## **Supporting information**

Unusual and highly bioactive sesterterpenes synthesized by *Pleurotus ostreatus* during the co-culture with *Trametes robiniophila Murr* 

Xiao-Ting Shen<sup>1†</sup>, Xu-Hua Mo<sup>1†</sup>, Li-Ping Zhu<sup>1†</sup>, Ling-Ling Tan<sup>1†</sup>, Feng-Yu Du<sup>2</sup>, Qian-Wen Wang<sup>3</sup>, Yuan-Ming Zhou<sup>3</sup>, Xiao-Jie Yuan<sup>1</sup>, Bin Qiao<sup>4</sup>, Song Yang<sup>1, 5\*</sup>

- School of Life Sciences, Qingdao Agricultural University, Shandong Province Key Laboratory of Applied Mycology, and Qingdao International Center on Microbes Utilizing Biogas, Qingdao, Shandong Province, China
- College of Chemistry and Pharmacy, Qingdao Agricultural University, Qingdao, Shandong Province, China.
- Central Laboratory, Qingdao Agricultural University, Qingdao, Shandong Province, China
- 4. School of Chemical Engineering and Technology, Tianjin University, Tianjin, China
- 5. Key Laboratory of Systems Bioengineering, Ministry of Education, Tianjin University, Tianjin, China

<sup>\*</sup>Correspondence: Song Yang, School of Life Sciences, Qingdao Agricultural University, Shandong Province Key Laboratory of Applied Mycology, and Qingdao International Center on Microbes Utilizing Biogas, Qingdao, Shandong Province, 266109, China. Email: yangsong1209@163.com. Telephone: +86-532-86080640

<sup>†</sup>Xiao-Ting Shen, Xu-Hua Mo, Li-Ping Zhuand Ling-Ling Tancontributed equally to this work.

Strain	Strain number	r Order	Family	Genus
Pleurotuso streatus	SY10	Agaricales	Pieurotaceae	Pleurotus
Lentinus edodes	SY103	Agaricales	Lentinula	Lentinus
Agaricus bisporus	SY153	Agaricales	Agaraceae	Agaricus
Flammulina velutipes	SY204	Agaricales	Physalacriaceae	Flammulina
Pleurotus eryngii	SY302	Agaricales	Pleurotaceae	Pleurotus
Pleurotus nebrodensis	SY429	Agaricales	Agaricales Pleurotaceae	
Schizophyllum commune	SY658	Agaricales	Schizophyllaceae	Schizophyllum
Grifola frondosa	SY251	Polyporales	Polyporaceae	Grigola
Ganoderma applanatum	SY330	Polyporales	GanodermataceaeDonk	Ganoderma
Ganoderma sinense	SY337	Polyporales	GanodermataceaeDonk	Ganoderma
Ganoderma lucidum	SY341	Polyporales	GanodermataceaeDonk	Ganoderma
Trametes versicolor	SY630	Polyporales	Polyporaceae	Trametes
Trametes robiniophia Murr	SY636	Polyporales	Polyporaceae	Trametes
Phellinus igniarius	SY489	Hymenochaetales	Hymenochaetaceae	Phellinus
Cordycep smilitaris	SY501	Hypocreales	Clavicipitaceae	Cordyceps
Sclerotium Xylariae Nigripis	SY687	Xylariales	Xylariaceae	Sclerotium

