

Supplementary Materials

Table S1. The major altered metabolic pathways in *S. aureus* GIM1.441 treated by Fraction 2 of *A. villosum* Lour.

Metabolic Pathway	Gene ID	Fold Change	Gene Description
Valine, leucine and isoleucine biosynthesis	B4602_RS11645	4.692	Acetolactate synthase AlsS
	B4602_RS10775	0.447	Ketol-acid reductoisomerase
	B4602_RS10780	0.390	2-isopropylmalate synthase
	B4602_RS10800	0.394	Threonine ammonia-lyase IlvA
	B4602_RS07310	2.450	Bifunctional threonine ammonia-lyase/L-serine ammonia-lyase TdcB
Biosynthesis of various other secondary metabolites	B4602_RS00415	2.968	Bifunctional transcriptional regulator/O-phospho-L-serine synthase SbnI
	B4602_RS00400	3.046	3-(L-alanin-3-ylcarbamoyl)-2-[(2-aminoethylcarbamoyl)methyl]-2-hydroxypropanoate synthase SbnF
	B4602_RS00395	4.626	L-2,3-diaminopropanoate--citrate ligase SbnE
	B4602_RS00385	2.880	Staphyloferrin B biosynthesis protein SbnC
	B4602_RS00410	2.571	Staphyloferrin B biosynthesis decarboxylase SbnH
Ascorbate and aldarate metabolism	B4602_RS11165	2.531	Aldehyde dehydrogenase family protein
	B4602_RS01530	8.846	PTS ascorbate transporter subunit IIC
	B4602_RS01540	7.963	PTS sugar transporter subunit IIA
	B4602_RS01535	6.872	PTS sugar transporter subunit IIB
	B4602_RS11755	2.573	30S ribosomal protein S8
Ribosome	B4602_RS11745	2.164	50S ribosomal protein L18
	B4602_RS11705	2.103	30S ribosomal protein S13
	B4602_RS11765	2.497	50S ribosomal protein L5
	B4602_RS11800	2.003	50S ribosomal protein L22
	B4602_RS11790	2.094	50S ribosomal protein L16
	B4602_RS11770	2.500	50S ribosomal protein L24
	B4602_RS11750	2.403	50S ribosomal protein L6
	B4602_RS11775	2.199	50S ribosomal protein L14
	B4602_RS11760	2.791	Type Z 30S ribosomal protein S14
	B4602_RS11805	2.116	30S ribosomal protein S19
	B4602_RS11780	2.240	30S ribosomal protein S17
	B4602_RS11735	2.008	50S ribosomal protein L30
	B4602_RS11710	2.304	50S ribosomal protein L36
	B4602_RS11785	2.067	50S ribosomal protein L29

C5-Branched dibasic acid metabolism	B4602_RS11640	4.678	Acetolactate decarboxylase
	B4602_RS10785	0.379	3-isopropylmalate dehydrogenase
	B4602_RS10790	0.414	3-isopropylmalate dehydratase large subunit
	B4602_RS10795	0.303	3-isopropylmalate dehydratase small subunit
Alanine, aspartate and glutamate metabolism	B4602_RS04620	2.062	Argininosuccinate lyase
	B4602_RS02195	2.141	Glutamate synthase large subunit
	B4602_RS00095	0.413	Adenylosuccinate synthase
	B4602_RS02200	2.014	Glutamate synthase subunit beta
	B4602_RS05210	0.472	Amidophosphoribosyltransferase
	B4602_RS07315	2.042	Alanine dehydrogenase
O-Antigen nucleotide sugar biosynthesis	B4602_RS00445	0.214	NAD-dependent epimerase/dehydratase family protein
	B4602_RS00575	4.175	Type 8 capsular polysaccharide synthesis protein Cap8F
	B4602_RS00570	4.080	Type 8 capsular polysaccharide synthesis protein Cap8E
	B4602_RS00580	3.171	Type 8 capsular polysaccharide synthesis protein Cap8G
Biosynthesis of various antibiotics	B4602_RS00375	8.641	2,3-diaminopropionate biosynthesis protein SbnA
	B4602_RS00380	3.155	N-[(2S)-2-amino-2-carboxyethyl]-L-glutamate dehydrogenase SbnB

Table S2. The major altered metabolic pathways in *B. cereus* Y1 treated by Fraction 2 of *A. villosum* Lour.

Metabolic Pathway	Gene ID	Fold Change	Gene Description
Bacterial chemotaxis	EJ379_25705	0.136	Methyl-accepting chemotaxis protein
	EJ379_08390	0.110	Chemotaxis signal transduction protein CheV
	EJ379_08260	0.199	Chemotaxis protein CheA
	EJ379_23055	0.148	Flagellar motor protein MotB
	EJ379_05160	0.311	Response regulator
	EJ379_02860	0.101	HAMP domain-containing protein
	EJ379_02170	0.188	Methyl-accepting chemotaxis protein
	EJ379_10215	0.120	HAMP domain-containing protein
	EJ379_25580	0.259	Methyl-accepting chemotaxis protein
	EJ379_23060	0.162	Flagellar motor protein MotA
	EJ379_08265	0.267	Flagellar motor switch phosphatase FlhY
	EJ379_08255	0.261	Response regulator
	EJ379_02085	0.188	Methyl-accepting chemotaxis protein
	EJ379_05155	0.312	Protein-glutamate O-methyltransferase CheR
	EJ379_08345	0.217	Flagellar motor switch protein FlhG
	EJ379_03465	0.358	Methyl-accepting chemotaxis protein
	EJ379_08280	0.369	Protein-glutamate O-methyltransferase CheR
	EJ379_08435	0.196	Flagellar motor switch protein FlhM

