

Table S1. Annotation and prediction of gene functions of aculeximycin biosynthesis gene cluster. Locus number is the numeric part of the locus_tag (e.g. locus number 6558 refers to gene KALB_6558).

Gene name	Locus number	Direction	Location start	Location end	Product
<i>acuX1</i>	6558	reverse	7364671	7362971	Hypothetical protein
<i>acuGT8</i>	6559	reverse	7366220	7365003	Glycosyltransferase
<i>acuAVIII</i>	6560	reverse	7377376	7366235	PKSI
<i>acuAVII</i>	6561	reverse	7386327	7377424	PKSI
<i>acuAVI</i>	6562	reverse	7409882	7386381	PKSI
<i>acuAV</i>	6563	reverse	7423160	7409934	PKSI
<i>acuAIV</i>	6564	reverse	7432829	7423185	PKSI
<i>acuAIII</i>	6565	reverse	7438114	7432850	PKSI
<i>acuAII</i>	6566	reverse	7453128	7438144	PKSI
<i>acuAI</i>	6567	reverse	7469754	7453189	PKSI
<i>acuO2</i>	6568	reverse	7471178	7469967	Cytochrome P450 hydroxylase
<i>acuGT7</i>	6569	reverse	7472406	7471171	Glycosyl transferase
<i>acuGT6</i>	6570	reverse	7473617	7472403	Glycosyltransferase
<i>acuS6</i>	6571	reverse	7474507	7473641	Glucose-1-phosphate thymidyltransferase
<i>acuW</i>	6572	reverse	7476426	7474630	ABC Transporter protein
<i>acuR5</i>	6573	forward	7476529	7477119	Transcription regulator, TetR family
<i>acuGT5</i>	6574	forward	7477412	7478632	Glycosyltransferase
<i>acuGT4</i>	6575	reverse	7480109	7478919	Glycosyltransferase
<i>acuS5</i>	6576	reverse	7480929	7480129	NDP-hexose-4-ketoreductase
<i>acuH</i>	6577	reverse	7482659	7481049	Beta-hexosaminidase
<i>acuN2</i>	6578	forward	7482946	7484181	Aminotransferase
<i>acuGT3</i>	6579	forward	7484178	7485428	Antibiotic resistance glycosyltransferase macrolide
<i>acuN1</i>	6580	forward	7485514	7486623	Aminotransferase
<i>acuGT2</i>	6581	forward	7486701	7487948	Glycosyltransferase
<i>acuS4</i>	6582	reverse	7489725	7488259	NDP-hexose 2,3-dehydratase
<i>acuS3</i>	6583	reverse	7490428	7489823	dTDP-4-dehydrorhamnose 3,5-epimerase
<i>acuGT1</i>	6584	forward	7490555	7491754	Glycosyltransferase
<i>acuS2</i>	6585	forward	7491783	7492757	dTDP-glucose 4,6-dehydratase
<i>acuR4</i>	6586	reverse	7493563	7492823	LuxR-family transcription regulator
<i>acuO1</i>	6587	forward	7494079	7494945	F420 Monooxygenase

<i>acuS1</i>	6588	reverse	7496334	7495132	NDP-hexose-C3-methyltransferase
<i>acuR3</i>	6589	reverse	7499231	7496448	LuxR-family transcription regulator
<i>acuR2</i>	6590	reverse	7501849	7499231	LuxR-family transcription regulator
<i>acuR1</i>	6591	reverse	7504512	7501846	LuxR-family transcription regulator

Table S2. Classification and characterization of secondary metabolism (SM) gene clusters identified in *Kutzneria albida* DSM43870 genome. Abbreviations of NRPS and PKS domains: C – condensation, A – adenylation, PCP – peptidyl-carrier protein, E – epimerase domain, nMT – N-methyltransferase, TE – thioesterase, KS – ketosynthase, AT – acyltransferase, ACP – acyl carrying protein, KR – ketoreductase, DH – dehydratase, ER – enoylreductase, AmT – aminotransferase, SDR – short chain dehydrogenase/reductase.