Table S1. List of 16 basidiomycetes fungi

M/Z (-)	RT/min	Predictive formula	Difference	Produced by fungus
136.042	3.43	C <sub>7</sub> H <sub>7</sub> NO <sub>2</sub>	newly synthesized	T. RobiniophiaMurr
138.0207	10.65	C <sub>6</sub> H <sub>5</sub> NO <sub>3</sub>	newly synthesized	T. RobiniophiaMurr
147.046	6.60	$C_9H_8O_2$	newly synthesized	T. RobiniophiaMurr
149.0256	8.23	C <sub>6</sub> H <sub>6</sub> N <sub>4</sub> O	newly synthesized	NL2
165.0554	6.60	$C_{9}H_{10}O_{3}$	newly synthesized	T. RobiniophiaMurr
176.0714	4.54	C <sub>10</sub> H <sub>11</sub> NO <sub>2</sub>	newly synthesized	T. RobiniophiaMurr
204.0564	4.54	C <sub>11</sub> H <sub>11</sub> NO <sub>3</sub>	newly synthesized	NL2
218.0808	13.02	C <sub>12</sub> H <sub>13</sub> NO <sub>3</sub>	newly synthesized	T. RobiniophiaMurr
269.1746	15.15	$C_{15}H_{26}O_{4}$	newly synthesized	P. ostreatus
271.0716	2.51	$C_{14}H_{12}N_2O_4$	newly synthesized	T. RobiniophiaMurr
345.2279	9.08	$C_{18}H_{34}O_{6}$	newly synthesized	T. RobiniophiaMurr
363.1112	10.89	$C_{20}H_{12}N_8$	newly synthesized	NL1
365.2677	21.16	$C_{18}H_{34}N_6O_2$	newly synthesized	NL2
371.1203	10.10	$C_{15}H_{16}N_8O_4$	newly synthesized	P. ostreatus
379.0918	3.40	$C_{20}H_{16}N_2O_6$	newly synthesized	NL1
385.1325	11.12	$C_{22}H_{18}N_4O_3$	newly synthesized	NL1
406.1034	2.27	$C_{21}H_{17}N_{3}O_{6}$	newly synthesized	NL1
421.2952	18.48	$C_{25}H_{42}O_5$	newly synthesized	NL1
423.3113	19.07	C <sub>25</sub> H <sub>44</sub> O <sub>5</sub>	newly synthesized	P. ostreatus
425.3266	20.07	$C_{25}H_{46}O_5$	newly synthesized	P. ostreatus
439.3084	15.73	$C_{25}H_{44}O_{6}$	newly synthesized	P. ostreatus
441.3218	15.95	$C_{25}H_{46}O_{6}$	newly synthesized	P. ostreatus
455.3381	21.58	$C_{26}H_{48}O_{6}$	newly synthesized	P. ostreatus
471.3312 *	15.28	$C_{25}H_{46}O_5$	newly synthesized	P. ostreatus
487.3269 *	13.89	$C_{25}H_{46}O_{6}$	newly synthesized	P. ostreatus

Table S2. List of induced features in the co-culture of *T. robiniophilaMurr* and *P. ostreatus*, and corresponding production fungus identified by  $^{13}$ C-labeling analysis.

489.3451 *	12.30	C <sub>25</sub> H <sub>48</sub> O <sub>6</sub>	newly synthesized	P. ostreatus
541.1326	4.29	$C_{27}H_{26}O_{12}$	newly synthesized	NL1
543.1519	2.53	$C_{28}H_{24}N_4O_8$	newly synthesized	NL2
563.3367	18.95	$C_{31}H_{44}N_6O_4$	newly synthesized	P. ostreatus
142.0609	3.39	C <sub>6</sub> H <sub>9</sub> NO <sub>3</sub>	increased ( 13.3±1.7 )	T. RobiniophiaMurr
212.0829	11.36	$C_{10}H_{15}NO_4$	increased ( 25.8±3.2 )	T. RobiniophiaMurr
216.1114	14.51	C <sub>13</sub> H <sub>15</sub> NO <sub>2</sub>	increased ( 23.2±3.7 )	T. RobiniophiaMurr
226.1140	14.04	C <sub>11</sub> H <sub>17</sub> NO <sub>4</sub>	increased ( 8.6±5.3 )	T. RobiniophiaMurr
243.1289	4.14	$C_7 H_{16} N_8 O_2$	increased ( 12.7±2.8 )	T. RobiniophiaMurr
269.1836	15.72	$C_{17}H_{22}N_2O$	increased ( 13.9±5.7 )	T. RobiniophiaMurr
329.1615	15.50	C <sub>25</sub> H <sub>30</sub>	increased ( 25.9±6.4 )	T. RobiniophiaMurr
249.1482	17.93	$C_{14}H_{22}N_2O_2$	increased ( 9.2±3.8 ) #	Both
251.1634	18.01	$C_{14}H_{24}N_2O_2$	increased ( 17.3±3.5 ) #	Both
281.1364	14.36	$C_{14}H_{22}N_2O_4$	increased ( 14.9±4.7 )	P. ostreatus
285.1696	13.31	$C_{14}H_{26}N_2O_4$	increased ( 15.4±3.5 )	P. ostreatus
287.1807	9.17	$C_{14}H_{28}N_2O_4$	increased ( 18.1±3.7 )	P. ostreatus
363.0139	15.88	$C_{21}H_{32}O_5$	increased ( 22.3±4.2 )	P. ostreatus
387.1484	11.70	$C_{\cdot 18}H_{24}N_6O_4$	increased ( 27.3±1.7 )	P. ostreatus
399.2743	14.13	$C_{21}H_{40}N_2O_5$	increased ( 32.1±5.7 )	P. ostreatus

