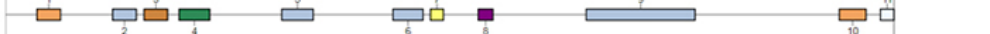


A

Region	Type	From	To	Most similar known cluster		Similarity	MIBIG BGC-ID
The following regions are from record MPLE01000001.1 (<i>Streptomyces viridifaciens</i>):							
							
Region 1	T3pks	55019	96101	Actinomycin	NRPS	10%	BGC0000296
Region 2	Lanthipeptide - Nrpsfragment	186747	228158	Viomycin	NRPS	9%	BGC0000458
Region 3	Arylpolyene	241651	282784	WS9326	NRPS	5%	BGC0001297
Region 4	Nrps	302617	356025				
Region 5	Nrps - Nucleoside	481446	536185	Tunicamycin	other	42%	BGC0000880
Region 6	T1pks - Nrps	675210	727626	Oxazolomycin	hybrid	15%	BGC0001106
Region 7	Lanthipeptide	740507	763068				
Region 8	Terpene	823523	849476	Carotenoid	terpene	45%	BGC0000633
Region 9	Nrps - T1pks	1011856	1201449	Candidicin	polyketide	76%	BGC0000034
Region 10	T1pks	1452695	1499210				
Region 11	Blactam	1524280	1547868	Clavams	other	64%	BGC0001151

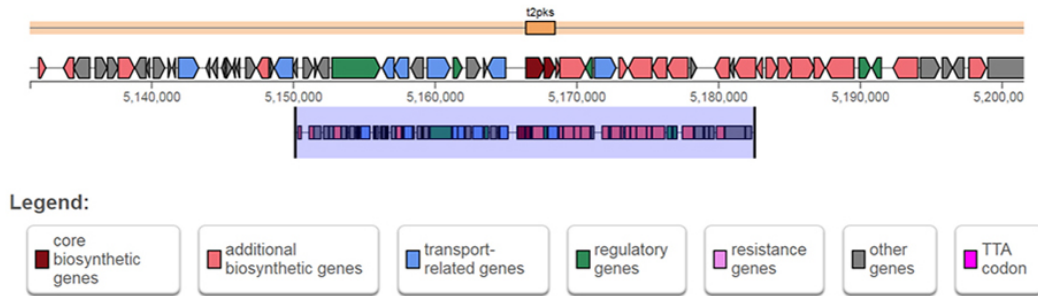
B

Region	Type	From	To	Most similar known cluster	Similarity	MiBIG BGC-ID
The following regions are from record MPLE01000004.1 (Streptomyces viridifaciens)						
Region 1	Nrps	43540	90359	Capreomycin	9%	BGC0000316
Region 2	Terpene	211185	230997			
Region 3	Nrps	340765	421797	Lipopeptide 8D1-1 / lipopeptide 8D1-2	15%	BGC0001370
Region 4	Nrpsfragment	596569	638812	Meilingmycin	4%	BGC0000093
Region 5	T2pks	683975	754674	Spore pigment	83%	BGC0000271
Region 6	Terpene	966842	986462	Acarviostatin	11%	BGC0000804
Region 7	Terpene	996986	1021419	Hopene	61%	BGC0000683
Region 8	Siderophore	1241877	1255028			
Region 9	Nrpsfragment	1418560	1460286			
Region 10	Others	1515975	1556086	Kijanamicin	4%	BGC0000082
Region 11	Nrpsfragment - T1pks	1626509	1677101	Vancomycin	17%	BGC0000455
Region 12	Nrps	1684526	1779221	Frulimicin	24%	BGC0000354
Region 13	Bacteriocin	2007281	2017303			
Region 14	Nrps - Betalactone	2064569	2142082	Lomaiviticin	6%	BGC0000240
Region 15	Siderophore	2274617	2287884			
Region 16	Nrps	2453955	2507665	Teleocidin B	50%	BGC0001085
Region 17	Lap	3307340	3330204			
Region 18	Nrps	3378027	3430494	Skylamycin	20%	BGC0000429
Region 19	Terpene	3760799	3781772	Geosmin	100%	BGC0001181
Region 20	Butyrolactone	4138981	4149459	Pristinamycin	3%	BGC0000952
Region 21	Thiopeptide - Lap	5051227	5080751			
Region 22	T2pks	5131444	5203500	Chlortetracycline	88%	BGC0000209
Region 23	T3pks	5550533	5589534	Herboxidiene	2%	BGC0001065
Region 24	Bacteriocin - Butyrolactone	5660652	5680142	Methylenomycin	28%	BGC0000914
Region 25	Lanthipeptide	6078936	6101773	A54145	5%	BGC0000291
Region 26	T3pks	6112996	6154051	Naringenin	100%	BGC0001310
Region 27	Nrps - T1pks	6284704	6457666	Gobichelin	27%	BGC0000366
Region 28	Nrps - Others	6461811	6548854			
Region 29	Nrpsfragment	6790211	6831191			
Region 30	Nrps	7128111	7192080	Cyclomarin	8%	BGC0000333
Region 31	Terpene	7457995	7479215	2-methylisoborneol	100%	BGC0000658
Region 32	Siderophore	7480413	7493514			
Region 33	Nrpsfragment	7706433	7750347	Herboxidiene	3%	BGC0001065

