

Fungal-Fungal Co-culture: A Primer for Generating Chemical Diversity

Sonja L. Knowles^a, Huzefa A. Raja^a, Christopher D. Roberts^a, Nicholas H. Oberlies^a

^a Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, Greensboro, NC, United States

Table S1. Fungal-Fungal Co-culture Papers from 2002 to early 2020

Figure S1. Structures of compounds isolated from co-culturing pairing. Refer to Supporting Information Table S1.

Table S1. Fungal-Fungal Co-culture Papers from 2002 to early 2020

Fungi	Taxonomy Phylum level/Ordinal level	Secondary Metabolites (N = New, K= Known)	Biological Activity	Reference
<i>Aspergillus sulphureus</i> and <i>Isaria felina</i>	Ascomycota/Eurotiales vs. Hypocreales	17-hydroxynotoamide D (N) 44 17-O-ethylnotoamide M (N) 45 10-O-acetylsclerotiamide (N) 46 10-O-ethylsclerotiamide (N) 47 10-O-ethylnotoamide R (N) 48 (-)-notoamide B (K) 49 notoamide C (K) 50 dehydronotoamide C (K) 51 notoamide D (K) 52 notoamide F (K) 53 notoamide Q (K) 54 17-epi-notoamide Q (K) 55 notoamide M (K) 56 sclerotiamide (K) 57	Inhibition of colony formation prostate cancer cells at non-cytotoxic concentration 10uM (45)	Afiyatullov, S.S., Zhuravleva, O.I., Antonov, A.S., Berdyshev, D.V., Pivkin, M.V., Denisenko, V.A., Popov, R.S., Gerasimenko, A.V., von Amsberg, G., Dyshlovoy, S.A., Leshchenko, E.V., Yurchenko, A.N. Prenylated indole alkaloids from co-culture of marine-derived fungi <i>Aspergillus sulphureus</i> and <i>Isaria felina</i> . <i>J. Antibiot.</i> 2018, 71.
<i>Eutypa lata</i> and <i>Botryosphaeria obtuse</i>		2-nonanone (K) 83 O-methylmellein (K) 84	Antifungal (83, 84)	Azzollini, A.; Boggia, L.; Boccard, J.; Sgorbini, B.; LeCoultrre, N.; Allard, P.-M.; Rubiolo, P.; Rudaz, S.; Gindro, K.; Bicchi, C. Dynamics of metabolite induction in fungal co-cultures by metabolomics at both volatile and non-volatile levels. <i>Front. Microbiol.</i> 2018, 9, 72.
<i>Aspergillus sclerotiorum</i> and <i>Penicillium citrinum</i>	Ascomycota/Onygenales vs. Hypocreales	sclerotiorumin A (N) 68 sclerotiorumin B (N) 69 sclerotiorumin C (N) 67 1-(4-benzyl-1H-pyrrol-3-yl)ethenone (N) 64 aluminiumneohydroxyaspergillin (N) 79 ferrineohydroxyaspergillin (N) 80	Cytotoxic (79)	Bao, J., Wang, J., Zhang, X.-Y., Nong, X.-H., Qi, S.-H. New furanone derivatives and alkaloids from the co-culture of marine-derived fungi <i>Aspergillus sclerotiorum</i> and

		neoaspergillic acid (K) 178		Penicillium citrinum. Chem. Biodiv. 2017, 14, e1600327
<i>Paraconiothyrium variabile</i> and <i>Fusarium oxysporum</i>		Beauvericin (K) 88	Fungi-static (88) Cell toxicity at higher levels	Bärenstrauch, M.; Mann, S.; Jacquemin, C.; Bibi, S.; Sylla, O.-K.; Baudouin, E.; Buisson, D.; Prado, S.; Kunz, C. Molecular crosstalk between the endophyte <i>Paraconiothyrium variabile</i> and the phytopathogen <i>Fusarium oxysporum</i> —modulation of lipoxygenase activity and beauvericin production during the interaction. Fungal Genet. Biol. 2020, 103383.
<i>Trichophyton rubrum</i> and <i>Bionectria ochroleuca</i> .		4-hydroxysulfoxy-2,2-dimethylthielavin P (N) 179		Bertrand, S., Schumpp, O., Bohni, N., Monod, M., Gindro, K., Wolfender, J.-L. De novo production of metabolites by fungal co-culture of <i>Trichophyton rubrum</i> and <i>Bionectria ochroleuca</i> . J. Nat. Prod. 2013, 76, 1157-1165.
<i>Sarocladium strictum</i> and <i>Fusarium oxysporum</i>		Fusaric acid (K) 180		Bohni, N., Hofstetter, V., Gindro, K., Buyck, B., Schumpp, O., Bertrand, S., Monod, M., Wolfender, J.-L. Production of Fusaric Acid by <i>Fusarium</i> spp. in Pure Culture and in Solid Medium Co-Cultures. Molecules 2016, 21, 370.
<i>Alternaria tenuissima</i> and <i>Nigrospora sphaerica</i>		Stemphyrylenol (K) 1 Alterperylenol (K) 2	Antifungal (1)	Chagas, F.O., Dias, L.G., Pupo, M.T. A mixed culture of