Nucleotide excision repair	EJ379_25710	0.108	Methyl-accepting chemotaxis protein
	EJ379_08245	0.243	Flagellar motor protein MotP
	EJ379_08250	0.463	Flagellar motor protein MotS
	EJ379_05760	0.175	Methyl-accepting chemotaxis protein
	EJ379_17320	0.406	Methyl-accepting chemotaxis protein
	EJ379_08430	0.479	Flagellar motor switch protein FlhN
	EJ379_00305	0.180	Transcription-repair coupling factor
	EJ379_26385	0.265	Excinuclease ABC subunit UvrA
	EJ379_23430	0.415	DNA polymerase I
	EJ379_23095	0.241	Excinuclease ABC subunit C
Histidine metabolism	EJ379_01760	0.260	NAD-dependent DNA ligase LigA
	EJ379_26390	0.431	Excinuclease ABC subunit B
	EJ379_01755	0.380	DNA helicase PcrA
	EJ379_06255	0.410	ATP-dependent helicase
	EJ379_05330	0.330	Helicase
	EJ379_14385	0.280	DNA helicase UvrD
	EJ379_18655	0.382	Formimidoylglutamate
	EJ379_18175	0.410	Aldehyde dehydrogenase DhaS
	EJ379_18660	0.409	Imidazolonepropionase
	EJ379_18665	0.353	Urocanate hydratase
Mismatch repair	EJ379_18670	0.486	Histidine ammonia-lyase
	EJ379_07680	0.491	Histidinol-phosphate transaminase
	EJ379_07135	0.265	Histidinol dehydrogenase
	EJ379_06560	0.398	Aldehyde dehydrogenase
	EJ379_07125	0.307	ATP phosphoribosyltransferase regulatory subunit
	EJ379_07170	0.220	Histidinol phosphate phosphatase domain-containing protein
	EJ379_07150	0.056	1-(5-phosphoribosyl)-5-((5-phosphoribosylamino)methylideneamino)imidazole 2-4-carboxamide isomerase
	EJ379_07130	0.185	ATP phosphoribosyltransferase
	EJ379_07145	0.089	Imidazole glycerol phosphate synthase subunit HisH
	EJ379_07140	0.263	Imidazoleglycerol-phosphate dehydratase HisB
	EJ379_15060	2.156	Histidinol-phosphate transaminase
	EJ379_07160	0.036	Phosphoribosyl-AMP cyclohydrolase
	EJ379_07155	0.068	Imidazoleglycerol phosphate synthase cyclase subunit
	EJ379_27960	0.382	Single-stranded DNA-binding protein
	EJ379_23520	0.263	DNA polymerase III subunit alpha
	EJ379_19260	0.332	DNA mismatch repair endonuclease MutL
	EJ379_19265	0.421	DNA mismatch repair protein MutS
	EJ379_00130	0.480	DNA polymerase III subunit gamma/tau

	EJ379_21375	0.332	Exodeoxyribonuclease VII large subunit
	EJ379_00010	0.242	DNA polymerase III subunit beta
	EJ379_19505	0.451	PolC-type DNA polymerase III
	EJ379_23250	0.391	Endonuclease MutS2
	EJ379_18460	0.462	3'-5' exonuclease
	EJ379_13795	0.388	DNA polymerase III subunit beta
	EJ379_21370	0.267	Exodeoxyribonuclease VII small subunit
	EJ379_17790	0.500	Endonuclease MutS2
Valine, leucine and isoleucine degradation	EJ379_21270	0.198	3-methyl-2-oxobutanoate dehydrogenase subunit beta
	EJ379_21275	0.188	3-methyl-2-oxobutanoate dehydrogenase subunit alpha
	EJ379_21280	0.180	Dihydrolipoyl dehydrogenase
	EJ379_21290	0.286	Leucine dehydrogenase
	EJ379_20560	0.413	Acetyl-CoA C-acetyltransferase
	EJ379_21265	0.179	2-oxo acid dehydrogenase subunit E2
	EJ379_20285	0.315	Dihydrolipoyl dehydrogenase
	EJ379_11710	0.490	CoA-acylating methylmalonate-semialdehyde dehydrogenase
	EJ379_12715	0.434	Hydroxymethylglutaryl-CoA lyase
	EJ379_27290	0.409	Acyl-CoA dehydrogenase AcdA
	EJ379_07085	0.319	Branched-chain-amino-acid transaminase
	EJ379_20660	0.484	NAD(P)-dependent oxidoreductase
	EJ379_01835	4.544	4-aminobutyrate-2-oxoglutarate transaminase
	EJ379_18540	4.023	Acetyl-CoA C-acyltransferase
O-Antigen nucleotide sugar biosynthesis	EJ379_27830	2.904	UDP-glucose 4-epimerase GalE
	EJ379_02515	0.118	SDR family NAD(P)-dependent oxidoreductase
	EJ379_26945	0.073	UTP-glucose-1-phosphate uridylyltransferase GalU
	EJ379_01610	0.118	NAD-dependent epimerase/dehydratase family protein
Biosynthesis of siderophore group nonribosomal peptides	EJ379_11790	0.338	Non-ribosomal peptide synthetase
	EJ379_11780	0.247	(2,3-dihydroxybenzoyl)adenylate synthase
	EJ379_10065	0.293	IucA/IucC family siderophore biosynthesis protein
	EJ379_11775	0.228	Isochorismate synthase Dhbc
	EJ379_10070	0.274	Siderophore biosynthesis protein
	EJ379_11785	0.327	Isochorismatase family protein
	EJ379_10075	0.349	Acyl-CoA synthetase
	EJ379_10085	0.270	Petrobactin biosynthesis protein AsbE
	EJ379_10090	0.079	Sugar phosphate isomerase/epimerase

Table S3. The major altered metabolic pathways in *V. parahaemolyticus* B2-28 treated by Fraction 2 of *A. villosum* Lour.