Type of SM	Cluster	Core enzymes locus tag and their domains architecture	Modification enzymes
NRPS			
	<i>kal7</i>	2585: A,PCP 2589: C,A,PCP,C,A,PCP,E,C,A,PCP,E,C,A,PCP,C,A,E,PCP 2590: C,A,PCP,C,A,PCP,E 2591: C,A,nMT,PCP,E,C,A,PCP,E,C,A,PCP,TE	Reductase (2586), oxygenase (2593), halogenase (2594), SARP transcriptional regulator (2597)
	<i>kal17</i>	3899: C,A,PCP;C,A,nMT,PCP,TE	ER (3875), reductase (3876),
	<i>kal18</i>	3904: A,PCP;C,A,PCP;E,C,A,PCP;C,PCP;C,A,PCP;C,PCP;C,A,PCP;C,A,PCP;C,A,PCP,E	LuxR transcriptional regulators (3906, 3908), cytochromes P450 (3912), SDR (3919)
	<i>kal36</i>	6133: PCP,C,A,PCP;C,A,PCP,TE 6134: A 6137: A,PCP;E,C,A,PCP;C,A,PCP,C	SDR (6127), dioxygenase (6139), SARP transcriptional regulator (6144)
	<i>kal37</i>	6150: A,PCP,TE 6152: A,KR,PCP 6154: C,A,PCP;C,A,PCP;C,A,PCP,TE 6155: A,PCP;C,PCP;E,C,PCP;C,A,PCP;C,PCP;C,A,PCP;C,A,PCP;C,A,PCP,E 6159: TE	ornithine cyclodeaminase (6148), dioxygenases (6149, 6160), amidase (6156), Ornithine transcarbamoylase (6158), glycosyltransferase (6172)
	<i>kal38</i>	6220: C,PCP 6221: A 6225: PCP 6227: A 6233: TE 6234: C,A PCP 6235: PCP 6240: A	dehydrogenases (6199, 6214, 6223), SDR (6201, 6232), phosphopantetheinyl transferase (6222), oxygenase , DAP diaminopimelate decarboxylase (6226), N-methyltransferase (6238)
Siderophore NRPS			

	<i>kal1</i>	0436: A,PCP, 700 aa N-terminal domain	Aminotransferase (0437)
	<i>kal9</i>	3278: A, PCP, 700 aa N-terminal domain	
	<i>kal14</i>	3665: A,PCP, 700 aa N-terminal domain	Aminotransferase (3666)
	<i>kal16</i>	3809: A,PCP, N-terminal catalytic domain (ϵ -poly-L-lysine synthases)	isochorismatase (3803)
	<i>kal22</i>	4308: A,PCP,C,PCP 4312: TE	Aminotransferase (4299), ornithine N-monooxygenase (4309), SDR (4301).
	<i>kal27</i>	4803: PCP 4805: A 4810: C,A,PCP;E,C,A,PCP,E 4811: C,A,PCP;C,A,PCP;C,A,PCP;E,C,A,PCP 4812: C,A,PCP;C,A,PCP;E,C,A,PCP;E,C,A,PCP,E	dioxygenases (6789), isochorismatase (4803, 4804), isochorismate synthase (4806), SDR (4808), iron ABC transporter (4809)
	<i>kal30</i>	5129: A,PCP, 700 aa N-terminal domain	Oxidoreductase (5135)
	<i>kal32</i>	5550: A 5551: C	Isochorismate synthase (5549), oxidoreductase (5552)
	<i>kal35</i>	5976: A,PCP, 700 aa N-terminal domain	
	<i>kal44</i>	7696: C,A,PCP,TD 7697: PCP 7698: A	Aminotransferase (7683), SDR (7687), isochorismatase (7689), iron ABC transporter (7693- 7695), dioxygenases (7700)
PKS			
Type I	<i>kal3</i>	1318: KS,AT,DH,ER,KR,ACP	ER (1311), KR (1313), epimerase (1319)
Type I	<i>kal6</i>	2529:KS,AT,ACP;KS,AT,KR,ACP;KS,AT,KR,ACP	KR (2525), ER (2526)
Type II	<i>kal21</i>	4117:KS α 4118:KS β 4114:ACP	cyclases (4113, 4115), oxygenases (4119), cytochromes P450 (4121)
Type I (IV)	<i>kal28</i>	5021: KS,AT,DH,DH,ACP 5022: KR 5023: KS,AT,ACP 5025: ACP	Aminotransferase (5014), dehydrogenases (5018, 5019, 5026), ACP-malonyltransferase (5020), TE (5024)