		altertoxin I (K) 3 alternariol (K) 4 alternariol monomethyl ether (K) 5		endophytic fungi increases production of antifungal polyketides. J. Chem. Ecol. 2013, 39, 1335- 1342.
<i>Paraconiothyrium variabile</i> and <i>Fusarium oxysporum</i>		13-oxo- 9,11-octadecadienoic acid (K) 81 13-hydroperoxy-9,11-octadecadienoic acid (K) 82 Beauvericin (K) 88		Combès, A., Ndoye, I., Bance, C., Bruzaud, J., Djediat, C., Dupont, J., Nay, B., Prado, S., 2012. Chemical Communication between the Endophytic Fungus <i>Paraconiothyrium</i> <i>Variabile</i> and the Phytopathogen <i>Fusarium oxysporum</i> . PLoS One 7(10), e47313.
Two mangrove fungi (strain Nos. K38 and E33)		(-)byssochlamic acid imide (N) 43	Antifungal (43)	Ding, W., Lu, Y., Feng, Z., Luo, S., Li, C., 2017. A New Nonadride Derivative from the Co-Culture Broth of Two Mangrove Fungi. Chem. Nat. Compd. 53(4), 691-693.
<i>Eutypa lata</i> and <i>Botryosphaeria obtusa</i>	Ascomycota/ Xylariales vs. Botryosphaerales	O-methylmellein (K) 84 Diastereoisomer 1 of 4-Hydroxy-8-O- methylmellein (K) 86 Diastereoisomer 2 of 4-Hydroxy-8-O- methylmellein (K) 87 5-Hydroxy-8-O-methylmellein (N) 85	Antifungal (84) Antigerminative (84)	Glauser, G., Gindro, K., Fringeli, J., De Joffrey, J.-P., Rudaz, S., Wolfender, J.-L. Differential analysis of mycoalexins in confrontation zones of grapevine fungal pathogens by ultrahigh pressure liquid chromatography/time- of-flight mass spectrometry and capillary nuclear magnetic resonance. J. Agric. Food Chem. 2009, 57, 1127-1134.
<i>Pseudoxylaria</i> sp. X802 and <i>Coriolopsis</i> sp.		pseudoxylallemycin A (N) 181 pseudoxylallemycin B (N) 182	Antimicrobial (181 – 184)	Guo, H., Kreuzenbeck, N.B., Otani, S., Garcia-Altares, M.,

		pseudoxylallemycin C (N) 183 pseudoxylallemycin D (N) 184 pseudoxylallemycin E (N) 185 pseudoxylallemycin F (N) 186 eucalyptene A (K) 187 terricollene C (K) 188 19,20-epoxycytochalasin C (K) 189 19,20-epoxycytochalasin D (K) 190 19,20- epoxycytochalasin Q (K) 191		Dahse, H.-M., Weigel, C., Aanen, D.K., Hertweck, C., Poulsen, M., Beemelmanns, C. Pseudoxylallemycins A–F, Cyclic Tetrapeptides with Rare Allenyl Modifications Isolated from <i>Pseudoxylaria</i> sp. X802: A Competitor of Fungus-Growing Termite Cultivars. <i>Org. Lett.</i> 2016, 18, 3338–3341.
<i>Hypoxyロン rubiginosum</i> (9969) and <i>Hymenoscyphus fraxineus</i> (VER/2)		Phomopsidin (K) 192 10-hydroxyphomopsidin (N) 193 Viridiol (K) 194	Antimicrobial (192, 194)	Halecker, S.; Wennrich, J.-P.; Rodrigo, S.; Andrée, N.; Rabsch, L.; Baschien, C.; Steinert, M.; Stadler, M.; Surup, F.; Schulz, B. Fungal endophytes for biocontrol of ash dieback: The antagonistic potential of <i>Hypoxyロン rubiginosum</i> . <i>Fungal Ecology</i> 2020, 45, 100918.
Phomopsis sp. K38 and <i>Alternaria</i> sp. E33	Ascomycota/ Pleosporales vs. Pleosporales	cyclo (D-Pro-L-Tyr-L-Pro-L-Tyr) (N) 59 cyclo (Gly-L-Phe-L-Pro-L-Tyr) (N) 58	Antifungal (58,59)	Huang, S., Ding, W., Li, C., Cox, D. Two new cyclopeptides from the co-culture broth of two marine mangrove fungi and their antifungal activity. <i>Pharmacogn. Mag.</i> 2014, 10, 410–414.
<i>Aspergillus fischeri</i> and <i>Xylaria flabelliformis</i>	.	Sartorypyrone A (K) 98 Aszonalenin (K) 92 Acetylaszonalenin (K) 93 Fumitremorgin A (K) 89 Fumitremorgin B (K) 90 C-11 epimer of verruclogen TR-2 91		Knowles, S. L.; Raja, H. A.; Isawi, I. H.; Flores-Bocanegra, L.; Reggio, P. H.; Pearce, C. J.; Burdette, J. E.; Rokas, A.; Oberlies, N. H. Wheldone: Characterization of a Unique Scaffold from