NL1: No <sup>13</sup>C-labeling was observed in the mono-culture after stimulation by the co-culture;NL2: No <sup>13</sup>C-labeling was observed due to low signal intensity in the co-culture;

\* m/z of features were [  $M+CH_2O_2-H$ ];

# Differences of the intensities of m/z 249.1482 and m/z 251.1634 were compared with those in the mono-culture of *P. ostreatus* and in the mono-culture of *T. robiniophilaMurr*, respectively.

Cluster	Scaffold accession	Product type	Start	End	Protein ID	Protein size A.A.	Putative function	Identity with the similar protein by NCBI-BlastP
cluster 1	KL198004.1	Terpene	1663722	1687415				
					KDQ33036	633	hypothetical protein	38%, KIM79710.1, Piloderma croceum F 1598
					KDQ33037	391	TAP42-like protein	59%, OCH93879.1, Obba rivulosa
					KDQ33038	212	GTP binding protein	92%, XP_001874941, Laccaria bicolor \$238N-H82
					KDQ33039	595	Methylenetetrahydrofolate reductase 2	67%, RDB21461.1, Hypsizygus marmoreus
					KDQ33040	183	Metallo-dependent phosphatase	88%, XP_007308813.1, Stereum hirsutum FP-91666 SS1
					KDQ33041	504	transcription factor/hypothetical protein	35%, KPA39034.1, Fusarium langsethiae
					KDQ33042	324	putative mnn4-regulates the mannosylphosphorylation	64%, ESK90200.1, Moniliophthora roreri MCA 2997
					KDQ33043	360	terpenoid synthase	75%, KZT27334.1, Neolentinus lepideus HHB14362 ss-1
					KDQ33044	330	activator of Hsp90 ATPase	61%, PAV23969.1, Pyrrhoderma noxium
					KDQ33045	321	cell division/GTP binding protein	91%, XP_001886019.1, Laccaria bicolor \$238N-H82
cluster 2	KL198004.1	Terpene	1791615	1800958				
					KDQ33083	309	terpenoid synthase	42%, XP_007385857.1, [Punctularia strigosozonata HHB-11173 SS5]
					KDQ33084	265	hypothetical protein	55%, KIM48617.1, Hebeloma cylindrosporum h7]
					KDQ33085	178	COX4 subunit of cytochrome c oxidase	65%, RDB23043.1, Hypsizygus marmoreus
					KDQ33086	363	Clavaminate synthase-like protein	57%, PCH44472.1, Wolfiporia cocos MD-104 SS10
clusster 3	KL198005.1	Terpene	580839	613276				
					KDQ31819	587	SAICAR synthase-like protein	64%, OSD04954.1, [Trametes coccinea BRFM310]
					KDQ31820	1372	Brefeldin A resistance protein	71%, RDB27068.1, [Hypsizygus marmoreus]
					KDQ31821	734	pre-mrna-splicing factor clf1	85%, GAW03472.1, [Lentinula edodes]
					KDQ31822	761	ATP-dependent RNA helicase MAK5	59%, RDB29879.1, [Hypsizygus marmoreus]
					KDQ31823	828	major facilitator superfamily MFS-1	61%, Armillaria gallica]
					KDQ32461	341	terpenoid synthase	77%, PBK90173.1, [Moniliophthora roreri MCA 2997]
					KDQ31824	457	glycosyltransferase family 32 protein	73%, XP_001881036.1, [Laccaria bicolor \$238N-H82]
					KDQ31825	156	hypothetical protein	56%, EGO03782.1, [Serpula lacrymans var. lacrymans \$7.3]
clusster 4	KL198006.1	Terpene	1236848	1268155	5		1	
		-			KDQ30320	313	hypothetical protein	37%, KIJ35026.1, Sphaerobolus stellatus SS14
					KDQ30321	238	lysophospholipase I	59%, XP_001837487.1, Coprinopsis cinerea okayama7#130
					KDQ30322	384	oxysterol binding protein	77%, ESK95501.1, Moniliophthora roreri MCA 2997
					KDQ30323	2084	hypothetical protein Hypma_015013	51%, RDB29315.1, Hypsizygus marmoreus
					KDQ30324	594	Histone-lysine N-methyltransferase	56%, RDB28649.1, Hypsizygus marmoreus
					KDQ30325	306	hypothetical protein	31%, KDQ30319.1, Pleurotus ostreatus PC15
					KDQ30326	168	hypothetical protein	No similar protein
					KDQ30327	60	XRE family transcriptional regulator	33%, WP_086684334.1, Streptomyces pseudogriseolus
					KDQ30328	317	terpenoid synthase	51%, XP_007385857.1, Punctularia strigosozonata HHB-11173 SS5
					KDQ30329	148	hypothetical protein	72%, KDQ54035.1, Jaapia argillacea MUCL 33604
					KDQ30330	703	Actin-like protein arp5	75%, RDB28997.1, Hypsizygus marmoreus
					KDQ30331	207	putative SEC4-like Rab/GTPase	90%, KZP30398.1, Fibularhizoctonia sp. CBS 109695