Metabolic Pathway	Gene ID	Fold Change	Gene Description
Glyoxylate and dicarboxylate metabolism	Vp_B2_28_3885	4.678	Hypothetical protein
	Vp_B2_28_3268	0.288	Membrane protein
	Vp_B2_28_4325	0.214	Transcriptional regulator
	Vp_B2_28_4324	0.253	Glycine cleavage system aminomethyltransferase T
	Vp_B2_28_4323	0.350	Glycine cleavage system aminomethyltransferase T
	Vp_B2_28_2435	0.466	tRNA guanosine(34) transglycosylase Tgt
	Vp_B2_28_2434	0.499	Preprotein translocase subunit YajC
	Vp_B2_28_1968	0.184	Preprotein translocase subunit SecD
	Vp_B2_28_4316	0.126	Multidrug transporter AcrB
	Vp_B2_28_0438	2.081	Catalase
Propanoate metabolism	Vp_B2_28_2170	0.271	Trypsin
	Vp_B2_28_2168	0.432	DNA mismatch repair protein MutT
	Vp_B2_28_5268	4.475	FMN-dependent NADH-azoreductase
	Vp_B2_28_5269	7.930	RNA helicase
	Vp_B2_28_2171	0.325	Histone acetyltransferase
	Vp_B2_28_5619	0.264	Phosphoenolpyruvate-protein phosphotransferase
	Vp_B2_28_2169	0.199	DNA mismatch repair protein MutT
	Vp_B2_28_2172	0.369	Histone acetyltransferase
	Vp_B2_28_2173	0.297	Propionyl-CoA synthetase
	Vp_B2_28_5544	0.350	Hypothetical protein
Lysine degradation	Vp_B2_28_5206	0.279	Formate dehydrogenase accessory protein FdhD
	Vp_B2_28_3274	0.453	Citrate (Si)-synthase
	Vp_B2_28_3823	2.086	Heavy metal-responsive transcriptional regulator
	Vp_B2_28_1176	0.482	Hypothetical protein
	Vp_B2_28_3822	2.616	Hypothetical protein
	Vp_B2_28_2037	0.216	Agmatine deiminase
	Vp_B2_28_2035	0.216	N-carbamoylputrescine amidase
	Vp_B2_28_2034	0.177	Gamma-glutamylputrescine oxidoreductase
	Vp_B2_28_2033	0.145	Gamma-glutamylputrescine oxidoreductase
	Vp_B2_28_1175	3.719	Cystatin domain protein
Fatty acid degradation	Vp_B2_28_4879	0.256	NAD(P)-dependent oxidoreductase
	Vp_B2_28_2279	0.180	Chemotaxis protein
	Vp_B2_28_0250	0.344	3-ketoacyl-CoA thiolase
	Vp_B2_28_0998	0.303	Acyl-CoA dehydrogenase
	Vp_B2_28_0996	0.326	Acyl-CoA dehydrogenase
	Vp_B2_28_0966	0.451	Long-chain-fatty-acid-CoA ligase
	Vp_B2_28_0997	0.174	Acyl-CoA dehydrogenase
Carbon fixation pathways in prokaryotes	Vp_B2_28_3275	0.374	Succinate dehydrogenase, cytochrome b556 subunit
	Vp_B2_28_0565	0.383	Aconitate hydratase B