		Griseofulvin (K) 94 Dechlorogriseofulvin (K) 95 Dechloro-5-hydroxygrisoefulvin (K) 96 5-hydroxygriseofulvin (K) 108 7-O-acetylcytochalasin B (K) 97 hirsutatin A (K) 103 zygosporin E (K) 102 cytochalasin C (K) 99 cytochalasin D (K) 100 cytochalasin Q (K) 101		the Coculture of <i>Aspergillus fischeri</i> and <i>Xylaria flabelliformis</i> . Org. Lett. 2020, 22, 1878-1882.
<i>Aspergillus fischeri</i> and <i>Xylaria cubensis</i>	Ascomycota/ Eurotiales vs. <i>Xylariales</i>	Wheldone (N) 104	Cytotoxic (104)	Knowles, S. L.; Raja, H. A.; Wright, A. J.; Lee, A. M. L.; Caesar, L. K.; Cech, N. B.; Mead, M. E.; Steenwyk, J. L.; Ries, L.; Goldman, G. H.; Rokas, A.; Oberlies, N. H. Mapping the Fungal Battlefield: Using <i>in situ</i> Chemistry and Deletion Mutants to Monitor Interspecific Chemical Interactions Between Fungi. <i>Front. Microbiol.</i> 2019, 10, 285.
<i>Penicillium</i> sp. and <i>Trichoderma</i> sp.		(Z)-2-ethylhex-2-enedioic acid (N) 195 (E)-4-oxo-2-propylideneoct-7-enoic acid (N) 196		Kossuga, M.H., Ferreira, A.G., Sette, L.D., Berlinck, R.G.S. Two Polyketides from a Co-culture of Two Marine-derived Fungal Strains. <i>Nat. Prod. Commun.</i> 2013, 8, 721-724.
<i>Camporesia sambuci</i> FT1061 and <i>Epicoccum sorghinum</i> FT1062	Ascomycota/ <i>Xylariales</i> vs. <i>Pleosporales</i>	11S-hydroxy-1-methoxyfusaricide (N) 34 epicoccarine B (K) 33 (+)-epipyridone (K) 35 D8646-2-6 (K) 36	Antifungal (36, 37) Anti-proliferative (33)	Li, C., Sarotti, A., Yang, B., Turkson, J., Cao, S. A New N-methoxypyridone from the Co-Cultivation of Hawaiian Endophytic Fungi <i>Camporesia</i>

		iso-D8646-2-6 (K) 37		sambuci FT1061 and Epicoccum sorghinum FT1062. Molecules 2017, 22, 1166
<i>Phomopsis</i> sp. K38 and <i>Alternaria</i> sp. E33	Ascomycota/ Pleosporales vs. Pleosporales	cyclo-(L-leucyl- trans-4-hydroxy-L-prolyl-D-leucyl-trans-4- hydroxy-L-proline) (N) 60	Antifungal (60)	Li, C., Wang, J., Luo, C., Ding, W., Cox, D.G. A new cyclopeptide with antifungal activity from the co-culture broth of two marine mangrove fungi. Nat. Prod. Res. 2014, 28, 616-621.
<i>Phomopsis</i> sp. K38 and <i>Alternaria</i> sp. E33	Ascomycota/ Pleosporales vs. Pleosporales	8-hydroxy-3-methyl-9-oxo-9H-xanthene-1- carboxylic acid methyl ether (N) 61	Antifungal (61)	Li, C., Zhang, J., Shao, C., Ding, W., She, Z., Lin, Y. A new xanthone derivative from the co-culture broth of two marine fungi (strain No. E33 and K38). Chem. Nat. Compd. 2011, 47, 382-384.
<i>Phomopsis</i> sp. K38 and <i>Alternaria</i> sp. E33	Ascomycota/ Pleosporales vs. Pleosporales	(-) -byssochlamic acid bisdiimide (N) 42	Weak cytotoxicity (42)	Li, C.-Y.; Ding, W.-J.; Shao, C.-L.; She, Z.-G.; Lin, Y.-C. A new diimide derivative from the co-culture broth of two mangrove fungi (strain no. E33 and K38). Journal of Asian Natural Products Research 2010, 12, 809-813
<i>Phoma</i> sp. and <i>Armillaria</i> sp.	Ascomycota vs. Basidiomycota/Pleosporales vs. Agaricales	Phexandiol A (N) 10 Phexandiol B (N) 11 Phomester A (N) 7 Phomester B (N) 8 Phomester C (N) 9		Li, H.-T., Zhou, H., Duan, R.-T., Li, H.-Y., Tang, L.-H., Yang, X.-Q., Yang, Y.-B., Ding, Z.-T. Inducing Secondary Metabolite Production by Co-culture of the Endophytic Fungus <i>Phoma</i> sp. and the Symbiotic Fungus <i>Armillaria</i> sp. J. Nat. Prod. 2019, 82, 1009–1013.