## Table S3 Putative gene clusters involved in terpene biosynthesis were predicted by AntiSMASH.

cluster 5	KL198007.1	Terpene	2979039	2996202				
				KDQ.	29683.1	415	NAD(P)/FAD-dependent oxidoreductase	60%, WP_117332655.1, Paraburkholderia sp. DHOC27
				KDQ	29913.1	372	hypothetical magnesium transporter, CorA-like protein	86%, XP_001876532.1, Laccaria bicolor \$238N-H82
				KDQ	29684.1	551	thiamin biosynthesis protein	59%, XP_001837535.1, Coprinopsis cinerea okayama7#130
				KDQ.	29685.1	307	terpenoid synthase	38%, OAX36101.1, Rhizopogon vinicolor AM-OR11-026
				KDQ.	29686.1	395	Mitochondrial distribution and morphology protein 34	64%, KNZ76017.1, Termitomyces sp. J132
				KDQ	29687.1	904	hypothetical protein K443DRAFT_95611	54%, KIK03142.1, Laccaria amethystina LaAM-08-1
				KDQ.	29688.1	328	phosphoribosylaminoimidazole-succinocarboxamide synthase	70%, XP_007388959.1, Punctularia strigosozonata HHB-11173 SS5
				KDQ.	29689.1	202	hypothetical protein	33%, RFN51705.1, Fusarium sp. FIESC_12
cluster 6	KL198007.1	Terpene	3003230	3036247				
				KDQ.	29691	262	Protein phosphatase inhibitor 2 (IPP-2)protein	51%, KEP54734.1, Rhizoctonia solani 123E
				KDQ.	29692	347	related to MTD1-methylenetetrahydrofolate dehydrogenase (?	73%, SJL02443.1, Armillaria ostoyae
				KDQ	29693	827	vesicular-fusion protein sec18	74%, GAW01008.1, Lentinula edodes
				KDQ.	29694	346	terpenoid synthase	55%, XP_007868800.1, Gloeophyllum trabeum ATCC 11539
				KDQ.	29695	169	Orm1 type endoplasmic reticulum protein	76%, PBK66949.1, Armillaria solidipes
				KDQ.	29696	250	vacuolar membrane protein	71%, GAW01014.1, Lentinula edodes
				KDQ.	29697	623	UPF0652 protein	77%, KNZ76028.1, Termitomyces sp. J132
				KDQ.	29698	614	Tripeptidyl-peptidase sed3	60%, RDB19145.1, Hypsizygus marmoreus
				KDQ.	29699	405	Eukaryotic translation initiation factor 3 subunit M	60%, RDB19879.1, Hypsizygus marmoreus
				KDQ.	29700	472	MFS general substrate transporter	55%, PCH42368.1, Wolfiporia cocos MD-104 SS10
				KDQ.	29701	499	hypothetical protein Hypma_012032	25%, RDB20806.1, Hypsizygus marmoreus
				KDQ.	29702	241	E3 ubiquitin-protein ligase RNF13	39%, KNZ72777.1, Termitomyces sp. J132
				KDQ.	29703	350	Transcription initiation factor IIB	87%, RDB19847.1, Hypsizygus marmoreus
cluster 7	KL198008.1	Terpene	3486503	3499654				
				KDQ.	28499	371	hypothetical protein	42%, KIM78294.1, Piloderma croceum F 1598
				KDQ.	28500	123	glycoside hydrolase family 3 protein	54%, XP_001878554.1, Laccaria bicolor \$238N-H82
				KDQ.	28501	337	terpenoid synthase	35%, XP_007362402.1, Dichomitus squalens LYAD-421 SS1
				KDQ.	28502	328	hypothetical protein SCP_1502810	39%, GBE89273.1, Sparassis crispa
				KDQ.	28503	312	NAD(P)-binding protein	63%, PCH40180.1, Wolfiporia cocos MD-104 SS10
chieter 8	KT 108000 1	Ternana	180/32	211568				-
cidster o	ALLIY0007.1	reipene	107452	KDO	26324	350	hypothetical protein	no other similar protein
				KDO	26325	209	cytosine permease	32% WP 079489404 1 Maledivibacter halophilus
				KDO	26326	445	Hercynylcysteine sulfoyide lyase	57% RDB27630.1 Hypsizymis marmoraus
				KD0	26327	62	small protein with six-cysteine motif-containing protein	5776, RDD27050.1, Hypsizygds mainteitets
				KDO	26328	496	soualene synthase	72% PBI 03238 1 Armillaria gallica
				KDO	26329	533	Protein RCC2	60% RDB27016 1 Hypsizyous marmoreus
				KDO	26330	428	Hercynylcysteine sulfoxide lyase	56% RDB27630.1 Hypsizygus marmoreus
				KDO	26331	1365	BTB/POZ domain-containing protein 1	46% OAX343361 Rhizoporn vinicolor AM-OR11-026
				KDO	26332	343	heta-lactamase/transpeptidase-like protein	52% PBK65178 Armillaria solidines
						2.2	ere arrange tunopopulato nuo protoni	