One carbon pool by folate	<i>Vp_B2_28_5208</i>	0.041	Hexose phosphate transporter
	<i>Vp_B2_28_3538</i>	0.491	LysR family transcriptional regulator
	<i>Vp_B2_28_0656</i>	0.453	Mannitol repressor family protein
	<i>Vp_B2_28_2724</i>	0.310	Dnd system-associated protein 3
	<i>Vp_B2_28_3815</i>	0.245	Hypothetical protein
	<i>Vp_B2_28_4318</i>	0.097	Multidrug transporter AcrB
	<i>Vp_B2_28_4317</i>	0.149	Multidrug transporter AcrB
	<i>Vp_B2_28_2725</i>	0.406	Hypothetical protein
	<i>Vp_B2_28_3454</i>	0.479	Fatty acid hydroxylase superfamily protein
	<i>Vp_B2_28_2764</i>	2.500	Met repressor
Methane metabolism	<i>Vp_B2_28_4138</i>	0.080	Ligase
	<i>Vp_B2_28_1542</i>	0.369	Universal stress protein
	<i>Vp_B2_28_4321</i>	0.257	TetR family transcriptional regulator
	<i>Vp_B2_28_4320</i>	0.099	Hypothetical protein
	<i>Vp_B2_28_3883</i>	4.586	Formate dehydrogenase
	<i>Vp_B2_28_5173</i>	2.388	Nitrate transporter system, permease component
	<i>Vp_B2_28_0682</i>	2.134	Formate dehydrogenase
	<i>Vp_B2_28_5174</i>	2.659	Nitrate ABC transporter ATP-binding protein
	<i>Vp_B2_28_2596</i>	2.270	Hypothetical protein
	<i>Vp_B2_28_3884</i>	4.607	Hypothetical protein
	<i>Vp_B2_28_0681</i>	2.262	Formate dehydrogenase
	<i>Vp_B2_28_0680</i>	2.430	Formate dehydrogenase
	<i>Vp_B2_28_0679</i>	3.703	Formate dehydrogenase subunit alpha
	<i>Vp_B2_28_2813</i>	0.088	Iron-hydroxamate ABC transporter substrate-binding protein
Sulfur metabolism	<i>Vp_B2_28_2811</i>	0.092	tRNA dihydrouridine synthase DusA
	<i>Vp_B2_28_2812</i>	0.098	Phage shock protein G
	<i>Vp_B2_28_2814</i>	0.110	Hypothetical protein
	<i>Vp_B2_28_4010</i>	0.196	Hypothetical protein
	<i>Vp_B2_28_4114</i>	4.401	Exonuclease
	<i>Vp_B2_28_5645</i>	4.972	Dimethylsulfoxide reductase subunit B
	<i>Vp_B2_28_2815</i>	0.080	Sulfite reductase
	<i>Vp_B2_28_4113</i>	3.789	Sensor domain-containing diguanylate cyclase
	<i>Vp_B2_28_5675</i>	3.883	3-hydroxyisobutyrate dehydrogenase
	<i>Vp_B2_28_2059</i>	3.905	Chemotaxis protein CheY
	<i>Vp_B2_28_4870</i>	2.491	Prevent-host-death family protein
	<i>Vp_B2_28_3206</i>	2.021	Amino acid acetyltransferase
ABC transporters	<i>Vp_B2_28_0738</i>	0.159	Amino acid ABC transporter periplasmic amino acid-binding protein
	<i>Vp_B2_28_0132</i>	0.215	Oligopeptide ABC transporter ATP-binding protein OppF
	<i>Vp_B2_28_0133</i>	0.236	Oligopeptide ABC transporter ATP-binding protein OppD
	<i>Vp_B2_28_0134</i>	0.176	Peptide ABC transporter permease

Vp_B2_28_0135	0.178	Peptide ABC transporter permease
Vp_B2_28_0136	0.306	Peptide ABC transporter substrate-binding protein
Vp_B2_28_0735	0.221	Serine protease
Vp_B2_28_0737	0.201	Amino acid transporter
Vp_B2_28_3870	5.298	Hypothetical protein
Vp_B2_28_5552	0.022	Choline ABC transporter substrate-binding protein
Vp_B2_28_5551	0.020	Methylmalonate-semialdehyde dehydrogenase (acylating)
Vp_B2_28_3093	0.052	DNA polymerase III subunit epsilon
Vp_B2_28_3096	0.062	Cyclic nucleotide-binding protein
Vp_B2_28_1128	27.425	RND transporter
Vp_B2_28_3097	0.057	Cyclic nucleotide-binding protein
Vp_B2_28_0062	0.364	ABC transporter substrate-binding protein
Vp_B2_28_3094	0.079	Cyclic nucleotide-binding protein
Vp_B2_28_0739	0.195	ABC transporter
Vp_B2_28_5553	0.014	Hypothetical protein
Vp_B2_28_4436	2.295	LysR family transcriptional regulator
Vp_B2_28_3393	0.225	Hypothetical protein
Vp_B2_28_3391	0.383	Orotate phosphoribosyltransferase
Vp_B2_28_3392	0.265	Ribonuclease PH
Vp_B2_28_3868	2.087	Flagellar synthesis chaperone protein
Vp_B2_28_3732	0.387	Thiol:disulfide interchange protein DsbE
Vp_B2_28_0736	0.193	Histidine/lysine/arginine/ornithine ABC transporter ATP -binding protein HisP
Vp_B2_28_4437	2.073	Cytochrome biogenesis protein
Vp_B2_28_2754	0.345	Iron transporter FeoA
Vp_B2_28_3730	0.483	C-type cytochrome biogenesis protein CcmI
Vp_B2_28_4300	0.343	ABC transporter permease
Vp_B2_28_4094	0.172	Hypothetical protein
Vp_B2_28_4301	0.299	Hypothetical protein
Vp_B2_28_3869	2.966	N-acetylglucosamine kinase
Vp_B2_28_4439	2.332	Universal stress protein UspA
Vp_B2_28_4386	2.479	LysR family transcriptional regulator
Vp_B2_28_3731	0.370	Cystathionine gamma-synthase
Vp_B2_28_4093	0.263	Alcohol dehydrogenase
Vp_B2_28_4499	2.963	FAD-linked oxidase
Vp_B2_28_4303	0.181	Collagenase
Vp_B2_28_4498	2.356	Arginine ABC transporter substrate-binding protein
Vp_B2_28_4385	2.495	Methyltransferase
Vp_B2_28_3639	0.219	Electron transporter RnfB
Vp_B2_28_2755	0.296	Hypothetical protein
Vp_B2_28_2575	4.648	Hypothetical protein
Vp_B2_28_4594	0.162	Thiaminase II