<p>Sexual <i>Aspergillus alliaceus</i> and asexual <i>Aspergillus alliaceus</i></p>	<p>Ascomycota/ Eurotiales vs. Eurotiales</p>	<p>Allianthrone A (N) 18 Allianthrone B (N) 19 Allianthrone C (N) 20</p>	<p>Cytotoxic (18)</p>	<p>Mandelare, P.; Adressa, D.; Kaweesa, E.; Zakharov, L.; Loesgen, S. Coculture of two developmental stages of a marine-derived <i>Aspergillus alliaceus</i> results in the production of the cytotoxic bianthrone allianthrone A. <i>J. Nat. Prod.</i> 2018, 81, 1014-1022.</p>
<p><i>Penicillium citrinum</i> and <i>Beauveria felina</i></p>		<p>Citrifelin A (N) 109 Citrifelin B (N) 110 dicitrinin A (K) 111 dihydrocitrinone (K) 112 decarboxydihydrocitrinone (K) 113 destruxin A (K) 114 roseotoxin B (K) 115 isaridin A (K) 116 isaridin B (K) 117</p>	<p>Antimicrobial (109, 110, 113)</p>	<p>Meng, L.-H., Liu, Y., Li, X.-M., Xu, G.-M., Ji, N.-Y., Wang, B.-G., 2015. Citrifelins A and B, Citrinin Adducts with a Tetracyclic Framework from Cocultures of Marine-Derived Isolates of <i>Penicillium citrinum</i> and <i>Beauveria feline</i>. <i>J. Nat. Prod.</i> 2015, 78, 2301-2305.</p>
<p><i>Talaromyces pinophilus</i> and <i>Paraphaeosphaeria</i> sp.</p>		<p>talarodone A (N) 118 penicidone C (K) 119 penicidone D (K) 120</p>		<p>Murakami, S.; Hayashi, N.; Inomata, T.; Kato, H.; Hitora, Y.; Tsukamoto, S. Induction of secondary metabolite production by fungal co-culture of <i>Talaromyces pinophilus</i> and <i>Paraphaeosphaeria</i> sp. <i>Journal of Natural Medicines</i> 2020, 1-5.</p>
<p><i>Penicillium pinophilum</i> FKI-5653 and <i>Trichoderma harzianum</i> FKI-5655</p>		<p>secopenicillide C (N) 121 penicillide (K) 122 MC-141 (K) 123 pestalasin A (K) 124 stromemycin (K) 125</p>		<p>Nonaka, K., Abe, T., Iwatsuki, M., Mori, M., Yamamoto, T., Shiomi, K., Omura, S., Masuma, R. Enhancement of metabolites productivity of <i>Penicillium</i></p>

				pinophilum FKI-5653, by co-culture with Trichoderma harzianum FKI-5655. J. Antibiot. 2011, 64, 769-774.
<i>Talaromyces siamensis</i> FKA-61 and <i>Phomopsis</i> sp. FKA-62		BE-31405 (K) 126	Antifungal(126)	Nonaka, K., Iwatsuki, M., Horiuchi, S., Shiomi, K., Omura, S., Masuma, R. Induced production of BE-31405 by coculturing of <i>Talaromyces siamensis</i> FKA-61 with a variety of fungal strains. J. Antibiot. 2015, 68, 573-578.
<i>IrpeX lacteus</i> and <i>Phaeosphaeria oryzae</i>	Basidiomycota vs. Ascomycota/ Polyporales vs. Pleosporales	IrpeXine (N) 41 Hypoxyxylone (K) 40		Sadahiro, Y.; Kato, H.; Williams, R. M.; Tsukamoto, S. IrpeXine, an Isoindolinone Alkaloid Produced by Coculture of Endophytic Fungi, <i>IrpeX lacteus</i> and <i>Phaeosphaeria oryzae</i> . J. Nat. Prod. 2020, 85, 1368-1373.
<i>Chaunopycnis</i> sp. and <i>Trichoderma hamatum</i>	Ascomycota/ Hypocreales vs. Hypocreales	chaunopyran A (N) 78 pyridoxatin (K) 66 methyl-pyridoxatin (N) 65		Shang, Z., Salim, A.A., Capon, R.J. Chaunopyran A: Co-Cultivation of Marine Mollusk-Derived Fungi Activates a Rare Class of 2-Alkenyl-Tetrahydropyran. J. Nat. Prod. 2017, 80, 1167-1172.
<i>Trametes robiniophila</i> Murr and <i>Pleurotus ostreatus</i>		postrediene A (N) 127 postrediene B (N) 128 postrediene C (N) 129	Antifungal(127, 128, 129)	Shen, X.-T., Mo, X.-H., Zhu, L.-P., Tan, L.-L., Du, F.-Y., Wang, Q.-W., Zhou, Y.-M., Yuan, X.-J., Qiao, B., Yang, S. Unusual and highly bioactive sesterterpenes synthesized by

