	T	V	M	L	A	<i>Streptomyces bungoensis</i>	TOM
WP_053671522.1	DH-EPL?	V	M	Y	T	V	M	L	A	<i>Streptomyces</i> sp. NRRL B-1140	TOM
KOG74888.1	DH-EPL?	V	M	Y	T	V	M	L	A	<i>Streptomyces antibioticus</i> NRRL B-2032	TOM
OQD56811.1	DH-EPL?	V	M	Y	T	V	M	L	A	<i>Streptomyces phaeoluteigriseus</i>	TOM
KMS87275.1	DH-EPL?	V	M	Y	T	V	M	L	A	<i>Streptomyces regensis</i>	TOM
NpsB	Pro	V	Q	Y	Y	T	L	V	C	<i>Klebsiella oxytoca</i>	Tilivalline
SEG83667.1	2C APD?	V	Q	Y	Y	T	I	L	C	<i>Actinomadura echinospora</i>	SIB
WP_040694105.1	DH-PPL?	V	L	F	Y	T	A	W	C	<i>Nocardioopsis prasina</i>	SIB
WP_047312981.1	2C APD?	V	E	F	Y	T	V	L	C	<i>Dermacoccus</i> sp. PE3	SIB
WP_073789160.1	DH-PPL?	V	E	F	Y	T	A	L	C	<i>Streptomyces uncialis</i>	SIB
SCK09874.1	DH-PPL?	V	E	F	Y	T	A	L	C	<i>Streptomyces</i> AmelKG-E11A	SIB
WP_071803261.1	DH-PPL?	V	M	F	C	T	A	L	V	<i>Couchioplanes caeruleus</i>	SIB
SCF39935.1	DH-PPL?	V	M	F	C	T	A	L	V	<i>Micromonospora echinospora</i>	SIB
SibD	DH-PPL	V	M	F	Y	T	A	L	V	<i>Streptosporangium sibiricum</i>	Sibiromycin
ORF22	DH-PPL	V	L	Y	Y	T	A	L	V	<i>Streptomyces refuineus</i>	Anthramycin
WP_014985045.1	DH-PPL?	V	L	Y	Y	T	A	L	C	<i>Nocardia brasiliensis</i>	ANT
WP_040743488.1	DH-PPL?	V	I	Y	Y	T	A	L	C	<i>Nocardia tenerifensis</i> I	ANT
WP_018681051.1	DH-PPL?	V	I	F	Y	T	A	L	C	<i>Actinokineospora enzanensis</i>	ANT
WP_043667671.1	DH-PPL?	V	L	Y	Y	T	A	L	C	<i>Nocardia vulneris</i>	ANT
WP_033289433.1	DH-PPL?	V	L	Y	Y	T	A	L	C	<i>Amycolatopsis jejuensis</i>	POR
Por21	DH-PPL	V	L	Y	Y	T	A	L	C	<i>Streptomyces albus</i>	Porothramycin
LmbC	PPL	V	A	L	V	A	I	G	C	<i>Streptomyces lincolnensis</i>	Lincomycin
CcbC	Pro	V	F	Y	C	A	L	V	C	<i>Streptomyces caelestis</i>	Celesticetin
AnaC (O)	Pro	L	F	Y	L	A	L	V	C	<i>Oscillatoria</i> PCC 6506	Anatoxin-a
AnaC (A)	Pro	L	F	Y	L	A	L	V	C	<i>Anabaena</i> sp.	Anatoxin-a
RedM	Pro	L	F	Y	L	A	L	V	C	<i>Streptomyces coelicolor</i>	Undecylprodigiosin
RphM	Pro	L	F	Y	L	A	L	V	C	<i>Streptomyces griseoviridis</i>	Prodigiosin
MarM	Pro	L	F	Y	L	A	L	V	C	<i>Streptomyces</i> sp. CNQ-617	Marineosins
HrmK	Pro	L	F	Y	A	A	L	V	C	<i>Streptomyces griseoflavus</i>	Hormaomycin
Pyr8	Pro	L	F	Y	I	A	W	V	C	<i>Streptomyces vitaminophilus</i>	Pyrrrolomycin
Pigl	Pro	L	F	Y	T	A	W	V	C	<i>Serratia marcescens</i>	Prodigiosin
Hapl	Pro	L	F	Y	I	A	F	V	C	<i>Hahella chejuensis</i>	Prodigiosin
Bmp4	Pro	L	F	Y	I	A	F	V	C	<i>Pseudoalteromonas</i> sp. PS5	Tetrabromopyrrole
NgnN4	Pro	L	L	Y	L	A	L	V	C	<i>Nocardia</i> sp.	Nargenicin A(1)
IdmJ	Pro	L	L	Y	L	A	L	V	C	<i>Streptomyces antibioticus</i>	Indanomycin
CalN2	Pro	L	L	Y	L	A	L	V	C	<i>Streptomyces chartreusis</i>	Calcimycin
CouN4	Pro	L	L	Y	L	A	L	V	C	<i>Streptomyces rishiriensis</i>	Coumermycin A1
CloN4	Pro	L	L	Y	L	A	L	V	C	<i>Streptomyces roseochromogenes</i>	Clorobiocin
DkxA (S)	Pro	L	L	Y	L	A	L	V	C	<i>Stigmatella aurantiaca</i>	Dkxanthenes
DkxA (M)	Pro	L	L	Y	L	A	L	V	C	<i>Myxococcus xanthus</i>	Dkxanthenes
Leu5	Pro	L	L	Y	L	A	L	V	C	<i>Sorangium cellulosum</i>	Leupyrrins
PITF	Pro	L	L	Y	L	A	L	V	C	<i>Pseudomonas fluorescens</i>	Pyoluteorin

Figure S1. Comparison of the nonribosomal codes of A-domains activating L-proline and L-proline derivatives. The highly conserved D and K residues at the boundaries of nonribosomal codes are omitted. The same set of A-domains is shown in phylogenetic tree in Figure 10. Amino acids are numbered at the top according to the A-domain of GrsA (PheA) (first row), CcbC (second row), and LmbC (third row). Residues of stand-alone A-domains in accordance with consensus of L-proline-specific stand-alone A-domains are in blue. Residues of modular A-domains in accordance with consensus of L-proline-specific modular A-domains are in red. \*Names of NRPSs obtained by the genome mining are represented by the GenBank accession number; number in parentheses behind the name of NRPS denotes the order of the A-domain in NRPS protein chain, if relevant; letter in parentheses denotes the source organism. †mePro – 4-methyl-L-proline; putative substrates of ten A-domains obtained by the genome mining are represented by the respective set of the APD biosynthetic proteins, the predicted products of these protein sets are presented in main text Table 1.