Type I	<i>kal39</i>	6321: ACP 6322: AT,DH 6323: KS,AT,KR	Glycosyltransferase (6320), SDR (6325)
Type I Acculeximycin biosynthesis gene cluster	<i>kal40</i>	6567 <i>acul</i> : KS,AT,DH,ER,KR,ACP;KS,AT,KR,ACP;KS,AT,DH,ER,KR,ACP 6566 <i>aculI</i> : KS,AT,KR,ACP;KS,AT,DH,ER,KR,ACP;KS,AT,KR,ACP 6565 <i>aculII</i> : KS,AT,DH,KR,ACP; 6564 <i>aculIV</i> : KS,AT,DH,KR ACP;KS,AT,KR, ACP 6563 <i>aculV</i> : KS,AT,KR,ACP;KS,AT,KR, ACP;KS,AT,KR,ACP; 6562 <i>aculVI</i> : KS,AT,KR,ACP;KS,AT,KR,ACP;KS,AT,DH,ACP;KS,AT,KR,ACP;KS,AT,DH,ER,KR,ACP 6561 <i>aculVII</i> : KS,AT,KR, ACP;KS,AT,KR, ACP 6560 <i>aculVIII</i> : KS,AT,DH,KR,ACP;KS,AT,DH,KR,ACP;TE	
Type II	<i>kal45</i>	7829: ACP 7830: KS β 7831: KS α	cyclases (7824), oxygenases (7826,7834,7839), SDR (7810,7822,7825,7833), glycosyltransferases (7812,7813,7814), O-methyltransferase (7835)
Type I	<i>kal46</i>	8454: KS,AT,KR 8455: KS,AT 8456: ACP	Aminotransferase (8447), glycosyltransferases (8458), cyclase (8466)
PKS-NRPS hybrid			
	<i>kal4</i>	1470:KS,AT,DH,KR,ACP;KS,AT,DH,KR,ACP 1471:KS,AT,KR,ACP 1472:KS,AT,DH,KR,ACP;KS,AT,DH,KR,ACP;KS,AT,DH,KR,ACP 1473:KS,AT,DH,KR,ACP,TE 1477: AT 1478:ACP 1479:A 1480:A 1483:ACP,KS,AT,DH,KR,ACP;KS,AT,DH,KR,ACP;KS,AT,DH,KR,ACP 1488:C,A	Cyclase, cytochromes P450 (1468,1475), glycosyltransferase (1474), diaminopimelate decarboxylase (1481)
	<i>kal10</i>	3293:C 3305: Acyl-CoA ligase 3306:ACP,KS,AT,DH,KR,ACP,TE	Cytochrome P450 (3295), dehydrogenase (3301), glycosyltransferase (3316)