				Pleurotus ostreatus during the co-culture with Trametes robiophila Murr. Appl. Environ. Microbiol. 2019, 85, AEM.00293-19
<i>Paraconiothyrium SSM001</i> and <i>Phomopsis</i> sp.		Taxol (K) 130		Soliman, S.S.M., Raizada, M.N. Interactions between co-habitating fungi elicit synthesis of Taxol from an endophytic fungus in host <i>Taxus</i> plants. Front. Microbiol. 2013, 4, 3
<i>Penicillium fuscum</i> and <i>Penicillium camembertii/clavigerum</i>	Ascomycota/ Eurotiales vs. Eurotiales	berkeleylactone A (N) 70 berkeleylactone B (N) 71 berkeleylactone C (N) 72 berkeleylactone D (N) 73 berkeleylactone E (N) 74 berkeleylactone F (N) 75 berkeleylactone G (N) 76 berkeleylactone H (N) 77 A26771B (K) 197	Antimicrobial (70 - 76)	Stierle, A.A., Stierle, D.B., Decato, D., Priestley, N.D., Alverson, J.B., Hoody, J., McGrath, K., Klepacki, D., The Berkeleylactones, Antibiotic Macrolides from Fungal Coculture. J. Nat. Prod. 2017, 80, 1150-1160.
<i>Moniliophthora roreri</i> and <i>Trichoderma harzianum</i>		T39 butenolide (K) 107 Harzianolide (K) 106 Sorbicillinol (K) 105		Tata, A., Perez, C., Campos, M.L., Bayfield, M.A., Eberlin, M.N., Ifa, D.R. Imprint Desorption Electrospray Ionization Mass Spectrometry Imaging for Monitoring Secondary Metabolites Production during Antagonistic Interaction of Fungi. Anal. Chem. 2015, 87, 12298-12305.
Two Marine Fungi (STRAIN Nos. E33 AND K38) (Wang, J.)	NA	Ethyl 5-Ethoxy-2-formyl-3-hydroxy-4-methylbenzoate (N) 63	Antifungal (63)	Wang, J., Ding, W., Li, C., Huang, S., She,

et al., 2013)				Z., Lin, Y. A New Polysubstituted Benzaldehyde from the co-culture broth of Two Marine Fungi (Strains Nos. E33 and K38). Chem. Nat. Compd. 2013, 49, 799-802.
Fungi E33 and K38 (Wang et al., 2015)		7-(γ,γ -dimethylallyloxy)-6-hydroxy-4-methylcoumarin (N) 62	Antifungal (62)	Wang, J., Huang, S., Li, C., Ding, W., She, Z., Li, C. A New Coumarin Produced by Mixed Fermentation of Two Marine Fungi. Chem. Nat. Compd. 2015, 51, 239-241.
<i>Fusarium tricinctum</i> and <i>Fusarium begoniae</i>		subenniatin A (N) 131 subenniatin B (N) 132		Wang, J.-p., Lin, W., Wray, V., Lai, D., Proksch, P. Induced Production of Depsipeptides by Co-Culturing <i>Fusarium tricinctum</i> and <i>Fusarium begoniae</i> . Tetrahedron Lett. 2013, 54, 2492-2496.
<i>Aspergillus flavipes</i> and <i>Chaetomium globosum</i>		Aspochalasinol A (N) 133 Aspochalasinol B (N) 134 Aspochalasinol C (N) 135 Aspochalasinol D (N) 136 Oxichaetoglobosin A (N) 137 Oxichaetoglobosin B (N) 138 Oxichaetoglobosin C (N) 139 Oxichaetoglobosin D (N) 140 Oxichaetoglobosin E (N) 141 Oxichaetoglobosin F (N) 142 Oxichaetoglobosin G (N) 143 Oxichaetoglobosin H (N) 144 Oxichaetoglobosin I (N) 145 chaetoglobosin D (K) 146 chaetoglobosin C (K) 147 epicoccine (K) 148 epicocconigrone (K) 149 chaetomugilide B (K) 150	antiproliferative activities (140, 143, 135, 139, 141, 142)	Wang, W.; Gong, J.; Liu, X.; Dai, C.; Wang, Y.; Li, X.-N.; Wang, J.; Luo, Z.; Zhou, Y.; Xue, Y.; Zhu, H.; Chen, C.; Zhang, Y. Cytochalasans produced by the coculture of <i>Aspergillus flavipes</i> and <i>Chaetomium globosum</i> . J. Nat. Prod. 2018, 81, 1578-1587.
<i>Trametes versicolor</i> and		2,5,6-trihydroxy-4,6-diphenylcyclohex-4-ene-	Antioxidant and anticancer	Xu, X.-Y., Shen, X.-