Figure S1. AntiSMASH 5.0 output revealing the biosynthetic gene clusters contained on the megaplasmid (top) and chromosome (bottom) of *K. viridifaciens*. The biosynthetic gene clusters are numbered according to their localization on the replicon.

Figure S2

A



B

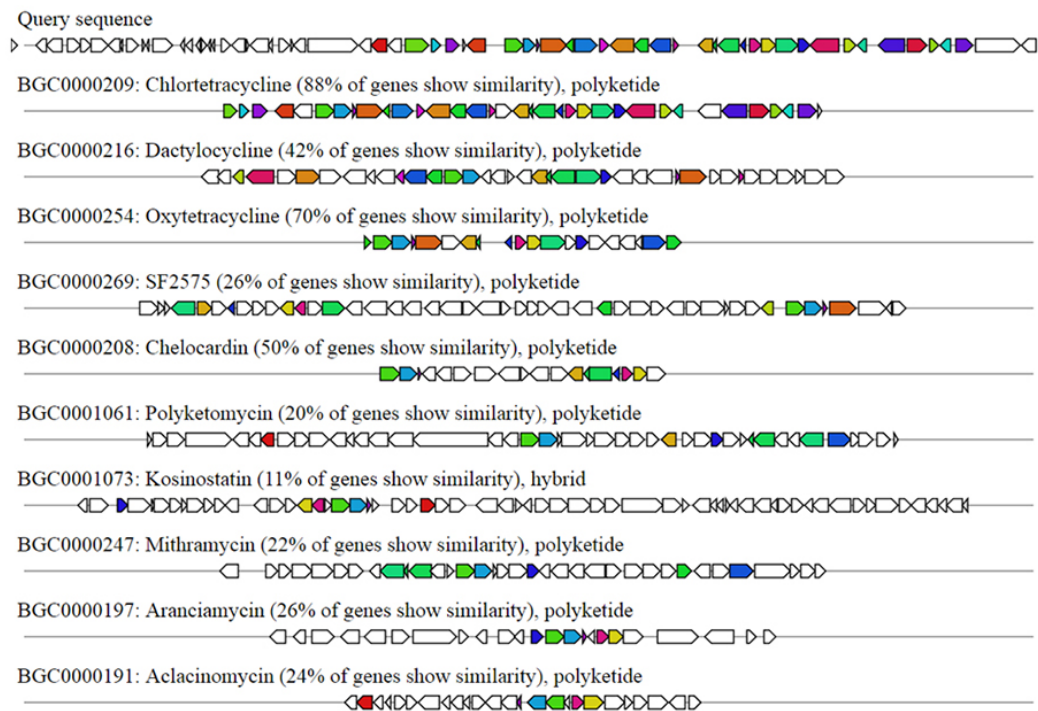


Figure S2. AntiSMASH 5.0 homology search of the *K. viridifaciens* tetracycline biosynthetic gene cluster. (A) Localization of the putative chlorotetracycline BGC in the chromosome of *K. viridifaciens*. (B) Comparison of the *K. viridifaciens* tetracycline biosynthetic gene cluster with known tetracycline gene clusters from *Streptomyces aureofaciens* (BGC0000209), *Dactylosporangium* sp. SC14051 (BGC0000216), *Streptomyces rimosus* (BGC0000254), *Streptomyces* sp. SF2575 (BGC0000269), *Amycolatopsis