

Modulation of Multiple Gene Clusters' Expression by the PAS-LuxR Transcriptional Regulator PteF

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Supplementary Figures S1 and S2, Supplementary Tables S1-S4

A

Gene	Description	log ₂ FC	Mc
<i>pteG</i>	cholesterol oxidase	2.153	2.046
<i>pteR</i>	SARP-LAL transcriptional regulator	4.622	2.183
<i>pteD</i>	cytochrome P450 monooxygenase	-4.655	-2.744
<i>pteC</i>	cytochrome P450 monooxygenase	-1.829	-2.325
<i>pteB</i>	dehydrogenase	-3.135	-2.339
<i>pteA4</i>	modular polyketide synthase	-0.544	-1.278
<i>fecB</i>	ABC transporter iron (III)/siderophore-binding protein	7.537	2.946
<i>aveR</i>	LuxR-family transcriptional regulator	5.273	2.001
<i>agaB1</i>	alpha-galactosidase	-1.969	-2.907
SAVERM2273	isomerase	-6.532	-7.240
<i>olmR1</i>	LuxR-family transcriptional regulator	-1.278	-1.560
<i>htpX1</i>	heat shock protein, protease	2.935	2.503

B

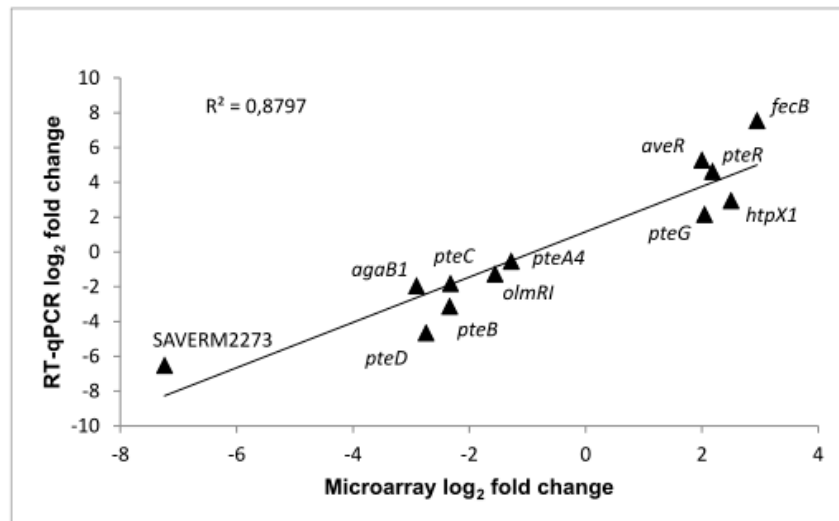


Figure S1.- Validation of microarray results using RT-qPCR. A) Comparison of the data obtained by RT-qPCR (log₂FC) and microarray analysis (Mc) for 12 different genes. B) Correlation between the results shown in panel A.