	<i>kal19</i>	3936: A,PCP;C,A,PCP;E,C,A,PCP;E,C,A,PCP;E,C,A,PCP 3937: C,A,PCP;E,C,A,PCP;C,A,PCP;E,C,A,PCP;C,A,PCP,E 3948: ACP 3951: Acyl-CoA ligase 3952: AT,ACP,KS,AT,KR,ACP 3953: KS,AT,DH,KR,ACP,TE	SDR (3919), methyltransferase (3934,3947), cytochromes P450 (3944,3945)
	<i>kal26</i>	4737: ACP,KS,AT,ACP,AmT,C,A,PCP,C,A,PCP 4740: Acyl-CoA ligase 4741: C,A,nMT,PCP,C 4742: C,A,PCP,TE 4759: A,PCP, terminal dehydrogenase	KR (4725), dehydrogenase (4726), ER (4746)
	<i>kal31</i>	5510: A,PCP 5511: KS 5512: A,PCP;C,PCP;C,A,PCP;C,A,PCP;C,A,PCP,TE 5522: A,PCP	Tyrosine 2,3-aminomutase (5509), methyltransferase (5514), dehydrogenase (5515), ornithine cyclodeaminase (5516)
	<i>kal33</i>	5790:A 5798: KS,ACP;C,A,PCP,TE 5802:A,PCP 5807:A	monooxygenase (5788), methyltransferase (5789), KR (5791), glycosyltransferases (5799, 5805), cytochromes P450 (5792,5800,5804), SDR (5809)
	<i>kal34</i>	5887: KS 5890: KS 5893: KS 5905: C,A,PCP;E,C,A,PCP;C,A,PCP,TE 5924:A, PCP;C,A,PCP 5925:C	methyltransferase (5884), SDR (5887), halogenase (5897), cytochromes P450 (5903), dioxygenases (5896,5911), aminotransferase (5917)
Terpene			
Geosmin	<i>kal2</i>	0676, geo1: germacradienol-geosmin synthase 0677, geo2: germacradienol synthase	Geranyl-geranyl-pyrophosphate synthetase (0679)
	<i>kal5</i>	2031 crtB5:phytoene synthase 2032crtX: carotene biosynthesis associated membrane protein	Geranyl-geranyl-pyrophosphate synthase (KALB_6731, ispA5), phytoene desaturase (KALB_6732, crtI5)
	<i>kal15</i>	3743: crtL type lycopene cyclase gene	

	<i>kal20</i>	4042: radical SAM protein 4044: squalene-hopene cyclase 4045: trans-Isoprenyl Diphosphate Synthases 4046: squalene-associated FAD-dependent desaturase 4047: phytoene synthase 4048: phytoene synthase	SDR (4040,4057), glycosyltransferases (4037), 4-Hydroxy-3-methylbut-2-enyl diphosphate reductase (4043)
2-MIB	<i>kal25</i>	4603: cyclo-AMP binding protein 4604: SAM dependent GPP methyltransferase 4605: monoterpene synthase	
Others			
Ectoine	<i>kal8</i>	3094: Ectoine hydroxylase 3095: L-ectoine synthase 3096: Diaminobutyrate-pyruvate aminotransferase 3097: acetyl-transferase	Transporter (3098)
Indolocarbazole	<i>kal11</i>	3408: tryptophan oxidase 3409: chromopyrrolic acid synthase 3410: flavin monooxygenase	cytochromes P450 (3411,3412),acyl-CoA dehydrogenase (3413,3414), SDR (3416,3417,3418)
Lantipeptide	<i>kal12</i>	3444: LanM type lanthionine synthetase 3445: putative prepropeptide	Acyl-CoA ligase (3448)
Lantipeptide	<i>kal13</i>	<i>lanA13</i> (3595): prepropeptide <i>lanB13</i> (3596): lanthionine-forming dehydratases <i>lanC13a</i> (3597): lanthionine-forming dehydratases <i>lanC13b</i> (3598): lanthionine-forming dehydratases 3599: peptide reductase/dehydrogenase 3600: thiazole/oxazole cyclodehydratase YcaO-like 3601: thiazole/oxazole cyclodehydratase YcaO-like	3588 - PKS: KS,AT,AmT
Aerobactin siderophore	<i>kal23</i>	4486: lucA/lucC domains protein	Transporter (4487), SDR (4488)
Bacteriocins	<i>kal24</i>	4567: linocin M18	ABC transporter (4568,4569)
Lantipeptide	<i>kal29</i>	5094: C,A (NRPS) 5095: LanM type lanthionine cyclase 5096: prepropeptide	Cyclase (5089), ER (5099),KR (5108), A-domain protein (5110)

Lantipeptide	<i>kal41</i>	6952: SpaB dehydratase, C-terminal domain protein 6953: Lantibiotic dehydratase 6954: prepropeptide 6955: LanC lanthionine cyclase	Methyltransferase (6948)
Lantipeptide	<i>kal42</i>	7175: LanC lanthionine cyclase 7176: LanB dehydratase 7177: prepropeptide 7167: thiazole/oxazole cyclodehydratase YcaO-like	
Diketopiperazine	<i>kal43</i>	7471: cyclodipeptide synthase	