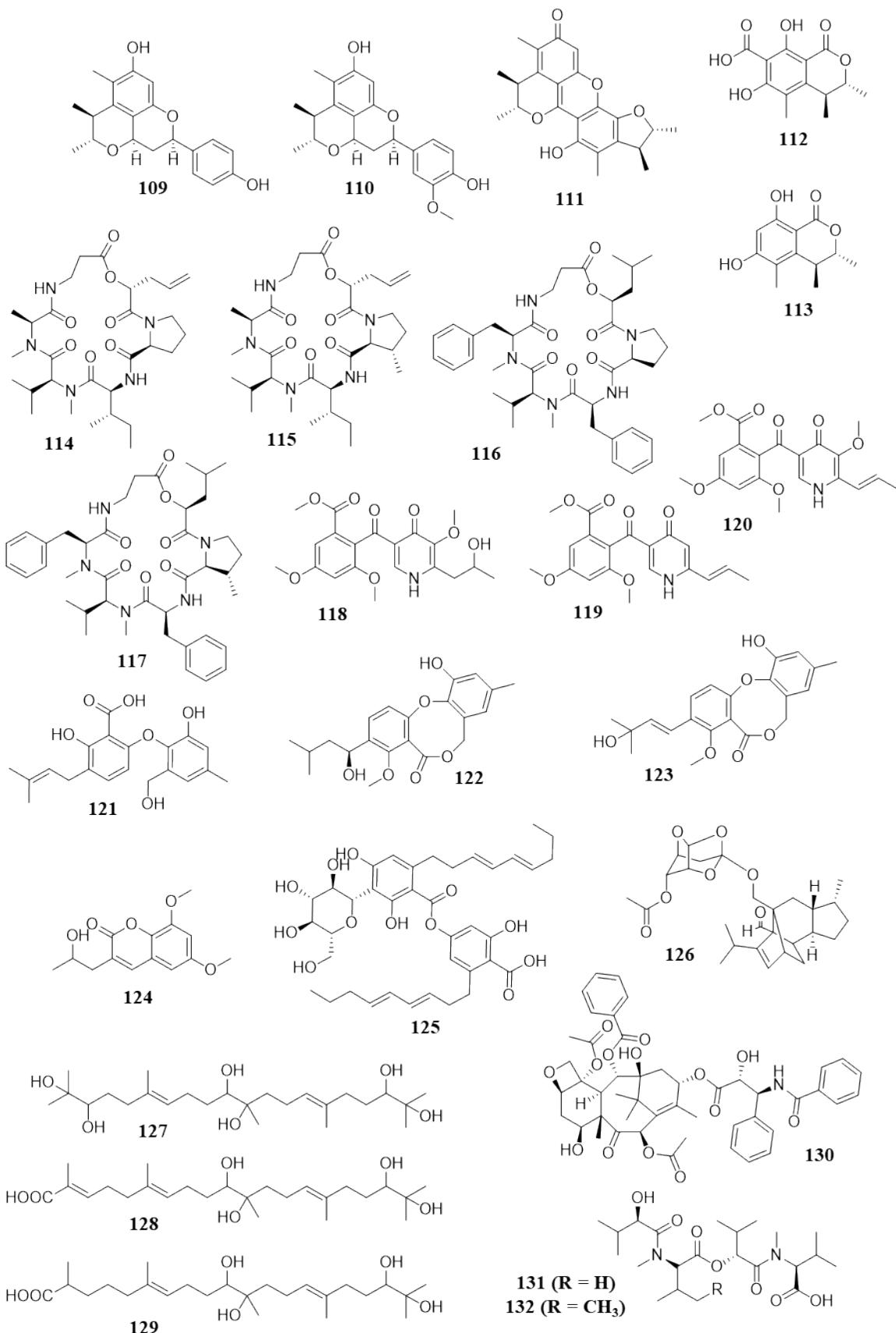
<i>Ganoderma applanatum</i>		1,3-dione) (N) 151 oresellinic acid (N) 152	(151 , 152)	T., Yuan, X.-J., Zhou, Y.-M., Fan, H., Zhu, L.-P., Du, F.-Y., Sadilek, M., Yang, J., Qiao, B., Yang, S. Metabolomics Investigation of an Association of Induced Features and Corresponding Fungus during the Co-culture of <i>Trametes versicolor</i> and <i>Ganoderma applanatum</i> . <i>Front. Microbiol.</i> 2018, 8, 2647.
<i>Aspergillus sydowii</i> EN-534 and <i>Penicillium citrinum</i> EN-535	Ascomycota/Eurotiales vs. Eurotiales	seco-penicitrinol A (N) 21 penicitrinol L (N) 22	Moderate anti-influenza (21)	Yang, S.-Q., Li, X.-M., Li, X., Li, H.-L., Meng, L.-H., Wang, B.-G. New citrinin analogues produced by coculture of the marine algal-derived endophytic fungal strains <i>Aspergillus sydowii</i> EN-534 and <i>Penicillium citrinum</i> EN-535. <i>Phytochem. Lett.</i> 2018, 25, 191-195
<i>Trametes versicolor</i> and <i>Ganoderma applanatum</i>		3-phenyllactic acid (K) 153 N-(4-methoxyphenyl)formamide 2-O- β -D-xyloside (N) 154 N-(4-methoxyphenyl)formamide 2-O- β -D-xylobioside (N) 155		Yao, L.; Zhu, L.-P.; Xu, X.-Y.; Tan, L.-L.; Sadilek, M.; Fan, H.; Hu, B.; Shen, X.-T.; Yang, J.; Qiao, B.; Yang, S. Discovery of novel xylosides in co-culture of basidiomycetes <i>Trametes versicolor</i> and <i>Ganoderma applanatum</i> by integrated metabolomics and bioinformatics. <i>Sci. Rep.</i> 2016, 6, 33237.
<i>Penicillium crustosum</i> PRB-2 and <i>Xylaria</i> sp. HDN13-249		Penixylarin A (N) 156 Penixylarin B (N) 157	Antibacterial (157 , 158 , 160 , 161)	Yu, G., Sun, Z., Peng, J., Zhu, M., Che, Q., Zhang, G., Zhu, T.,