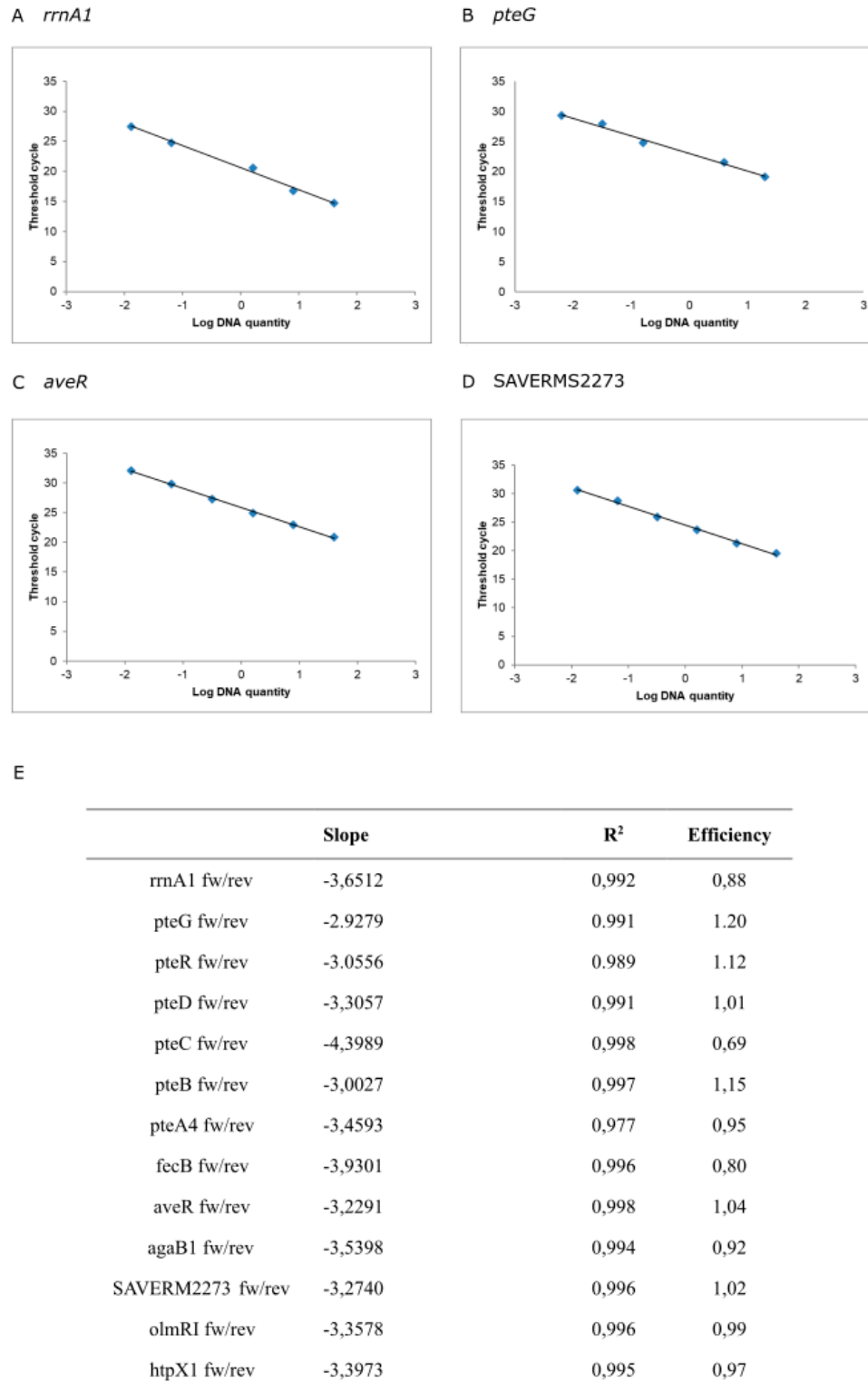


Figure S2: Primer efficiency. The efficiency of each set of primers was calculated according to the equation $E = 10^{[-1/\text{slope}] - 1}$. Using 5-fold dilutions of genomic DNA, the resulting Ct values were plotted against the logarithm of the DNA quantity as shown in A (primers for *rrnA1*), B (primers for *pteG*), C (primers for *aveR*), or D (primers for *SAVERM2273*). Data are from three replicates, values represent the mean and the vertical bars \pm SD. Panel E summarizes information obtained from all plotted data.

Table S1: Differentially expressed genes in *S. avermitilis* Δ *pteF* when compared to its parental strain. Genes are ordered firstly by functional class, secondly by reduced or enhanced transcription, and then by chromosomal position with the aim of highlighting the coincidence of profiles among clustered genes. The primary annotation source is the StrepDB server (<http://strepdb.streptomyces.org.uk>). Some genes are included in more than one functional category if they are implicated in several processes. Mc values higher than 1 and the corresponding fold-change values above 2 are in bold. The *p*-values are indicated in bold type when found statistically significant (see Materials and methods). A few genes that did not meet criteria are also included (see footnotes). For simplicity, designations “putative” have been removed.

Gene	Description	Fold change	Mc	Corrected <i>p</i> -value	<i>p</i> -value	
Genes involved in genetic information- and protein-processing, and amino acid metabolism						
t1						
2723	<i>rocA</i>	delta-1-pyrroline-5-carboxylate dehydrogenase	3,56	-1.83	0.0219	0.0005
2724	<i>putA</i>	proline dehydrogenase	2,66	-1.41	0.0095	0.0002
2795	<i>zmp4</i>	griselysin (secreted neutral zinc metalloprotease)	2,06	-1.04	0.0473	0.0014
4551		ornithine aminotransferase	3,71	-1.89	0.0166	0.0004
4561 ^a	<i>sig40</i>	RNA polymerase ECF-subfamily sigma factor	1,75	-0.81	0.1009	0.0045
4562 ^a		hypothetical protein	2,06	-1.04	0.0039	0.0000
7112	<i>rocD2</i>	ornithine aminotransferase	3,01	-1.59	0.0212	0.0005
213	<i>sig60</i>	RNA polymerase ECF-subfamily sigma factor	3,43	1.78	0.0135	0.0003
321	<i>prpB1</i>	magnesium or manganese-dependent protein phosphatase	2,99	1.58	0.0054	0.0001
459	<i>hsp18_1</i>	heat shock protein	2,30	1.20	0.0106	0.0002
692	<i>hsp18_2</i>	heat shock protein	3,81	1.93	0.0002	0.0000
703		Acetyltransferase	2,41	1.27	0.0022	0.0000
758		Acetyltransferase	2,23	1.16	0.0063	0.0001
826	<i>cspD1</i>	cold-shock protein	2,79	1.48	0.0011	0.0000
898	<i>sig10</i>	RNA polymerase ECF-subfamily sigma factor	5,82	2.54	0.0007	0.0000
997	<i>sig13</i>	RNA polymerase ECF-subfamily sigma factor	2,68	1.42	0.0071	0.0001
1061		cysteine desulfurase	6,68	2.74	0.0002	0.0000
1986	<i>paaI</i>	phenylacetic acid degradation protein	2,58	1.37	0.0031	0.0000
2718	<i>leuB</i>	3-isopropylmalate dehydrogenase	4,69	2.23	0.0252	0.0006
4891	<i>htpX1</i>	heat shock protein. protease	5,66	2.50	0.0064	0.0001

t2						
2675	<i>rpmB1</i>	ribosomal protein L28	2,25	-1.17	0.0397	0.0005
3016	<i>wblE</i>	WhiB-family transcriptional regulator	2,17	-1.12	0.0451	0.0006
3888	<i>sig32</i>	RNA polymerase ECF-subfamily sigma factor	12,21	-3.61	0.0010	0.0000
4561 ^a	<i>sig40</i>	RNA polymerase ECF-subfamily sigma factor	1,68	-0.75	0.1641	0.0074
4820	<i>cspD6</i>	cold-shock protein	4,06	-2.02	0.0350	0.0004
459	<i>hsp18_1</i>	heat shock protein	3,23	1.69	0.0027	0.0000
692	<i>hsp18_2</i>	heat shock protein	3,58	1.84	0.0006	0.0000
758		Acetyltransferase	2,03	1.02	0.0286	0.0003
826	<i>cspD1</i>	cold-shock protein	2,13	1.09	0.0168	0.0001
898	<i>sig10</i>	RNA polymerase ECF-subfamily sigma factor	3,05	1.61	0.0283	0.0003
1061		Aminotransferase	3,18	1.67	0.0087	0.0000