Quorum sensing	Vp_B2_28_4169	0.430	Hypothetical protein
	Vp_B2_28_5464	0.196	HNH endonuclease
	Vp_B2_28_5432	0.435	GGDEF domain-containing protein
	Vp_B2_28_2324	0.366	Arylsulfatase
	Vp_B2_28_0378	0.294	Phosphate ABC transporter, permease protein PstA
	Vp_B2_28_5366	0.103	TetR family transcriptional regulator
	Vp_B2_28_5602	0.066	Phosphoribosylglycinamide formyltransferase
	Vp_B2_28_2576	0.380	PreQ(1) synthase
	Vp_B2_28_3965	0.426	Hypothetical protein
	Vp_B2_28_4833	0.465	Glyoxalase
	Vp_B2_28_1994	0.149	Membrane protein
	Vp_B2_28_0547	0.116	Peptide ABC transporter substrate-binding protein
	Vp_B2_28_4613	0.429	Peptide ABC transporter, periplasmic peptide-binding protein
	Vp_B2_28_0587	0.282	LuxR family transcriptional regulator
	Vp_B2_28_4612	0.448	ABC transporter ATP-binding protein
	Vp_B2_28_4614	0.315	Transcriptional regulator IlvY
	Vp_B2_28_4615	0.434	Ketol-acid reductoisomerase
	Vp_B2_28_1993	0.154	Carotenoid dehydrogenase
	Vp_B2_28_0549	0.140	Peptide ABC transporter permease
	Vp_B2_28_3425	2.705	LPS biosynthesis protein
	Vp_B2_28_1951	0.495	Conserved hypothetical protein
	Vp_B2_28_0548	0.191	Peptide ABC transporter permease
	Vp_B2_28_0965	0.411	Transcriptional regulator
	Vp_B2_28_0551	0.215	Peptide ABC transporter ATP-binding protein
	Vp_B2_28_0550	0.166	Peptide ABC transporter ATP-binding protein
	Vp_B2_28_3389	0.474	Nucleoid occlusion factor SlmA
	Vp_B2_28_2766	3.787	Bifunctional aspartate kinase/homoserine dehydrogenase II
	Vp_B2_28_4289	0.257	Transcription regulator
	Vp_B2_28_3640	0.241	Electron transporter RnfB
	Vp_B2_28_4302	0.141	Collagenase
	Vp_B2_28_5462	0.331	OtnA protein
	Vp_B2_28_4292	0.310	Amino acid dehydrogenase
Arginine and proline metabolism	Vp_B2_28_3777	0.234	Histidine kinase
	Vp_B2_28_2907	70.055	Endonuclease I
	Vp_B2_28_4180	0.283	PTS glucose transporter subunit IIBC
	Vp_B2_28_4181	0.284	Nuclease
	Vp_B2_28_2021	0.077	Lactoylglutathione lyase
	Vp_B2_28_2026	0.091	Glutamine synthetase
	Vp_B2_28_2027	0.137	Hypothetical protein
	Vp_B2_28_2032	0.143	Gamma-glutamylputrescine oxidoreductase

	Vp_B2_28_2030	0.123	Aldehyde dehydrogenase
	Vp_B2_28_2025	0.144	Na ⁺ /H ⁺ antiporter family protein
	Vp_B2_28_2028	0.090	Glutamine amidotransferase
	Vp_B2_28_4290	0.198	Aldehyde dehydrogenase
	Vp_B2_28_2031	0.169	Aldehyde dehydrogenase
	Vp_B2_28_0934	0.071	Carboxynorspermidine decarboxylase
Taurine and hypotaurine metabolism	Vp_B2_28_2494	0.353	RNA chaperone ProQ
	Vp_B2_28_0127	2.320	Phosphate acetyltransferase
	Vp_B2_28_0126	2.413	Acetate kinase
	Vp_B2_28_2331	3.087	Hypothetical protein
	Vp_B2_28_2493	0.488	Hypothetical protein
	Vp_B2_28_2495	0.420	Tail-specific protease
	Vp_B2_28_4228	0.471	Hypothetical protein
Purine metabolism	Vp_B2_28_4988	0.327	Membrane protein
	Vp_B2_28_1503	0.048	ATP-dependent RNA helicase
	Vp_B2_28_1504	0.052	Crp/Fnr family transcriptional regulator
	Vp_B2_28_3533	3.272	Hypothetical protein
	Vp_B2_28_1508	0.054	Sulfate adenylyltransferase subunit 2
	Vp_B2_28_3814	0.351	S-adenosyl-L-homocysteine hydrolase NAD-binding protein
	Vp_B2_28_0927	0.486	Ribonucleotide-diphosphate reductase subunit alpha
	Vp_B2_28_1725	0.350	Molecular chaperone DnaJ
	Vp_B2_28_2334	0.449	RNA helicase
	Vp_B2_28_0222	0.446	Amidophosphoribosyltransferase
	Vp_B2_28_2527	0.375	Hypothetical protein
	Vp_B2_28_2526	0.392	Prepilin-type cleavage/methylation protein
	Vp_B2_28_0493	2.476	Purine-nucleoside phosphorylase
	Vp_B2_28_3625	0.456	Conserved hypothetical protein
	Vp_B2_28_0929	0.367	Ribonucleotide-diphosphate reductase subunit beta
	Vp_B2_28_2411	0.478	Membrane protein
	Vp_B2_28_1500	2.027	Peptidoglycan-binding protein LysM
	Vp_B2_28_1354	3.089	Permease
	Vp_B2_28_5596	0.395	Hypothetical protein
	Vp_B2_28_3305	2.235	tRNA pseudouridine synthase TruD
	Vp_B2_28_5595	0.450	Flagellar sheath protein A
	Vp_B2_28_2529	0.310	Conserved hypothetical protein
	Vp_B2_28_4080	0.496	Patatin family protein
	Vp_B2_28_2528	0.430	Aminobenzoyl-glutamate transporter
	Vp_B2_28_1552	0.495	50S ribosomal protein L27
	Vp_B2_28_4987	0.399	Hypothetical protein
	Vp_B2_28_4549	0.465	Chaperone protein ClpB