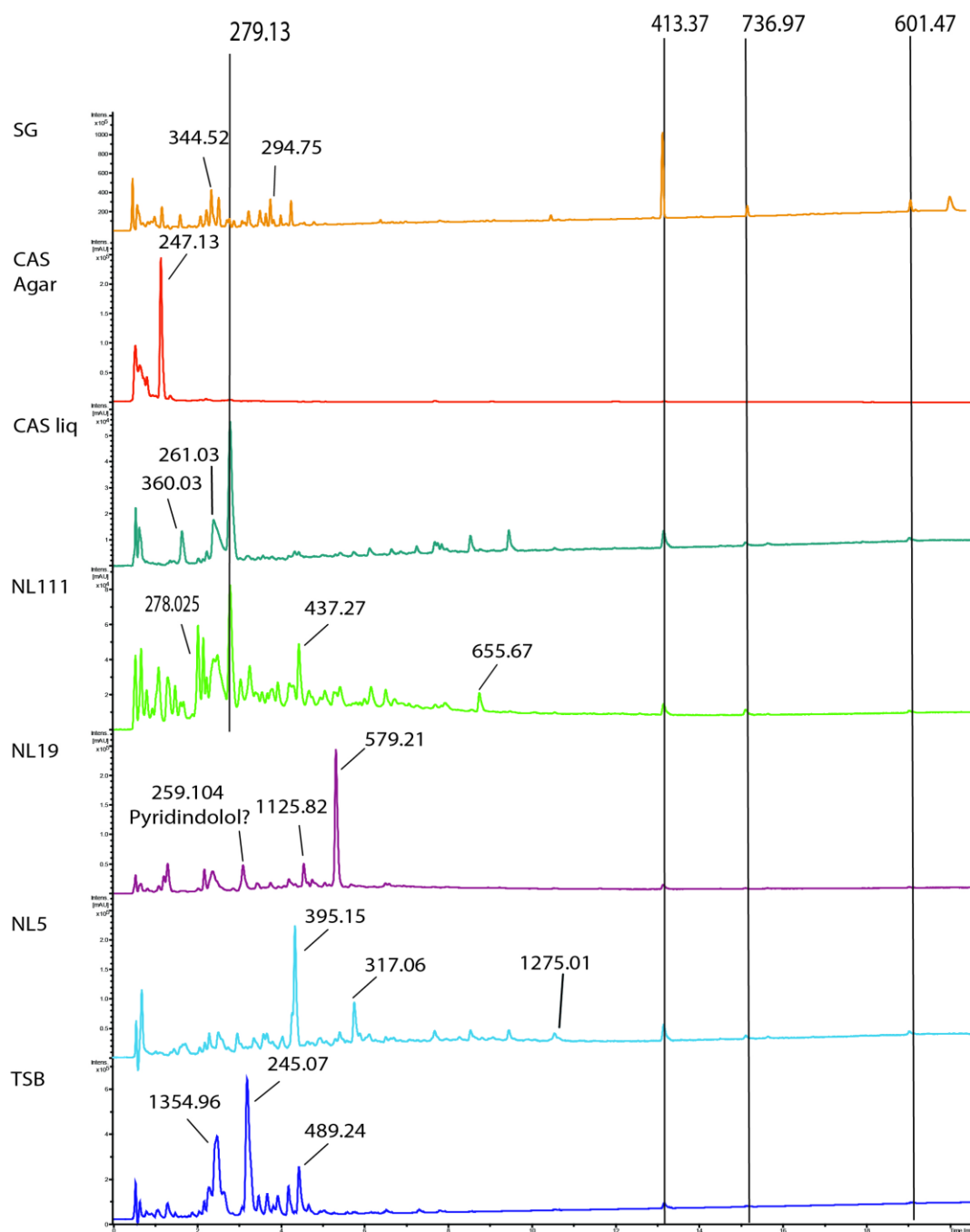


Figure S1. HPLC-MS analysis of extracts from *K. albida* culture grown in different media. UV-Vis traces are shown. Masses of some compound are marked. Compounds that have hits in DNP are also indicated.