sulphurea* (BGC0000208), *Streptomyces diastatochromogenes* (BGC0001061), *Micromonospora* sp. TP-A0468 (BGC0001073), *Streptomyces argillaceus* (BGC0000247), *Streptomyces echinatus* (BGC0000197) and *Streptomyces galilaeus* (BGC0000191).

Figure S3

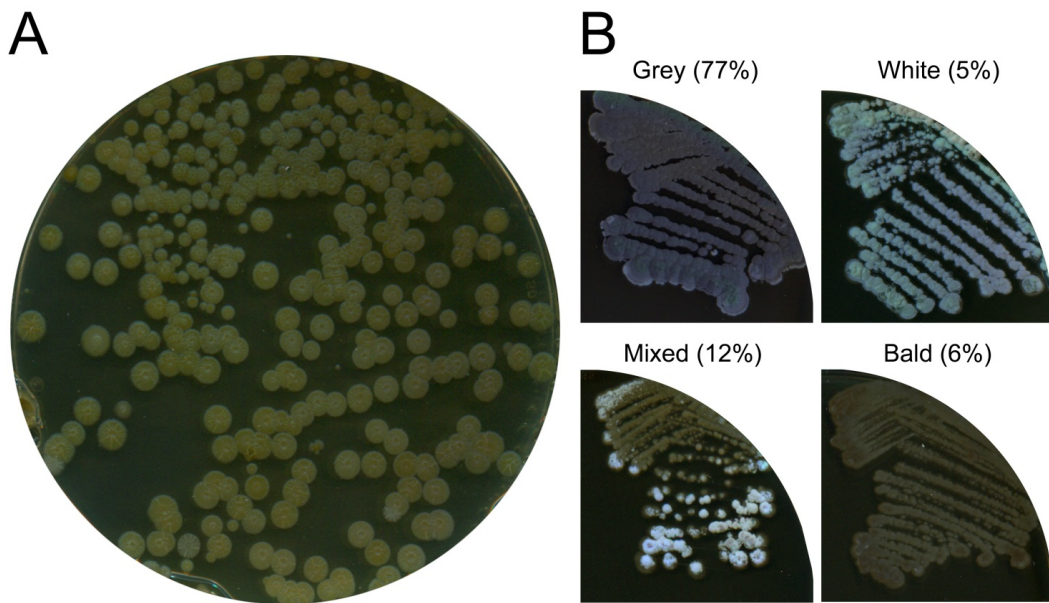


Figure S3. Protoplast regeneration generates morphological diversity in osmotically balanced medium. (A) Protoplasts regenerated on R5 medium yielded colonies that are unable to sporulate due to the high sucrose levels. (B) Subculturing of 149 randomly-picked colonies on MYM medium revealed dramatic developmental defects in 23% of the colonies. Whereas 77% of the colonies were able to form grey-pigmented sporulating colonies (similar to the wild-type), 5% of the colonies were white, 6% were bald, while 12% had a mixed appearance.