alpha-Linolenic acid metabolism	<i>Vp_B2_28_5043</i>	0.286	Hypothetical protein
	<i>Vp_B2_28_5133</i>	0.379	Haloacid dehalogenase
	<i>Vp_B2_28_1729</i>	0.494	DNA helicase
Non-alcoholic fatty liver disease	<i>Vp_B2_28_1595</i>	0.279	Penicillin-binding protein activator
	<i>Vp_B2_28_1596</i>	0.254	Conserved hypothetical protein
	<i>Vp_B2_28_1597</i>	0.238	DnaA initiator-associating protein DiaA
Butanoate metabolism	<i>Vp_B2_28_5427</i>	2.825	Hypothetical protein
	<i>Vp_B2_28_3272</i>	0.464	Type II citrate synthase
	<i>Vp_B2_28_3271</i>	0.420	Phosphoglucomutase, alpha-D-glucose phosphate-specific
	<i>Vp_B2_28_5121</i>	3.969	PrkA family serine protein kinase
	<i>Vp_B2_28_5042</i>	0.398	Redox-sensitive transcriptional activator SoxR
	<i>Vp_B2_28_0249</i>	0.386	Multifunctional fatty acid oxidation complex subunit alpha
	<i>Vp_B2_28_3270</i>	0.391	SeqA protein
	<i>Vp_B2_28_1970</i>	0.189	Hypothetical protein
	<i>Vp_B2_28_1967</i>	0.148	Hypothetical protein
	<i>Vp_B2_28_2291</i>	0.271	Hypothetical protein
	<i>Vp_B2_28_2290</i>	0.413	Hypothetical protein
	<i>Vp_B2_28_3628</i>	0.299	Transcriptional regulator
	<i>Vp_B2_28_3627</i>	0.344	Oxidoreductase

Table S4. Comparison of the major altered metabolic pathways in the three target strains treated by Fraction 2 of *A. villosum* Lour.

Metabolic Pathway	Gram-positive strain		Gram-negative strain
	<i>S. aureus</i> GIM1.441	<i>B. cereus</i> Y1	<i>V. parahemolyticus</i> B2-28
Valine, leucine and isoleucine biosynthesis	+	-	-
Biosynthesis of various other secondary metabolites	+	-	-
Ascorbate and aldarate metabolism	+	-	-
Ribosome	+	-	-
C5-Branched dibasic acid metabolism	+	-	-
Alanine, aspartate and glutamate metabolism	+	-	-
O-Antigen nucleotide sugar biosynthesis	+	+	-
Biosynthesis of various antibiotics	+	-	-
Bacterial chemotaxis	-	+	-
Nucleotide excision repair	-	+	-
Histidine metabolism	-	+	-
Mismatch repair	-	+	-
Valine, leucine and isoleucine degradation	-	+	-
Biosynthesis of siderophore group nonribosomal peptides	-	+	-
Glyoxylate and dicarboxylate metabolism	-	-	+
Propanoate metabolism	-	-	+

Lysine degradation	-	-	+
Fatty acid degradation	-	-	+
Carbon fixation pathways in prokaryotes	-	-	+
One carbon pool by folate	-	-	+
Methane metabolism	-	-	+
Sulfur metabolism	-	-	+
ABC transporters	-	-	+
Quorum sensing	-	-	+
Arginine and proline metabolism	-	-	+
Taurine and hypotaurine metabolism	-	-	+
Purine metabolism	-	-	+
alpha-Linolenic acid metabolism	-	-	+
Non-alcoholic fatty liver disease	-	-	+
Butanoate metabolism	-	-	+
Central carbon metabolism in cancer	-	-	+

Note: +: altered. -: not altered.

Table S5. The oligonucleotide primers designed and used in the RT-qPCR assay.