cluster 9	KL198009.1	Terpene	1413181	1436188				
					KDQ26760	254	hypothetical protein	no other similar protein
					KDQ26761	328	terpenoid synthase	33%, XP_007385857.1, Punctularia strigosozonata HHB-11173 SS5
					KDQ26762	305	P34-Arc-domain-containing protein	80%, KZP27392.1, Fibularhizoctonia sp. CBS 109695
					KDQ26763	284	NADPH-dependent methylglyoxal reductase GRE2	39%, KIM38281.1, Grifola frondosa
					KDQ26764	513	hypothetical protein PHLGIDRAFT_287083	44%, KIP02588.1, Phlebiopsis gigantea 11061_1 CR5-6
					KDQ26765	174	diaminohydroxyphosphoribosylamino-pyrimidine deaminase	70%, XP_007307627.1, Stereum hirsutum FP-91666 SS1
					KDQ26766	357	CAMK/CAMKL/GIN4 protein kinase	69%, GAT46733.1, Mycena chlorophos
					KDQ26767	1026	Polydeoxyribonucleotide synthase [ATP] 4	70%, Q7Z7W5.1
					KDQ26768	901	Forkhead box protein I3	43%, KXN86593.1, Leucoagaricus sp. SymC.cos
					KDQ26769	520	hypothetical protein PILCRDRAFT_7602	39%, KIM82689.1, Piloderma croceum F 1598
cluster 10	KL1980010.1	Terpene	377075	409519				
					KDQ25267	517	putative monooxygenas	33%, XP_007321663.1, Serpula lacrymans var. lacrymans \$7.9
					KDQ25268	534	squalene epoxidase/Squalene monooxygenase	55%, ALJ76841.1, Taiwanofungus camphoratus
					KDQ25269	350	hypothetical protein	28%, EJD40764.1, Auricularia subglabra TFB-10046 SS5
					KDQ25270	733	terpene synthase/Lanosterol synthase	70%, XP_007870900.1, Gloeophyllum trabeum ATCC 11539
					KDQ25271	406	squalene synthase/farnesyl-diphosphate farnesyltransferase	49%, PAV19342.1, Pyrrhoderma noxium
					KDQ25272	568	putative monooxygenase	33%, XP_007321666.1, Serpula lacrymans var. lacrymans \$7.9
					KDQ25273	553	subtilisin-like protein	56%, XP_007261610.1, Fomitiporia mediterranea MF3/22
					KDQ25274	271	S-adenosylmethionine transporter	75%, OCH91648.1, Obba rivulosa
					KDQ25275	400	putative tRNA-splicing endonuclease subunit sen54	50%, KNZ79720.1, Termitomyces sp. J132
					KDQ25276	214	glycoside hydrolase family 61 protein	68%, KEP47514.1, Rhizoctonia solani 123E
					KDQ25277	242	short chain oxidoreductase	55%, XP_007305294.1, Stereum hirsutum FP-91666 SS1
					KDQ25278	371	Peroxisomal membrane protein PEX29	41%, OBZ68884.1, Grifola frondosa
cluster 11	KL1980010.1	Terpene	1360621	1370113				
					KDQ25605	234	cyclin-like protein	58%, PBK97780.1
					KDQ25606	354	terpenoid synthase	34%, XP_007772031.1
					KDQ25607	683	Nuclear control of ATPase protein 2	41%, RDB17868.1
					KDQ25608	206	hypothetical protein	38%, GAT60266.1
					KDQ25609	405	26S proteasome subunit P45	93%, KZP05231.1
					KDQ25610	197	hypothetical protein	no other similar protein
cluster 12	KL1980010.1	Terpene	1874217	1895254				
					KDQ25806.1	341	hypothetical protein STEHIDRAFT_168254	42%, XP_007303762.1, Stereum hirsutum FP-91666 SS1
					KDQ25807.1	529	adenylate cyclase	42%, CUA69745.1, Rhizoctonia solani
					KDQ25808.1	476	hypothetical protein K443DRAFT_676857	40%, KIK03377.1, Laccaria amethystina LaAM-08-1
					KDQ26263.1	360	terpenoid synthase	75%, KZT27334.1, Neolentinus lepideus HHB14362 ss-1
					KDQ25809.1	380	leucine-rich repeat containing protein	32%, EAY25202.1, Microscilla marina ATCC 23134
					KDQ258010	166	Serine/threonine-protein kinase PLK4	60%, RDB17944.1, Hypsizygus marmoreus