Genes involved in nucleotide and vitamin metabolism, and DNA replication, recombination and repair

t1						
5915	<i>phoA</i>	alkaline phosphatase	5,24	-2.39	0.0013	0.0000
6215	<i>cpdB</i>	2'.3'-cyclic-nucleotide 2'-phosphodiesterase	2,97	-1.57	0.0341	0.0009
6407	<i>cobJ</i>	precorrin methylase	2,04	-1.03	0.0166	0.0004
6413	<i>cobA</i>	cob(I)alamin adenosyltransferase	1,53	-0.61	0.0315	0.0008
47		IS605 family IS1136A-like transposase	3,36	1.75	0.0135	0.0003
61		IS605 family IS1136A0-like transposase	3,27	1.71	0.0145	0.0003
120		IS701 family ISRhosp2-like transposase	2,38	1.25	0.0293	0.0007
288		IS630 family ISMac13-like transposase	2,53	1.34	0.0082	0.0001
757		IS630 family IS885-like transposase	2,73	1.45	0.0095	0.0002
803	<i>pgmA</i>	Phosphoglucomutase	3,18	1.67	0.0155	0.0003
821		IS200/IS605 family ISFsp4-like transposase	3,03	1.60	0.0003	0.0000
879	<i>ku2</i>	Ku70/Ku80 protein	2,01	1.01	0.0135	0.0003
3445	<i>purN</i>	phosphoribosylglycinamide formyltransferase	2,45	1.29	0.0005	0.0000
3463	<i>uvrD1</i>	ATP-dependent DNA helicase	1,71	0.77	0.0312	0.0008

4139	<i>purQ</i>	phosphoribosyl formylglycinamidine synthase I	1,80	0.85	0.0313	0.0008
4265	<i>thiC</i>	thiamine biosynthesis protein	3,03	1.60	0.0018	0.0000
t2						
4626	<i>int12</i>	tyrosine-family recombinase/integrase	2,85	-1.51	0.0125	0.0001
288		IS630 family ISMac13-like transposase	2,25	1.17	0.0358	0.0004
289		IS701 family ISAzvi8-like transposase	2,69	1.43	0.0078	0.0001
757		IS630 family IS885-like transposase	2,85	1.51	0.0160	0.0001

Carbohydrate metabolism genes

t1						
1082	<i>agaB1</i>	alpha-galactosidase	7,52	-2.91	0.0000	0.0000
2060		polysaccharide deacetylase. secreted	2,08	-1.06	0.0116	0.0002
6534		Glycosyltransferase	2,46	-1.30	0.0126	0.0002
649	<i>ard</i>	Phosphotransferase	2,77	1.47	0.0009	0.0000
803	<i>pgmA</i>	Phosphoglucomutase	3,18	1.67	0.0155	0.0003
1009		Glycosyltransferase	2,93	1.55	0.0067	0.0001
1011	<i>galE5</i>	UDP-glucose 4-epimerase	3,84	1.94	0.0027	0.0000
1013	<i>mpg2</i>	mannose-1-phosphate guanyltransferase	3,97	1.99	0.0101	0.0002
1014		NDP-hexose 4-ketoreductase	2,77	1.47	0.0077	0.0001
1911	<i>ccrA2</i>	crotonyl-CoA reductase	2,50	1.32	0.0040	0.0000
1912	<i>meaA1</i>	methylmalonyl-CoA mutase. coenzyme B12-dependent α -subunit	3,81	1.93	0.0003	0.0000
1913	<i>citE2</i>	citrate lyase beta chain	2,58	1.37	0.0016	0.0000
3859	<i>citA2</i>	citrate synthase	2,60	1.38	0.0144	0.0003
t2						
1082	<i>agaB1</i>	alpha-galactosidase	2,39	-1.26	0.0180	0.0001

Lipid metabolism genes

t1						
2944 ^{a,b}	<i>fabB2</i>	3-oxoacyl-ACP synthase II	1,79	-0.84	0.3338	0.0410
217	<i>fabC4</i>	acyl carrier protein	3,20	1.68	0.0011	0.0000
492	<i>echA1</i>	enoyl-CoA hydratase	2,25	1.17	0.0474	0.0014

1485 ^a	<i>plsC1</i>	1-acylglycerol-3-phosphate O-acyltransferase	1,84	0.88	0.3542	0.0471
1912	<i>meaA1</i>	methylmalonyl-CoA mutase. coenzyme B12-dependent alpha subunit	3,81	1.93	0.0003	0.0000
4208	<i>ltp3</i>	nonspecific lipid-transfer protein	2,23	1.16	0.0092	0.0001
4209		MaoC-like dehydratase	3,14	1.65	0.0067	0.0001
4210	<i>fadE28</i>	acyl-CoA dehydrogenase	3,03	1.60	0.0035	0.0000
t2						
217	<i>fabC4</i>	acyl carrier protein	2,83	1.50	0.0048	0.0000
1485 ^a	<i>plsC1</i>	1-acylglycerol-3-phosphate O-acyltransferase	1,85	0.89	0.3609	0.0463
2944 ^{a,b}	<i>fabB2</i>	3-oxoacyl-ACP synthase II	2,17	1.12	0.1908	0.0098
3866	<i>accA2</i>	acetyl/propionyl CoA carboxylase alpha subunit	2,07	1.05	0.0138	0.0001
Energy production genes						
t1						
4846	<i>nuoJ1</i>	NADH dehydrogenase I chain J (complex I)	3,27	-1.71	0.0434	0.0012
4847	<i>nuoK1</i>	NADH dehydrogenase I chain K (complex I)	3,18	-1.67	0.0100	0.0002
t2						
2885	<i>atpF</i>	F-type proton-transporting ATPase b chain	2,58	-1.37	0.0110	0.0001
Transport and external signals processing						
t1						
2246		simple sugar ABC transporter ATP-binding protein	2,14	-1.10	0.0155	0.0003
2247		simple sugar ABC transporter substrate-binding protein	3,12	-1.64	0.0327	0.0009
2455		MFS transporter protein	5,35	-2.42	0.0090	0.0001
2609		ABC transporter substrate-binding protein	2,30	-1.20	0.0229	0.0005
2963		ABC transporter permease protein	1,75	-0.81	0.0396	0.0011
3618		transmembrane transport protein	2,19	-1.13	0.0314	0.0008
4247		ABC transporter permease protein	1,67	-0.74	0.0252	0.0006
4248 ^c		ABC transporter ATP-binding protein	2,07	-1.05	0.0564	0.0018
4249 ^c		ABC transporter permease protein	1,92	-0.94	0.1647	0.0099