Bacterial Strain	Primer	Sequence (5' to 3')
<i>S. aureus</i> GIM1.441	B4602_RS10775-F	AAATACCGCAAGAACCCAA
	B4602_RS10775-R	GCGATACGCTGAACACTCG
	B4602_RS01530-F	TACCGCAAGAACCCAAGA
	B4602_RS01530-R	CGATACGCTGAACACTCG
	B4602_RS02195-F	GTGTTGAACGAGCGACCAG
	B4602_RS02195-R	AACGCATCTTCCAAATCCC
	B4602_RS00385-F	CAATTACGATAGAGGGAAGG
	B4602_RS00385-R	TACACTTGATAATCCGCTTC
	B4602_RS00410-F	TTTTGGTGGCCCTGGTAAG
	B4602_RS00410-R	TTGGGAAATGGTCCTGCTA
<i>B. cereus</i> Y1	EJ379_25705-F	GCAAGAACCCAAGAAACTAT
	EJ379_25705-R	CAATGACTTTATTCCCATCA
	EJ379_05155-F	CTGAGATGTTCCGTAACCCTG
	EJ379_05155-R	GTTGCGTAAATAACCGACTT
	EJ379_01760-F	GCAGCAGCAGGTTCAATA
	EJ379_01760-R	GAAGGGCAACATCATCTA
	EJ379_19260-F	CGCCCTGCTTCAGTCGTA
	EJ379_19260-R	ACTCGGCAATGCCTCACC
	EJ379_27830-F	CGGAAATGACTATCCAACGA
	EJ379_27830-R	ACCTGGGCGACGCTCTGTAA
<i>V. parahaemolyticus</i> B2-28	Vp_B2_28_4316-F	AGGTGGTTTCCCAGGTGC
	Vp_B2_28_4316-R	CCCATTGATACTGGCTTACC
	Vp_B2_28_2625-F	CAAGTGGAAGTGC GTGAA
	Vp_B2_28_2625-R	GTGCCTGGAAGACCGATA
	Vp_B2_28_2812-F	CACCTTACCGTTGGATTG
	Vp_B2_28_2812-R	CTGGCAGTTTGAAGTTATTG
	Vp_B2_28_0737-F	TGTTGCTCAAGCGAAAGAA

Vp_B2_28_0737-R	GAATAATGCCATCCCAATC
Vp_B2_28_0737-F	GTTATCTCCATCATTGGCTCT
Vp_B2_28_0737-R	CGAACGAATACGCTGAAC

Table S6. The relative expression of the representative DEGs by the RT-qPCR assay.

Bacterial Strain	Gene	Predicted Protein	Fold Change	
			RNA-Seq.	RT-qPCR
<i>S. aureus</i> GIM1.441	B4602_RS10775	Ketol-acid reductoisomerase	0.447	0.236
	B4602_RS01530	PTS ascorbate transporter subunit IIC	8.846	1.532
	B4602_RS02195	Glutamate synthase large subunit	2.141	1.901
	B4602_RS00385	Staphyloferrin B biosynthesis protein SbnC	2.88	5.375
	B4602_RS00410	Staphyloferrin B biosynthesis decarboxylase SbnH	2.571	3.309
<i>B. cereus</i> Y1	EJ379_25705	Methyl-accepting chemotaxis protein	0.136	0.097
	EJ379_05155	Protein-glutamate O-methyltransferase CheR	0.312	0.377
	EJ379_01760	NAD-dependent DNA ligase LigA	0.26	0.075
	EJ379_19260	DNA mismatch repair endonuclease MutL	0.332	0.694
	EJ379_27830	UDP-glucose 4-epimerase GalE	2.904	3.320
<i>V. parahaemolyticus</i> B2-28	Vp_B2_28_4316	Multidrug transporter AcrB	0.126	0.041
	Vp_B2_28_2625	RpoS	2.64	7.21
	Vp_B2_28_2812	Phage shock protein G	0.098	0.549
	Vp_B2_28_0737	Amino acid transporter	0.201	0.033
	Vp_B2_28_0735	Serine protease	0.221	0.652

Table S7. The bacterial strains and media used in this study.

Bacterial Strain	Culture Medium	Source
<i>Aeromonas hydrophila</i> ATCC35654	TSB	ATCC, United States
<i>Bacillus cereus</i> Y1	TSB	LS-SHOU, China
<i>Enterobacter cloacae</i> ATCC13047	TSB	Biobw, China
<i>Enterobacter cloacae</i> D1	TSB	Biobw, China
<i>Escherichia coli</i> ATCC8739	TSB	Biobw, China
<i>Escherichia coli</i> K12	TSB	IIM, China
<i>Escherichia coli</i> ATCC25922	TSB	IIM, China
<i>Enterobacter sakazakii</i> CMCC45401	TSB	Biobw, China
<i>Klebsiella pneumoniae</i> 7-17-16	EE	LS-SHOU, China
<i>Pseudomonas aeruginosa</i> ATCC9027	TSB	Biobw, China
<i>Pseudomonas aeruginosa</i> ATCC27853	TSB	Biobw, China
<i>Staphylococcus aureus</i> GIM1.481	TSB	ATCC, United States
<i>Staphylococcus aureus</i> GIM1.441	TSB	ATCC, United States
<i>Staphylococcus aureus</i> GIM1.160	TSB	ATCC, United States
<i>Shigella dysenteriae</i> CMCC51252	TSB	GCCC, China
<i>Salmonella choleraesuis</i> ATCC13312	TSB	ATCC, United States
<i>Shigella flexneri</i> GIM1.238	TSB	GCCC, China
<i>Shigella flexneri</i> GIM1.539	TSB	GCCC, China