cluster 13	KL1980011.1	Terpene	1022162	1045821				
		•			KDQ24516.1	501	hypothetical protein A7U60_g7568	24%, OCB85557.1, Sanghuangporus baumii
					KDQ24517.1	268	hypothetical protein GALMADRAFT_246490	43%, KDR77205.1, Galerina marginata CBS 339.88
					KDQ24518.1	643	DNA/RNA polymerase	55%, PBK75521.1, Armillaria solidipes
					KDQ24519.1	659	hypothetical protein Hypma	42%, RDB26384.1, Hypsizygus marmoreus
					KDQ24520.1	99	Zinc finger HIT domain-containing protein 1	65%, RDB26081.1, Hypsizygus marmoreus
					KDQ24521.1	910	Cystathionine beta-lyase	73%, RDB26082.1, Hypsizygus marmoreus
					KDQ25140.1	339	terpenoid synthase	70%, PBL03761.1, Armillaria gallica
					KDQ24522.1	208	DNA-directed RNA polymerase RPB5 subunit	84%, XP_007388983.1, Punctularia strigosozonata HHB-11173 SS5
					KDQ24523.1	246	Select seq PCH42341.1 WD40 repeat-like protein	82%, PCH42341.1, Wolfiporia cocos MD-104 SS10
					KDQ24524.1	260	Increased recombination centers protein 22	60%, RDB26386.1, Hypsizygus marmoreus
					KDQ24525.1	320	class I glutamine amidotransferase-like protein	67%, KLO13044.1, Schizopora paradoxa
cluster 14	KL1980011.1	Terpene	1246999	1273897				
					KDQ24603.1	790	AP-3 complex subunit beta-2	61%, RDB31011.1, Hypsizygus marmoreus
					KDQ24604.1	629	Methyltransferase ausD	58%, RDB23458.1, Hypsizygus marmoreus
					KDQ24605.1	1003	calcofluor white hypersensitive protein	61%, ESK82818.1, Moniliophthora roreri MCA 2997
					KDQ24606.1	348	COBW domain-containing protein C15D4.05	67%, RDB31054.1, Hypsizygus marmoreus
					KDQ24607.1	345	terpenoid synthase	30%, XP_007772031.1, Coniophora puteana RWD-64-598 SS2
					KDQ24608.1	191	hypothetical protein Hypma_016157	48%, RDB14947.1, Hypsizygus marmoreus
					KDQ24609.1	500	Membrane protein TMS1	78%, RDB31006.1, Hypsizygus marmoreus
					KDQ24610.1	1028	WD40 repeat-like protein	51%, GBE80545.1, Sparassis crispa
cluster 15	KL1980012.1	Terpene	1308937	1350261				
					KDQ24002.1	205	B-cell receptor-associated 31-like protein	69%, OAX32675.1, Rhizopogon vinicolor AM-OR11-026
					KDQ24003.1	626	L-sorbose 1-dehydrogenase/glucose dehydrogenase	48%, RDB27735.1, Hypsizygus marmoreus
					KDQ24004.1	324	terpenoid synthase	41%, KIY51852.1, Fistulina hepatica ATCC 64428
					KDQ24005.1	514	putative CyP450 monooxygenase	94%, CAJ00405.1, Pleurotus sapidus
					KDQ24006.1	504	cytochrome P450	46%, PBK63697.1, Armillaria solidipes
					KDQ24007.1	339	hypothetical protein	51%, KIM79191.1, Piloderma croceum F 1598
					KDQ24008.1	593	GMC oxidoreductase/L-sorbose 1-dehydrogenase	49%, KIL63993.1, Amanita muscaria Koide BX008
					KDQ24186.1	132	NdufA6 NADH-ubiquinone oxidoreductase 14.8 kDa subunit	72%, OAX37719.1, Rhizopogon vinicolor AM-OR11-026
					KDQ24009.1	204	casein kinase substrate phosphoprotein PP28 protein	59%, EUC64528.1, Rhizoctonia solani AG-3 Rhs1AP
					KDQ24010.1	347	Aldo-keto reductase yakc [NADP(+)]	69%, RDB23525.1, Hypsizygus marmoreus
					KDQ24011.1	582	DUF1365-domain-containing protein	52%, RDB23789.1, Hypsizygus marmoreus
					KDQ24012.1	617	hypothetical protein	38%, KIK38162.1, Suillus luteus UH-Slu-Lm8-n1
					KDQ24013.1	633	hypothetical protein	39%, ESK95859.1, Moniliophthora roreri MCA 2997
					KDQ24014.1	225	hypothetical protein	38%, RXI77973.1, Lactobacillus sp. BCRC 12945
					KDQ24015.1	611	Pyranose dehydrogenase/aryl-alcohol oxidase-like protein	71%, RDB23531.1, Hypsizygus marmoreus