		Penixylarin C (N) 158 Penixylarin D (N) 159 1,3-dihydroxy-5-(12-hydroxyheptadecyl)benzene (K) 160 1,3-dihydroxy-5-(12-sulfoxyheptadecyl)benzene (K) 161		Gu, Q., Li, D. Secondary Metabolites Produced by Combined Culture of <i>Penicillium crustosum</i> and a <i>Xylaria</i> sp. J. Nat. Prod. 2019, 82, 2013–2017
<i>Talaromyces aculeatus</i> and <i>Penicillium variabile</i>		Penitalarin A (N) 162 Penitalarin B (N) 163 Penitalarin C (N) 164 nafuredin B (N) 165 nafuredin A (K) 166	Cytotoxic (165)	Zhang, Z., He, X., Zhang, G., Che, Q., Zhu, T., Gu, Q., Li, D. Inducing Secondary Metabolite Production by Combined Culture of <i>Talaromyces aculeatus</i> and <i>Penicillium variabile</i> . J. Nat. Prod. 2017, 80, 3167–3171
<i>Nigrospora oryzae</i> and <i>Beauveria bassiana</i>	Ascomycota/Xylariales vs. Hypocreales	Nigbeauvin A (N) 28 Nigbeauvin B (N) 29 Nigbeauvin C (N) 30 Nigbeauvin D (N) 31 Nigbeauvin E (N) 32		Zhang, Z.-X., Yang, X.-Q., Zhou, Q.-Y., Wang, B.-Y., Hu, M., Yang, Y.-B., Zhou, H., Ding, Z.-T. New Azaphilones from <i>Nigrospora oryzae</i> Co-Cultured with <i>Beauveria bassiana</i> . Molecules 2018, 23, 1816.
<i>Nigrospora oryzae</i> and <i>Irpe lacteus</i>	Ascomycota vs. Basidiomycota/Xylariales vs. Polyporales	Nigirpexin A (N) 23 Nigirpexin B (N) 24 Nigirpexin C (N) 25 Nigirpexin D (N) 26 Nigrosirpexin A (N) 27		Zhou, Q.-Y., Yang, X.-Q., Zhang, Z.-X., Wang, B.-Y., Hu, M., Yang, Y.-B., Zhou, H., Ding, Z.-T. New azaphilones and tremulane sesquiterpene from endophytic <i>Nigrospora oryzae</i> cocultured with <i>Irpe lacteus</i> . Fitoterapia 2018, 130, 26–30
Two isolates of <i>Aspergillus</i> sp.	Ascomycota/Eurotiales vs. Eurotiales	Asperginin (N) 6 Neoaspergillic acid (K) 178	Antibacterial (6)	Zhu, F., Chen, G., Chen, X., Huang, M., Wan, X. Asperginin, a new antibacterial alkaloid produced by mixed fermentation of