4250 ^c		ABC transporter ATP-binding protein	2,62	-1.39	0.0816	0.0032
5915	<i>phoA</i>	alkaline phosphatase	5,24	-2.39	0.0013	0.0000
5971	<i>phoC</i>	acid phosphatase	6,19	-2.63	0.0354	0.0009
515		oxidoreductase, iron-sulfur subunit	3,14	1.65	0.0035	0.0000
600	<i>fecC1</i>	ABC transporter iron(III)/siderophore transport system ATP-binding protein	5,28	2.40	0.0003	0.0000
602	<i>fecB</i>	ABC transporter iron(III)/siderophore-binding protein	7,73	2.95	0.0006	0.0000
610		MFS transporter protein	2,28	1.19	0.0166	0.0004
694		ABC transporter permease protein	4,53	2.18	0.0027	0.0000
695		ABC transporter ATP-binding protein	3,46	1.79	0.0224	0.0005
4600		MFS membrane protein (sulfate transport)	2,17	1.12	0.0019	0.0000
6941		MFS transporter protein	12,21	3.61	0.0000	0.0000
t2						
1804		hypothetical protein	2,00	-1.00	0.0486	0.0007
4066		ABC transporter ATP-binding protein	1,83	-0.87	0.0343	0.0004
4106		MFS transporter protein	2,85	-1.51	0.0468	0.0006
4247		ABC transporter permease protein	1,66	-0.73	0.0500	0.0007
602	<i>fecB</i>	ABC transporter iron(III)/siderophore-binding protein	4,72	2.24	0.0094	0.0001
610		MFS transporter protein	2,69	1.43	0.0122	0.0001
2436		sodium:solute symporter	1,91	0.93	0.0297	0.0003
2534		serine protease	2,10	1.07	0.0297	0.0003

Genes involved in cell envelope biosynthesis and morphological differentiation

t1						
1431 ^a	<i>spoVK</i>	sporulation protein K-like protein	1.49	0,577	0,1444	0,0082
2505	<i>clgR</i>	DNA-binding protein	1,85	-0.89	0.0129	0.0002
2600 ^a	<i>clpC1</i>	ATP-dependent Clp protéase	1,49	-0.58	0.7027	0.2294
3188		protein sporulation related domain-protein	2,62	-1.39	0.0456	0.0013
7486	<i>sti2</i>	subtilisin inhibitor	2,13	-1.09	0.0298	0.0007
617	<i>ctpB</i>	cation-transporting P-type ATPase	3,43	1.78	0.0009	0.0000

2754	<i>ampD1</i>	N-acetylmuramoyl-L-alanine amidase	2,60	1.38	0.0095	0.0002
5456	<i>mreC</i>	rod shape-determining protein	1,91	0.93	0.0443	0.0012
6937	<i>kipA</i>	antagonist of KipI	5,94	2.57	0.0022	0.0000
6938 ^b	<i>kipI</i>	inhibitor of KinA	2,85	1.51	0.0593	0.0020
t2						
2505	<i>clgR</i>	DNA-binding protein	1,78	-0.83	0.0375	0.0004
3016	<i>wblE</i>	WhiB-family transcriptional regulator	2,17	-1.12	0.0451	0.0006
4130	<i>bldC</i>	MerR-family transcriptional regulator	3,68	-1.88	0.0279	0.0002
7486	<i>sti2</i>	subtilisin inhibitor	3,34	-1.74	0.0039	0.0000
617	<i>ctpB</i>	cation-transporting P-type ATPase	3,66	1.87	0.0017	0.0000
Regulatory genes						
t1						
1081		ROK-family transcriptional regulator	3,63	-1.86	0.0035	0.0000
2268	<i>avaL2</i>	TetR-family transcriptional regulator (γ-butyrolactone)	8,88	-3.15	0.0078	0.0001
2270	<i>avaL1</i>	TetR-family transcriptional regulator (γ-butyrolactone)	6,41	-2.68	0.0035	0.0000
2301		regulatory protein	15,24	-3.93	0.0252	0.0006
2404	<i>cutS</i>	two-component system sensor kinase	2,13	-1.09	0.0035	0.0000
2505	<i>clgR</i>	DNA-binding protein	1,85	-0.89	0.0129	0.0002
2901 ^b	<i>olmRII</i>	LuxR-family transcriptional regulator (oligomycin)	2,77	-1.47	0.0712	0.0026
2902	<i>olmRI</i>	LuxR-family transcriptional regulator (oligomycin)	2,95	-1.56	0.0006	0.0000
2989		MarR-family transcriptional regulator (neopentalenolactone)	2,08	-1.06	0.0487	0.0015
4327		DNA-binding protein	2,28	-1.19	0.0336	0.0009
4398		regulatory protein	3,97	-1.99	0.0396	0.0011
4561 ^a	<i>sig40</i>	RNA polymerase ECF-subfamily sigma factor	1.75	-0,81	0,1009	0,0045
4903		TetR-family transcriptional regulator	2,66	-1.41	0.0095	0.0002
218		transcriptional regulatory protein	2,16	1.11	0.0396	0.0011
244		MerR-family transcriptional regulator	6,41	2.68	0.0029	0.0000
323		MerR-family transcriptional regulator	3,94	1.98	0.0028	0.0000