cluster 16	KL1980012.1	Terpene	1749778	1765491				
					KDQ24136.1	208	hypothetical protein	41%, KDR82944.1, Galerina marginata CBS 339.88
					KDQ24137.1	449	glycoside hydrolase family 47	59%, KZP30628.1, Fibularhizoctonia sp. CBS 109695
					KDQ24138.1	407	terpenoid synthase	53%, PBK67540.1, Armillaria solidipes
					KDQ24139.1	273	hypothetical protein	33%, XP_027620911.1, Sparassis crispa
					KDQ24140.1	1024	hypothetical protein	44%, XP_024334700.1, Postia placenta MAD-698-R-SB12
					KDQ24141.1	76	hypothetical cold-regulated 413 plasma membrane protein 2	33%, XP_010690970.1, Beta vulgaris subsp. vulgaris
cluster 17	KL1980013.1	Terpene	618641	642045				
					KDQ23215.1	197	ste ste20 ysk protein kinase	36%, ESK94320.1, Moniliophthora roreri MCA 2997
					KDQ23216.1	500	aldehyde dehydrogenase	74%, GAW04170.1, Lentinula edodes
					KDQ23217.1	514	cytochrome P450 monooxygenase 65	37%, XP_009553326.1, Heterobasidion irregulare TC 32-1
					KDQ23218.1	195	terpenoid synthase	39%, KZT73357.1, Daedalea quercina L-15889
					KDQ23219.1	596	alcohol oxidase	47%, KZV83135.1, Exidia glandulosa HHB12029
					KDQ23220.1	278	GTP-binding protein	49%, KZP07191.1, ibularhizoctonia sp. CBS 109695
					KDQ23221.1	111	Sulfoacetaldehyde acetyltransferase	37%, VDC32956.1, Xinfangfangia sp. CIP 111625
					KDQ23222.1	803	ubiquitin carboxyl-terminal hydrolase 14	70%, KZT00902.1, Laetiporus sulphureus 93-53
					KDQ23223.1	630	actin-like ATPase domain-containing protein	65%, GAW05934.1, Lentinula edodes

Note: The proteins in red color indicates they are oxidases, and the proteins marked with yellow indicates they are terpene synthases.