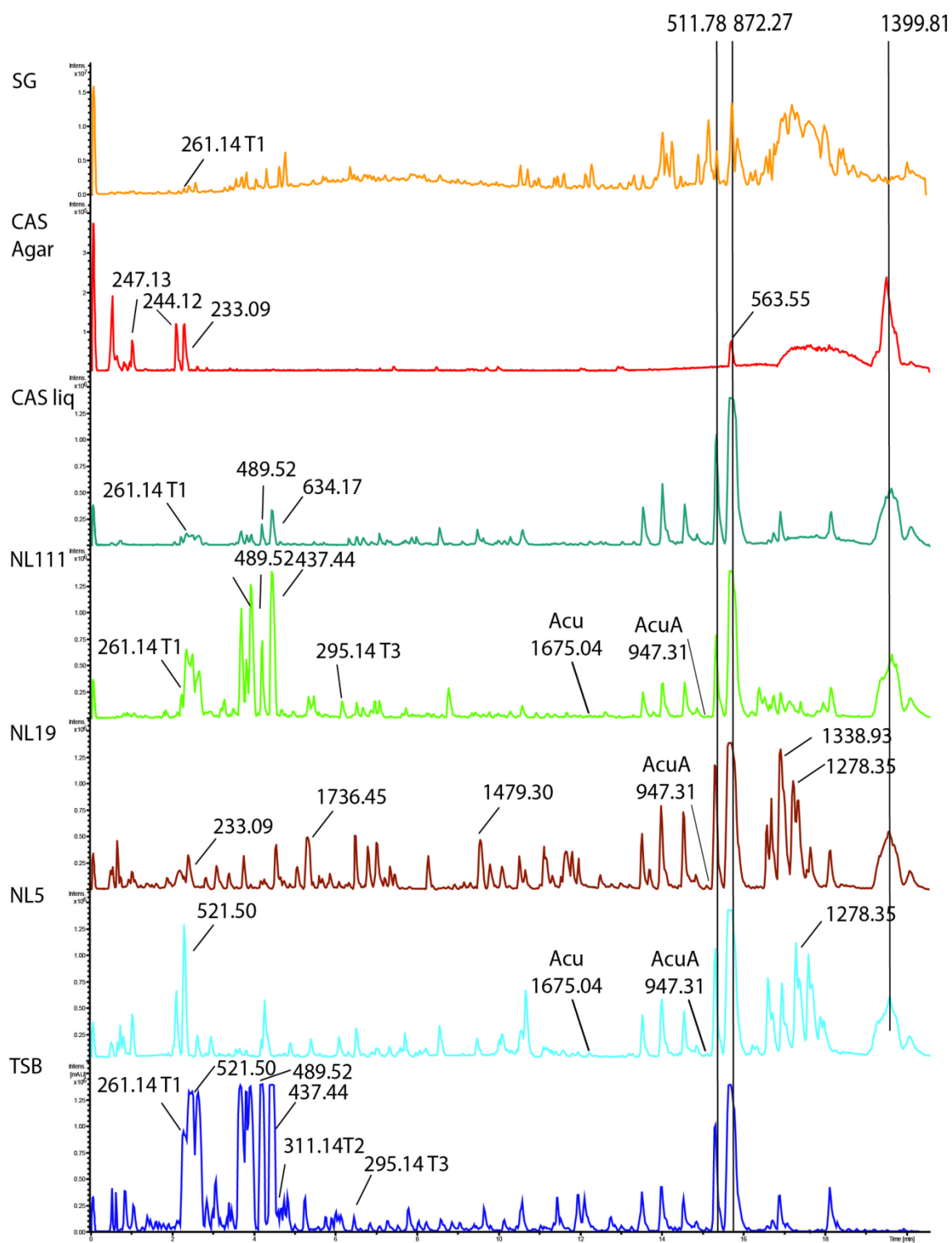


Figure S2. HPLC-MS analysis of extracts from *K. albidia* culture grown in different media. Base peak chromatogram traces are shown. Masses of some compound are marked. Aculeximycin and its aglycone are marked as Acu and AcuA respectively. Cyclic dipeptides are marked as T1 (cFL), T2 (cFY) and T3 (cFF).