343		regulatory protein	3,05	1.61	0.0148	0.0003
410	<i>pteR</i>	SARP-LAL transcriptional regulator (filipin)	4,53	2.18	0.0009	0.0000
448		TetR-family transcriptional regulator	2,17	1.12	0.0126	0.0002
513	<i>bdpJ</i>	AraC-family transcriptional regulator	2,73	1.45	0.0137	0.0003
576		TetR-family transcriptional regulator	4,23	2.08	0.0014	0.0000
678		transcriptional regulator	2,95	1.56	0.0045	0.0001
705		TetR-family transcriptional regulator	2,23	1.16	0.0145	0.0003
742		AraC-family transcriptional regulator	2,10	1.07	0.0443	0.0012
831		LacI-family transcriptional regulator	2,31	1.21	0.0035	0.0000
935	<i>aveR</i>	LuxR-family transcriptional regulator (avermectin)	4,00	2.00	0.0049	0.0001
980		GntR-family transcriptional regulator	2,00	1.00	0.0116	0.0000
5755		regulatory protein	3,07	1.62	0.0280	0.0007
6982 ^a		MerR-family regulatory protein	1.50	0,586	0,1726	0,0110
t2						
2505	<i>clgR</i>	DNA-binding protein	1,78	-0.83	0.0375	0.0004
3705 ^c	<i>avaR1</i>	gamma-butyrolactone receptor protein (avenolide)	1,89	-0.92	0.1344	0.0043
4130	<i>bldC</i>	MerR-family transcriptional regulator	3,68	-1.88	0.0279	0.0002
4561 ^a	<i>sig40</i>	RNA polymerase ECF-subfamily sigma factor	1.68	-0,75	0,1641	0,0074
218		transcriptional regulatory protein	2,33	1.22	0.0386	0.0005
244		MerR-family transcriptional regulator	5,98	2.58	0.0079	0.0000
323		MerR-family transcriptional regulator	3,61	1.85	0.0093	0.0000
410	<i>pteR</i>	SARP-LAL transcriptional regulator (filipin)	2,71	1.44	0.0266	0.0002
576		TetR-family transcriptional regulator	2,48	1.31	0.0436	0.0006
678		transcriptional regulator	2,39	1.26	0.0343	0.0004
3850		transcriptional regulator	2,66	1.41	0.0094	0.0000
5754		DNA-binding protein	3,56	1.83	0.0032	0.0000
5755		regulatory protein	3,56	1.83	0.0279	0.0002

Secondary metabolite genes

t1						
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407	<i>pteH</i>	Thioesterase	1,93	0.95	0.1395	0.0076
408	<i>pteG</i>	cholesterol oxidase	4,14	2.05	0.0025	0.0000
411 ^b	<i>pteE</i>	ferredoxin (filipin)	2,14	-1.10	0.2533	0.0233
412	<i>pteD</i>	cytochrome P450 monooxygenase (filipin)	6,68	-2.74	0.0005	0.0000
413	<i>pteC</i>	cytochrome P450 monooxygenase (filipin)	5,03	-2.33	0.0004	0.0000
414	<i>pteB</i>	dehydrogenase (filipin)	5,06	-2.34	0.0000	0.0000
415 ^b	<i>pteA5</i>	modular polyketide synthase (filipin)	2,01	-1.01	0.1136	0.0054
416	<i>pteA4</i>	modular polyketide synthase (filipin)	2,43	-1.28	0.0095	0.0002
417 ^b	<i>pteA3</i>	modular polyketide synthase (filipin)	1,56	-0.64	0.3514	0.0457
418 ^b	<i>pteA2</i>	modular polyketide synthase (filipin)	1,83	-0.87	0.3639	0.0506
419 ^b	<i>pteA1</i>	modular polyketide synthase (filipin)	1,74	-0.80	0.4388	0.0752
1136	<i>melC1</i>	tyrosinase co-factor protein	3,20	-1.68	0.0776	0.0015
1137 ^c	<i>melC2</i>	tyrosinase (melanin)	1,99	-0.99	0.1151	0.0055
2266 ^c	<i>avaC</i>	phosphatase (γ-butyrolactone)	1,97	-0.98	0.0794	0.0030
2267 ^c	<i>avaB</i>	oxidoreductase (γ-butyrolactone)	2,30	-1.20	0.2777	0.0279
2269 ^c	<i>avaA</i>	gamma-butyrolactone biosynthesis protein (γ- butyrolactone)	3,01	-1.59	0.1456	0.0083
2272 ^c		hypothetical protein (pk3)	5,46	-2.45	0.2000	0.0150
2273		isomerase (pk3)	151,17	-7.24	0.0208	0.0005
2274		secreted protein (pk3)	32,45	-5.02	0.0473	0.0014
2275 ^c		transmembrane efflux protein (pk3)	19,97	-4.32	0.1124	0.0053
2276 ^c	<i>fabH7</i>	3-oxoacyl-ACP synthase III (pk3)	18,90	-4.24	0.1242	0.0063
2277 ^c		thioesterase (pk3)	12,30	-3.62	0.2222	0.0183
2278 ^c		F420-dependent dehydrogenase (pk3)	11,47	-3.52	0.3037	0.0327
2279 ^c		acyl-CoA synthetase (pk3)	7,84	-2.97	0.3522	0.0462
2285 ^c	<i>rocD3</i>	ornithine aminotransferase)pks3)	9,65	-3.27	0.3205	0.0377
2290 ^c	<i>fabH3</i>	3-oxoacyl-ACP synthase III (pk3)	9,85	-3.30	0.3281	0.0397
2724	<i>putA</i>	proline dehydrogenase	2,66	-1.41	0.0095	0.0002
2890 ^b	<i>ccrA1</i>	crotonyl-CoA reductase (oligomycin)	1,34	-0.42	0.4368	0.0743
2891 ^c		hypothetical (oligomycin)	2,27	-1.18	0.2280	0.0193
2892 ^b	<i>olmA4</i>	modular polyketide synthase (oligomycin)	1,26	-0.33	0.4760	0.0913