**Table S4.** Comparisonof genes expression of cluster 15 and cluster 17 between the coculture and mono-culture of *P. ostreatus*. Data were acquired from three independent biological replicates.

Protein ID	Description	MPleos readcount	MPleos FPKM	CPleos readcount	CPleos FPKM	Fold change
Cluster 15						U
KDQ24002	B-cell receptor-associated 31-like protein	1325	12.9	2232	23.1	1.68
KDQ24003	L-sorbose 1-dehydrogenase	1325	12.9	2232	23.1	1.68
KDQ24004	terpenoid synthase	1325	12.9	2232	23.1	1.68
KDQ24005	putative CyP450 monooxygenase	405	10.9	411	11.4	1.01
KDQ24006	cytochrome P450	2704	29	1806	19.9	0.66
KDQ24007	hypothetical protein	2704	29	1806	19.9	0.66
KDQ24008	GMC oxidoreductase	3349	63.7	1201	23.5	0.36
KDQ24186	NdufA6 NADH-ubiquinone oxidoreductase 14.8 kDa subunit	815	38.13	580	28.2	0.71
KDQ24009	casein kinase substrate phosphoprotein PP28 protein	2941	54.3	2571	50.1	0.87
KDQ24010	Aldo-keto reductase	559	176.9	314	96.6	0.56
KDQ24011	DUF1365-domain-containing protein	5914	81.2	1626	22.8	0.27
Cluster 17						
KDQ23215	ste ste20 ysk protein kinase	115	2.1	141	2.68	1.23
KDQ23216	aldehyde dehydrogenase	1587	20.04	539	7.08	0.34
KDQ23217	cytochrome P450 monooxygenase	ND	ND	ND	ND	
KDQ23218	terpenoid synthase	660	13.01	893	18.71	1.35
KDQ23219	GMC oxidoreductase/alcohol oxidase	660	13.01	893	18.71	1.35
KDQ23220	GTP-binding protein	727	32.9	426	20.22	0.59
KDQ23221	Sulfoacetaldehyde acetyltransferase	ND	ND	ND	ND	
KDQ23222	ubiquitin carboxyl-terminal hydrolase 14	726	9.35	934	12.55	1.28
KDQ23223	actin-like ATPase domain- containing protein	2181	51.4	1521	37.88	0.69

Note: MPleos and CPleos stand for the mono-culture and the co-culture, respectively.

Bold label means that genes expression was confirmed by subsequent qRT-PCR analysis.

ND stands for not detected.

Diameter of inhibition zone  $\geq 16$ mm



**Figure S1** Agar diffusion test to screen out an appropriate co-culture system for efficiently inhibiting the growth of *C. albicans* and *C. neoformans*. The results of *C. neoformans* are not shown for brevity.



Figure S2 MS/MS spectra of induced sesterterpene derivatives.



**Figure S3A**<sup>13</sup>C-spectrum of sesterterpene **1** (methanol)



Figure S3B DEPT90° and EPT135° spectrum of sesterterpene 1



Figure S3C<sup>1</sup>H-spectrum of sesterterpene 1



Figure S3D COSY spectrum of sesterterpene 1



Figure S3E HSQC spectrum of sesterterpene1



Figure S3F HMBC spectrum of sesterterpene 1



Figure S3G NOESY spectrum of sesterterpene 1



**Figure S3H**<sup>1</sup>H-spectrum of sesterterpene 2

## 13C NMR AV III 600 in MeOD 439



**Figure S3I**<sup>13</sup>C-spectrum of sesterterpene **2** 



Figure S3J DEPT90° and DEPT135° spectrum of sesterterpene 2



Figure S3K HSQC spectrum of sesterterpene 2



Figure S3L COSY spectrum of sesterterpene 2







Figure S30<sup>1</sup>H-spectrum of sesterterpene 3