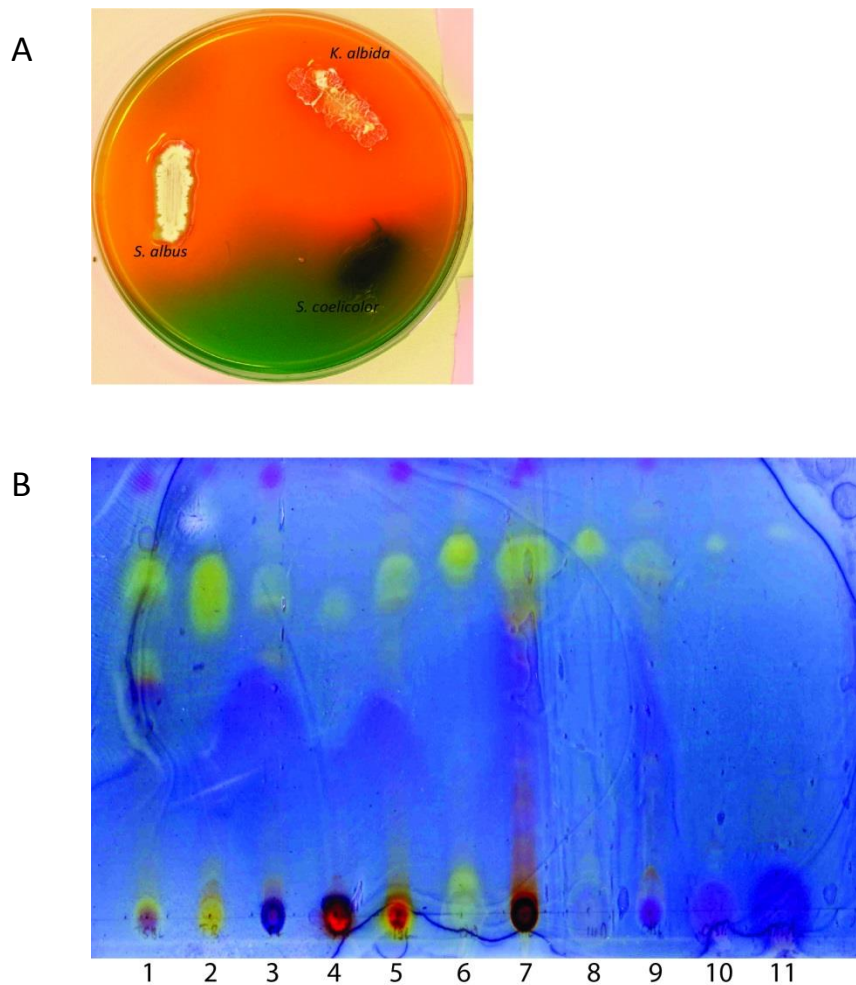


Figure S3. A. Modified CAS siderophore production test. Strains were grown for 7 days on CAS agar media and plates were overlaid with 0.8% agar containing Chrome azurol S (CAS), hexadecyltrimethyl ammonium bromide (HDTMA) in PIPES, and 1 mMFeCl₃·6H₂O [1]. Change in color was monitored after 3 hours. Orange color indicates siderophores accumulation. B. TLC analysis of extracts from *K. albida* cultures grown in different media (1 – TSB supernatant, 2 – TSB biomass, 3 – NL5 supernatant, 4 – NL5 biomass, 5 – NL19 supernatant, 6 – NL19 biomass, 7 – NL111 supernatant, 8 – NL111 biomass, 9 – CAS supernatant, 10 – CAS biomass, 11 – SG supernatant). The solvent phase was acetone-methanol 9:1. Plate was overlaid with 0.8% agar containing Chrome azurol S (CAS), hexadecyltrimethyl ammonium bromide (HDTMA) in PIPES, and 1 mMFeCl₃·6H₂O. Changes in color were monitored after 30 minutes of incubation.

1. Perez-Miranda S, Cabirol N, George-Tellez R, Zamudio-Rivera LS, Fernandez FJ: **O-CAS, a fast and universal method for siderophore detection.** *J Microbiol Methods* 2007, **70**(1):127-131.