2893	<i>olmA5</i>	modular polyketide synthase (oligomycin)	1,16	-0.22	0.6421	0.1789
2894^c	<i>olmB</i>	cytochrome P450 monooxygenase (oligomycin)	2,13	-1.09	0.1512	0.0087
2895^c	<i>olmA7</i>	modular polyketide synthase (oligomycin)	1,56	-0.64	0.0746	0.0028
2896^c	<i>olmA6</i>	modular polyketide synthase (oligomycin)	1,67	-0.74	0.1443	0.0080
2897^c	<i>olmA3</i>	modular polyketide synthase (oligomycin)	1,25	-0.32	0.3610	0.0493
2898^{a,b}	<i>olmA2</i>	modular polyketide synthase (oligomycin)	1,24	-0.31	0.5785	0.1377
2899^{a,b}	<i>olmA1</i>	modular polyketide synthase (oligomycin)	1,53	-0.61	0.1817	0.0121
2900^c		P450-like protein (oligomycin)	1,48	-0.57	0.2474	0.0224
2901	<i>olmRII</i>	LuxR-family transcriptional regulator	2,77	-1.47	0.0712	0.0026
2902	<i>olmRI</i>	LuxR-family transcriptional regulator	2,95	-1.56	0.0006	0.0000
2903^c	<i>olmC</i>	thioesterase (oligomycin)	3,63	-1.86	0.1235	0.0062
2990^c	<i>gap1</i>	glyceraldehyde-3-phosphate dehydrogenase (neopentalenolactone)	2,57	-1.36	0.2469	0.0222
2991^c	<i>ptlH</i>	1-deoxypentalenic acid 11-beta hydroxylase (neopentalenolactone)	1,91	-0.93	0.1529	0.0089
2993^c	<i>ptlF</i>	1-deoxy-11beta-hydroxypentalenic acid dehydrogenase (neopentalenolactone)	1,69	-0.76	0.2639	0.0251
2994	<i>ptlE</i>	Baeyer-Villiger monooxygenase (neopentalenolactone)	2,46	-1.30	0.0087	0.0001
2995^c	<i>ptlD</i>	dioxygenase (neopentalenolactone)	2,31	-1.21	0.0962	0.0041
3155^c		MbtH-like protein (nrp3)	2,27	-1.18	0.2696	0.0261
3156^c	<i>nrps3-1</i>	non-ribosomal peptide synthetase (nrp3)	2,95	-1.56	0.0867	0.0035
3161^c	<i>dapF2</i>	diaminopimelate epimerase (nrp3)	2,04	-1.03	0.5045	0.1029
3162^c		hypothetical protein (nrp3)	2,87	-1.52	0.1668	0.0101
3163^c		hypothetical protein (nrp3)	2,36	-1.24	0.3227	0.0384
3164		hypothetical protein (nrp3)	3,01	-1.59	0.0003	0.0000
7112	<i>rocD2</i>	ornithine aminotransferase	3,01	-1.59	0.0212	0.0005
7184^c	<i>pks4</i>	modular polyketide synthase (pks4)	9,32	-3.22	0.2980	0.0315
7185^c		UDP-glucose:sterol glucosyltransferase (pks4)	8,28	-3.05	0.2753	0.0271
7186^c	<i>cyp26</i>	cytochrome P450 monooxygenase (pks4)	7,36	-2.88	0.2419	0.0213
7469	<i>cyp28</i>	cytochrome P450 monooxygenase	2,93	-1.55	0.0359	0.0010

109	<i>cyp1</i>	cytochrome P450 monooxygenase	1,99	0.99	0.0319	0.0008
407 ^b	<i>pteH</i>	thioesterase (filipin)	1,93	0.95	0.1395	0.0076
408	<i>pteG</i>	cholesterol oxidase (filipin)	4,14	2.05	0.0025	0.0000
442		monooxygenase involved in antibiotic biosynthesis	3,78	1.92	0.0116	0.0002
600	<i>fecC1</i>	ABC transporter iron(III)/siderophore transport system ATP-binding protein (nrp6)	5,28	2.40	0.0003	0.0000
602	<i>fecB</i>	ABC transporter iron(III)/siderophore-binding protein (nrp6)	7,73	2.95	0.0006	0.0000
603	<i>nrps6</i>	non-ribosomal peptide synthetase (nrp6)	1,60	0.68	0.3119	0.0342
604		hypothetical protein (nrp6)	2,27	1.18	0.0224	0.0005
605	<i>fadD2</i>	acyl-CoA synthetase. long-chain fatty acid:CoA ligase (nrp6)	2,30	1.20	0.0049	0.0001
606 ^c		hypothetical protein (nrp6)	1,65	0.72	0.3525	0.0464
607		taurine catabolism dioxygenase (nrp6)	2,22	1.15	0.0017	0.0000
608 ^c	<i>fabC2</i>	acyl carrier protein (nrp6)	2,03	1.02	0.1136	0.0054
609 ^c	<i>fabH4</i>	3-oxoacyl-ACP synthase III (nrp6)	2,22	1.15	0.1182	0.0058
610		MFS transporter protein (nrp6)	2,28	1.19	0.0166	0.0004
611		beta-hydroxylase (nrp6)	3,12	1.64	0.0005	0.0000
803	<i>pgmA</i>	Phosphoglucomutase	3,18	1.67	0.0155	0.0003
885		monooxygenase involved in antibiotic biosynthesis	5,54	2.47	0.0003	0.0000
938 ^c	<i>aveA1</i>	type I polyketide synthase (avermectin)	2,27	1.18	0.1820	0.0122
941 ^c	<i>aveE</i>	cytochrome P450 monooxygenase (avermectin)	2,06	1.04	0.1376	0.0074
947 ^c	<i>aveBIII</i>	glucose-1-phosphate thymidyltransferase (avermectin)	2,11	1.08	0.2027	0.0154
951	<i>aveBVII</i>	dTDP-6-deoxy-L-hexose 3-O-methyltransferase (avermectin)	4,03	2.01	0.0020	0.0000
952	<i>aveBVIII</i>	dTDP-4-keto-6-deoxy-L-hexose 2,3-reductase (avermectin)	3,56	1.83	0.0049	0.0001
953	<i>aveG</i>	thioesterase (avermectin)	4,59	2.20	0.0018	0.0000
1002		polyketide cyclase	2,10	1.07	0.0239	0.0006
2718	<i>leuB</i>	3-isopropylmalate dehydrogenase	4,69	2.23	0.0252	0.0006
3031	<i>cyp14</i>	epi-isozizaene hydroxylase (cytochrome P450) (ezs)	2,00	1.00	0.2918	0.0301
3032	<i>ezs</i>	epi-isozizaene synthase (sesquiterpene cyclase) (ezs)	2,14	1.10	0.1621	0.0097