<i>Shigella flexneri</i> GIM1.231	TSB	GCCC, China
<i>Salmonella paratyphi</i> GIM1.235	TSB	GCCC, China
<i>Shigella sonnei</i> GIM1.424	TSB	ATCC, United States
<i>Shigella sonnei</i> GIM1.239	TSB	ATCC, United States
<i>Salmonella enterica</i> subsp. <i>enterica</i> (ex Kauffmann and Edwards)		
Le Minor and Popoff serovar Vellore ATCC15611	LB	LS-SHOU, China
<i>Vibrio cholerae</i> GIM1.449	TSB	GCCC, China
<i>Vibrio cholerae</i> B1	TSB	LS-SHOU, China
<i>Vibrio parahaemolyticus</i> B2-28	TSB	LS-SHOU, China
<i>Vibrio parahaemolyticus</i> N2-5	TSB	LS-SHOU, China
<i>Vibrio parahaemolyticus</i> N9-20	TSB	LS-SHOU, China
<i>Vibrio alginolyticus</i> ATCC33787	TSB	ATCC, United States
<i>Vibrio fluvialis</i> ATCC33809	Marine 2216	ATCC, United States
<i>Vibrio harveyi</i> ATCC BAA-1117	Marine 2216	ATCC, United States
<i>Vibrio harveyi</i> ATCC33842	Marine 2216	ATCC, United States
<i>Vibrio metschnikovi</i> ATCC700040	TSB	LS-SHOU, China
<i>Vibrio mimicus</i> bio-56759	Marine 2216	ATCC, United States
<i>Vibrio parahaemolyticus</i> ATCC17802	TSB	ATCC, United States
<i>Vibrio parahaemolyticus</i> ATCC33847	TSB	ATCC, United States
<i>Vibrio vulnificus</i> ATCC27562	Marine 2216	Biobw, China

Note: ATCC: American Type Culture Collection, United States; GCCC, Guangdong Culture Collection Center, Guangzhou, China; IIM, Institute of Industrial Microbiology, Shanghai, China; LS-SHOU, Laboratory stock, Shanghai Ocean University, Shanghai, China.

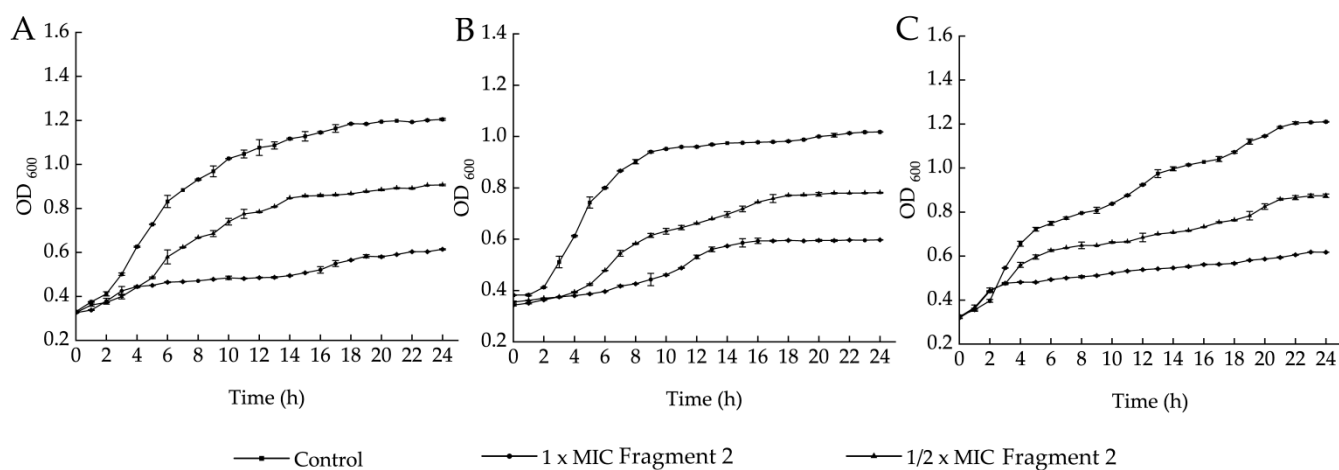


Figure S1. Growth curves of target strains treated by Fraction 2 from *A. villosum* Lour. (A–C): *S. aureus* GIM1.441, *B. cereus* Y1, and *V. parahemolyticus* B2-28, respectively. The strains were incubated in the TSB medium at 37 °C.

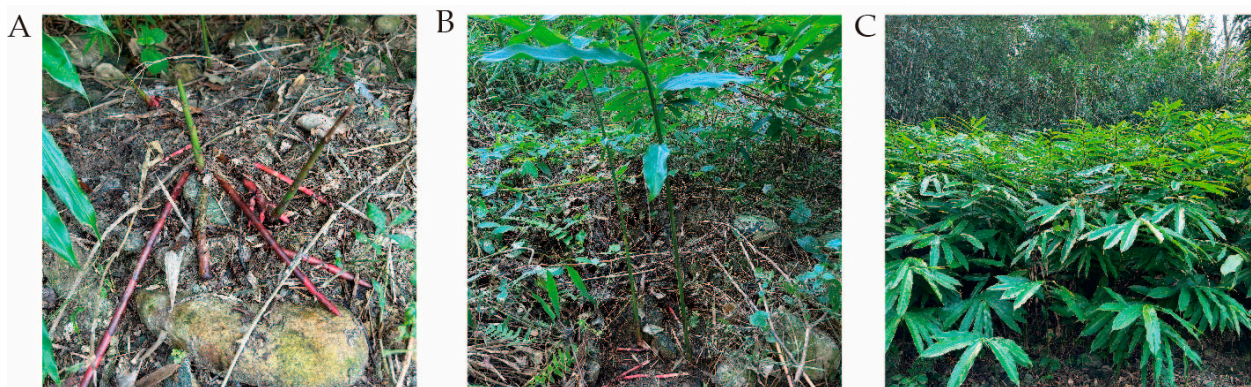


Figure S2. The plant of *A. villosum* Lour. (A–C): the different plant growth period.