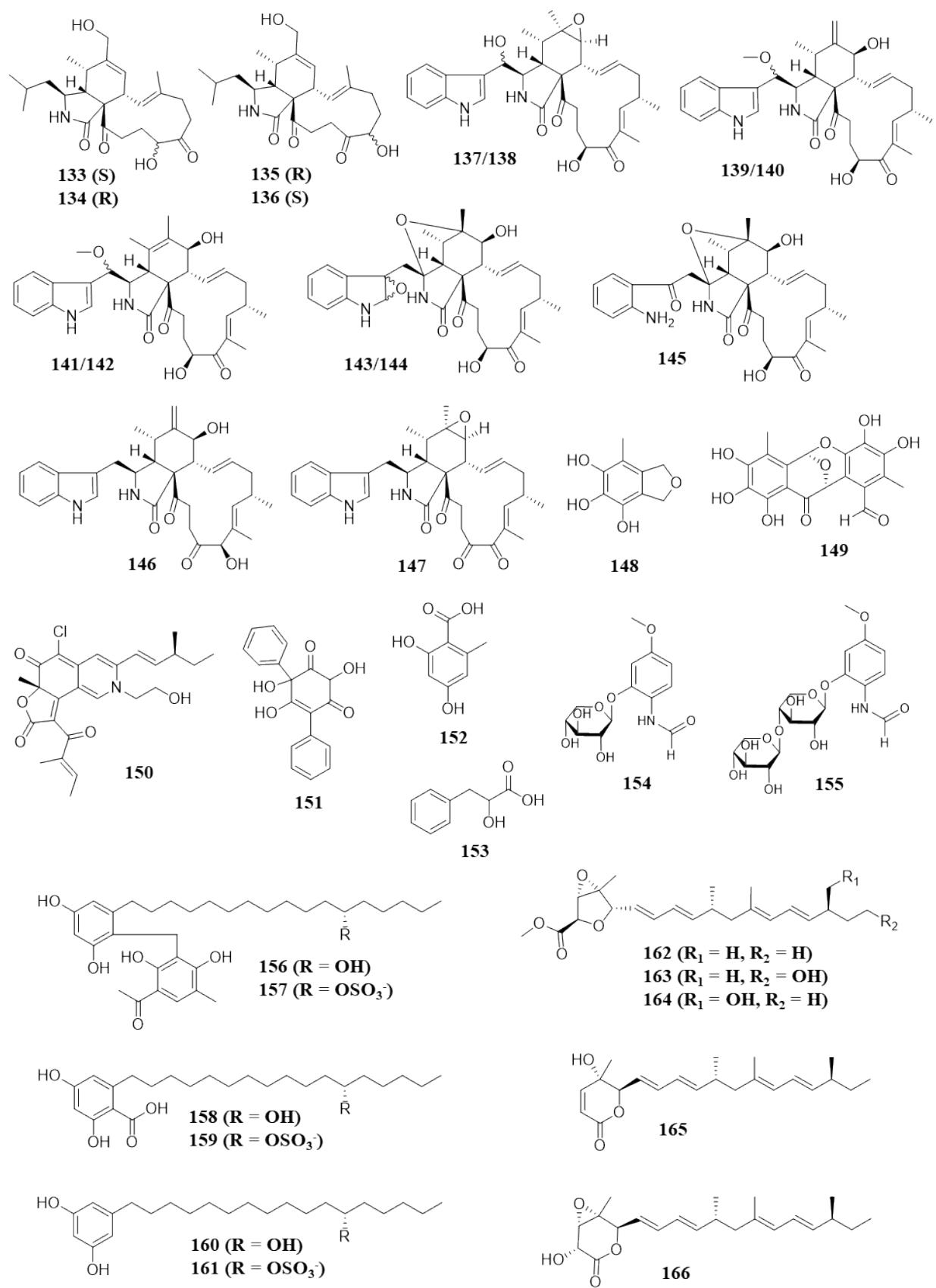
				two marine-derived mangrove epiphytic fungi. <i>Chem. Nat. Compd.</i> 2011, 47, 767-769.
Marine fungal strains (Nos. 1924 and 3893)	NA	Marinamide (N) 38 methyl ester Marinamide (N) 39	Cytotoxic (38, 39) Antibacterial (38, 39)	Zhu, F., Lin, Y. Marinamide, a novel alkaloid and its methyl ester produced by the application of mixed fermentation technique to two mangrove endophytic fungi from the South China Sea. <i>Chinese Sci. Bull.</i> 2006, 51, 1426-1430. Structural revision Zhu, F.; Chen, G.; Wu, J.; Pan, J. Structure revision and cytotoxic activity of marinamide and its methyl ester, novel alkaloids produced by co-cultures of two marine-derived mangrove endophytic fungi. <i>Natural product research</i> 2013, 27, 1960-1964.
<i>Nigrospora oryzae</i> and <i>Collectotrichum gloeosporioides</i> , <i>Irpe lacticus</i>		nigrosirpxin B (N) 167 nigrosirpxin C (N) 168 nigirpxin E (N) 169 nigrosirpxin D (N) 170 nigrosirpxin E (N) 171 nigcollin A (N) 172 nigcollin B (N) 173 nigcollin C (N) 174 nigcollin D (N) 175 nigcollin E (N) 176 nigrosirpxin F (N) 177		Shi, L.-J.; Wu, Y.-M.; Yang, X.-Q.; Xu, T.-T.; Yang, S.; Wang, X.-Y.; Yang, Y.-B.; Ding, Z.-T. The Cocultured <i>Nigrospora oryzae</i> and <i>Collectotrichum gloeosporioides</i> , <i>Irpe lacticus</i> , and the Plant Host <i>Dendrobium officinale</i> Bidirectionally Regulate the Production of Phytoxins by Anti-phytopathogenic Metabolites. <i>J. Nat.</i>

				Prod. 2020, 83, 1374-1382.
<i>Phoma</i> sp. YUD17001 and <i>Armillaria</i> sp.	Ascomycota vs. Basidiomycota/Pleosporales vs. Agaricales	phomretone A (N) 12 phomretone B (N) 13 phomretone C (N) 14 phomretone D (N) 15 phomretone E (N) 16 phomretone F (N) 17		Li, H.-T.; Liu, T.; Yang, R.; Xie, F.; Yang, Z.; Yang, Y.; Zhou, H.; Ding, Z.-T. Phomretones A–F, C 12 polyketides from the co-cultivation of <i>Phoma</i> sp. YUD17001 and <i>Armillaria</i> sp. RSC Adv. 2020, 10, 18384-18389.

Figure S1. Structures of compounds isolated from co-culturing pairing. Refer to Supporting Information Table S1.



Continued....



Continued....