3445	<i>purN</i>	phosphoribosylglycinamide formyltransferase	2,45	1.29	0.0005	0.0000
3859	<i>citA2</i>	citrate synthase	2,60	1.38	0.0144	0.0003
4006	<i>mshA</i>	Glycosyltransferase	1,69	0.76	0.0422	0.0012
6068		secreted cholesterol oxidase	2,27	1.18	0.0060	0.0001
7319	<i>fhuF2</i>	ferric iron reductase	2,39	1.26	0.0071	0.0001
7320	<i>avsA</i>	siderophore synthetase component (polyhydroxycarboxylate siderophore)	2,16	1.11	0.0295	0.0007
7321 ^c	<i>avsB</i>	siderophore synthetase component (polyhydroxycarboxylate siderophore)	1,71	0.77	0.2474	0.0224
7586	<i>mcjB1</i>	hypothetical protein (micromicin)	2,23	1.16	0.0063	0.0001
t2						
1136 ^c	<i>melC1</i>	tyrosinase co-factor protein (melanin)	3,20	-1.68	0.0776	0.0015
1137	<i>melC2</i>	tyrosinase (melanin)	3,61	-1.85	0.0078	0.0000
3164		hypothetical protein (nrp3)	2,69	-1.43	0.0015	0.0000
604		hypothetical protein (nrp6)	2,33	1.22	0.0357	0.0004
605	<i>fadD2</i>	acyl-CoA synthetase. long-chain fatty acid:CoA ligase (nrp6)	3,03	1.60	0.0019	0.0000
606		hypothetical protein (nrp6)	2,71	1.44	0.0484	0.0007
607		taurine catabolism dioxygenase (nrp6)	3,36	1.75	0.0006	0.0000
608 ^c	<i>fabC2</i>	acyl carrier protein (nrp6)	1,99	0.99	0.1573	0.0066
609 ^c	<i>fabH4</i>	3-oxoacyl-ACP synthase III (nrp6)	2,11	1.08	0.1774	0.0085
7586	<i>mcjB1</i>	hypothetical protein (micromicin)	2,03	1.02	0.0286	0.0003

Miscellaneous

t1						
1149		secreted esterase	1,82	-0.86	0.0212	0.0005
1745		Monooxygenase	2,01	-1.01	0.0116	0.0002
2622		secreted protein	3,56	-1.83	0.0020	0.0000
2764		secreted metalloproteinase	2,55	-1.35	0.0320	0.0008
3319		SAM-P45 peptidase	5,10	-2.35	0.0022	0.0000
4202		secreted protein	2,28	-1.19	0.0208	0.0005
4718		hypothetical protein	2,07	-1.05	0.0321	0.0008

5292	secreted protein	2,58	-1.37	0.0049	0.0001
5827	secreted protein	5,43	-2.44	0.0035	0.0000
6208	trypsin-like protease	1,77	-0.82	0.0474	0.0014
6295	carboxypeptidase T (secreted zinc-binding carbopeptidase)	5,28	-2.40	0.0438	0.0012
194	Acetyltransferase	3,78	1.92	0.0001	0.0000
200	large secreted protein	2,55	1.35	0.0487	0.0015
468	Oxygenase	3,78	1.92	0.0468	0.0014
613	secreted protein	3,39	1.76	0.0024	0.0000
615	secreted protein	4,20	2.07	0.0033	0.0000
616	secreted protein	3,51	1.81	0.0047	0.0001
769	Dioxygenase	5,21	2.38	0.0003	0.0000
787	choramphenicol phosphotransferase	2,55	1.35	0.0038	0.0000
871	Fe(II)/alpha-ketoglutarate dependent hydroxylase	2,41	1.27	0.0088	0.0001
897	secreted alpha-amylase inhibitor	4,69	2.23	0.0343	0.0009
899	secreted protein	7,16	2.84	0.0001	0.0000
903	membrane protein	2,14	1.10	0.0110	0.0002
923	Hydrolase	2,11	1.08	0.0156	0.0003
974	non-heme chloroperoxidase	2,48	1.31	0.0224	0.0005
990	secreted protein	3,51	1.81	0.0022	0.0001
993	cysteine transferase	3,12	1.64	0.0077	0.0001
996	secreted protein	2,13	1.09	0.0027	0.0000
1008	secreted protein	5,82	2.54	0.0002	0.0000
1048	DNA-binding protein	2,87	1.52	0.0070	0.0001
1749	phosphoesterase (SimX4 homolog)	2,22	1.15	0.0125	0.0002
2164	Hydrolase	1,89	0.92	0.0429	0.0012
4008	NLP/P60-family secreted protein (PgpA peptidase)	1,72	0.78	0.0449	0.0013
4330	membrane protein	3,18	1.67	0.0088	0.0001
4668	secreted protein	1,69	0.76	0.0456	0.0013
5004	secreted beta-lactamase	2,27	1.18	0.0437	0.0014
6908	membrane protein	1,73	0.79	0.0496	0.0015

6939		lactam utilization protein	4,63	2.21	0.0035	0.0000
7350		integral membrane protein	7,78	2.96	0.0030	0.0000
t2						
3095		ATP-binding protein	2,48	-1.31	0.0372	0.0004
51		Acetyltransferase	2,28	1.19	0.0372	0.0004
194		Acetyltransferase	1,88	0.91	0.0321	0.0003
615		secreted protein	5,70	2.51	0.0020	0.0000
812		small hydrophilic protein	1,60	0.68	0.0484	0.0007
871		Fe(II)/alpha-ketoglutarate dependent hydroxylase	2,27	1.18	0.0283	0.0003
899		secreted protein	6,54	2.71	0.0006	0.0283
923		Hydrolase	2,77	1.47	0.0050	0.0000
990		secreted protein	2,77	1.47	0.0156	0.0001
996		secreted protein	1,89	0.92	0.0162	0.0000
1008		secreted protein	3,05	1.61	0.0085	0.0000
1048		DNA-binding protein	2,69	1.43	0.0204	0.0002
1275		stress-inducible protein	1,87	0.90	0.0484	0.0007
1499		integral membrane protein	2,41	1.27	0.0279	0.0002
1501		secreted protein	2,53	1.34	0.0455	0.0006
1512		secreted protein	2,10	1.07	0.0184	0.0001
4438		secreted protein	4,89	2.29	0.0404	0.0005
6553	<i>sprD1</i>	streptogrisin D (secreted serine protease)	3,34	1.74	0.0486	0.0001
7350		integral membrane protein	5,90	2.56	0.0160	0.0001

^a PimM binds to its promoter region [7]

^b Gene included considering previous [7] or present RT-qPCR results

^c Gene included because its transcription profile matches those of genes functionally related

Table S2: Determination of the quality flag for array spots. The Feature Extraction software quantifies spot fluorescence and provides a set of Boolean values to assess the quality of the results. These quality indicators evaluate both red and green channel data of each spot (indicators are listed in the first row). Based on previous observations of the significance of each quality indicator, we classified the indicated combinations of Boolean values into a unique quality flag. Although spots with the best quality results were flagged as "1.00", other flag values were arbitrary.

Step	glsPosAndSignif	rlsPosAndSignif	glsWellAboveBG	rlsWellAboveBG	glsFeatNonUnifOL	rlsFeatNonUnifOL	glsBGNNonUnifOL	rlsBGNNonUnifOL	glsSaturated	rlsSaturated	Flag
1 st	1	1	1	1	0	0	0	0	0	0	1.00
2 nd		0									0.01
3 rd					0	0	0	0			0.95
					0	0	0	1			1.00
					0	0	1	0			
					0	1	0	0			
					1	0	0	0			
					0	1	1	0			0.85
					1	0	0	1			
					1	1	0	0			0.80
					1	0	1	0			0.70
					0	1	0	1			0.60
					0	0	1	1			0.50
					0	1	1	1			0.40
					1	0	1	1			
					1	1	0	1			
					1	1	1	0			
					1	1	1	1			0.30

Table S3: Assigned weights to each spot flags. To obtain spot quality weights that could be entered into the data analysis, we followed the idea behind the array weight estimation of Ritchie et al. [59]. In our case, the data of the 12 array hybridizations (4 conditions x 3 biological replicates) were normalized, the array weights calculated, and a linear model was fitted as indicated in Materials and Methods. In this initial stage, all spots were equally weighted irrespective of their quality flags. Spots with more reproducible transcription values —less variable— between replicates indicate a higher data quality. Hence, means of spot variances for each flag group were calculated. Spot weights were simply obtained by the normalized inverse of the mean variance.

Quality flag	Mean of variances	Quality weight	Percentage of total spots
1.00	4.296	1.000	62.601%
0.80	4.827	0.890	4.110%
0.95	5.209	0.825	0.015%
0.01	6.366	0.675	32.611%
0.60	11.985	0.358	0.005%
0.40	20.589	0.209	0.002%
0.85	23.558	0.182	0.002%
0.30	35.496	0.121	0.051%
0.70	36.000	0.119	0.006%
0.50	44.424	0.097	0.597%

Table S4: Sequence of primers used for qPCR.

Primer	Sequence (5'to 3')	Transcripts quantification	Product size (bp)
Q-rrnA1 fw	GACGCAACGCGAAGAACC	<i>rrnA1</i>	137
Q-rrnA1 rev	TGCGGGACTTAACCCAACATC		
Q-pteG fw	CGGTGCCGACCACGAC	<i>pteG</i>	100
Q-pteG rev	GCGGGGCAGACTACGATCAC		
Q-pteR fw	GGCCCTGCTGCTCATCC	<i>pteR</i>	153
Q-pteR rev	CCTGTTCCCGCCTTTGTG		
Q-pteD fw	GCCAGCATGTCGTCCAAGAG	<i>pteD</i>	141
Q-pteD rev	CTTCCCCCTGATCGGTGTC		
Q-pteC fw	GTGCTCCGGCTCGTCCTG	<i>pteC</i>	118
Q-pteC rev	CCTGCTGCGCGACTCCTC		
Q-pteB fw	CCAGCGAGGACCACACG	<i>pteB</i>	116
Q-pteB rev	GCCGAAGCAGGCGTTCC		
Q-pteA4 fw	TCAGGCCAAGGAAGTACGAGAC	<i>pteA4</i>	125
Q-pteA4 rev	CGCCATGTGGGACGACTAC		
Q-sav602 fw	CGGGCGCCTTGGTGAAC	<i>fecB</i>	97
Q-sav602 rev	GCCACCGGCGACAAGGC		
Q-sav935 fw	GCACGGTGAACTGCTCGTC	<i>aveR</i>	131
Q-sav935 rev	GTGGTCCGCGGGAAGCC		
Q-sav1082 fw	GCAGACCGAGTGTGGGAGAG	<i>agaB1</i>	115
Q-sav1082 rev	CCGGTGGGCTGCCATTCTG		
Q-sav2273 fw	GCCAGCGGATCGATGTACGG	SAVERM2273	97
Q-sav2273 rev	AGTACCTCGCCCTGTGGAAC		
Q-sav2902 fw	GAGGTCGTCCGGGAAAGGAG	<i>olmRI</i>	104
Q-sav2902 rev	TCGGCCTGATCGCTCTGC		
Q-sav4891 fw	GTCGTCGCACTCTTCATCGC	<i>htpX1</i>	108
Q-sav4891 rev	GGCCTCGAACTCGCTCACC		