

Supplementary Materials

Influence of OSMAC-Based Cultivation in Metabolome and Anticancer Activity of Fungi Associated with the Brown Alga *Fucus vesiculosus*

Bicheng Fan ¹, Delphine Parrot ¹, Martina Blümel ¹ Antje Labes ^{1,†} and Deniz Tasdemir ^{1,2,*}

¹ GEOMAR Centre for Marine Biotechnology, Research Unit Marine Natural Products Chemistry, GEOMAR Helmholtz Centre for Ocean Research Kiel, Am Kiel-Kanal 44, 24106 Kiel, Germany; bfan@geomar.de (B.F.); delphine.parrot@gmail.com (D.P.); mbluemel@geomar.de (M.B.); antje.labes@hs-flensburg.de (A.L.)

² Faculty of Mathematics and Natural Sciences, Kiel University, Christian-Albrechts-Platz 4, 24118 Kiel, Germany

[†] Current address: Flensburg University of Applied Sciences, Department Energy and Biotechnology, Kanzleistraße 91-93, 24943 Flensburg, Germany

* Correspondence: dtasdemir@geomar.de; Tel.: +49-431-600-4430

Table S1. Identification of 87 fungal strains isolated from *Fucus vesiculosus* and its surrounding environment (sediment and seawater). Identification was done according to Sanger sequencing comparison of the ITS1-5.8S rRNA gene-ITS2 fragment to NCBI GenBank nucleotide database using BLASTn (incl. respective assigned Genbank accession numbers). The 3 first BLAST hits incl. respective accession numbers are given. WM: Modified Wickerham medium, PDM: Potato Dextrose medium, GCM: Glucose Casein medium, GYP: Glucose Yeast Peptone medium. SE: sediment. SA: seawater. FVE: *F. vesiculosus* endophytic fungi. FVS: *F. vesiculosus* surface epiphytic fungi. *Strain could not be identified to genus level but only to higher taxa (order) level.

Series no.	I.D.	Source	Isolation Medium	Sequence length	Closest relative in NCBI GenBank	NCBI accession number	Order	Sequence similarity %	Accession number
1*	1	FVE	WM	297	<i>Pyrenochaetopsis</i> sp. HKU62 <i>Pyrenochaetopsis</i> sp. CBS:119739 Uncultured <i>Leptosphaeria</i> sp.2KK-2015	LC158605.1 LT623227.1 KP747710.1	Pleosporales	100	MH881440
2	2	SE	PDM	172	<i>Fusarium lateritium</i> 3821 <i>Fusarium tricinctum</i> IBL277f <i>Fusarium avenaceum</i> SFC101774	MG066631.1 MF162319.1 MF186082.1	Hypocreales	100	MH881441
3	6	SE	GCM	261	<i>Fusarium culmorum</i> F165 <i>Fusarium graminearum</i> PGTU10 18S <i>Fusarium culmorum</i> Ba4	KU891563.1 MF497389.1 MH361213.1	Hypocreales	100	MH881442
4	8	SE	PDM	270	<i>Penicillium sanguifluum</i> IG103 <i>Penicillium</i> sp. S1a1 <i>Penicillium sanguifluum</i> 17_3N1	MG973279.1 KY784181.1 KY859378.1	Eurotiales	100	MH881443
5*	10	SE	GYP	426	<i>Pyrenochaetopsis microspora</i> MUT4941 <i>Roussoellaceae</i> sp. MUT4859 <i>Phoma</i> sp. MUT 5462	LT623227.1 KR014355.1 KU314985.1	Pleosporales	100	MH881444
6	11	FVS	GCM	385	<i>Gibellulopsis</i> sp. MYf203 <i>Gibellulopsis</i> sp. P2 <i>Gibellulopsis nigrescens</i> LG1401	KX079890.1 KY465972.1 KX359602.1	Hypocreales	100	MH881445
7	12	FVE	WM	400	<i>Acremonium furcatum</i> MUT1194 <i>Acremonium antarcticum</i> AY913 <i>Acremonium antarcticum</i> CBS 987.87	KR709189.1 LT549083.1 JX158422.1	Hypocreales	99	MH881446
8	13	FVE	WM	301	<i>Trichoderma gamsii</i> SCAU130 <i>Trichoderma koningii</i> ACCC32855 <i>Trichoderma koningii</i> ACCC32853	MF061792.1 MF780862.1 MF780861.1	Hypocreales	100	MH881447
9	14	SE	WM	306	<i>Penicillium</i> sp. L2-3C <i>Penicillium</i> sp. UCD161305F	MG813426.1 MG686509.1	Eurotiales	100	MH881448

10	15	SE	WM	227	<i>Penicillium thomii</i> MUT<ITA>:2257	MG813165.1	Eurotiales	100	MH881449
					<i>Penicillium</i> sp. L2-3C	MG813426.1			
					<i>Penicillium</i> sp. UCD161305F	MG686509.1			
11	16	SE	PDM	358	<i>Penicillium thomii</i> MUT<ITA>:2257	MG813165.1	Eurotiales	100	MH881450
					<i>Penicillium glabrum</i> KAS5827	KY469043.1			
					<i>Penicillium glabrum</i> SFC101259	MF185992.1			
12	20	SE	PDM	287	<i>Penicillium spinulosum</i> Su-XII-4	MF475933.1	Eurotiales	100	MH881451
					<i>Penicillium</i> sp. L2-3C	MG813426.1			
					<i>Penicillium</i> sp. UCD161305F	MG686509.1			
13	24	SE	GCM	376	<i>Penicillium thomii</i> MUT<ITA>:2257	MG813165.1	Eurotiales	100	MH881452
					<i>Penicillium murcianum</i> PM1	MF668969.1			
					<i>Penicillium nucicola</i> KAS 2101	KT887846.1			
14	25	SE	GYP	482	<i>Penicillium</i> sp. SFC102007	MF186110.1	Eurotiales	98	MH881453
					<i>Cladosporium sloanii</i> DTO:130-D5	MF473253.1			
					<i>Cladosporium psychrotolerans</i> DTO:307-H2	MF473224.1			
15	26	SE	GCM	232	<i>Cladosporium psychrotolerans</i> DTO:305-G3	MF473223.1	Eurotiales	99	MH881454
					<i>Penicillium</i> sp. EMA-2011d	JF429677.1			
					<i>Penicillium thomii</i> MUT<ITA>:2257	MG813165.1			
16	27	SE	GYP	352	<i>Penicillium glabrum</i> SFC101259	MF185992.1	Eurotiales	99	MH881455
					<i>Penicillium coralligerum</i> YK247	LC214562.1			
					<i>Penicillium atrovenetum</i> bqW5	MF599167.1			
17	29	SE	GYP	430	<i>Penicillium</i> sp. 8	KY401130.1	Eurotiales	100	MH881456
					<i>Penicillium glabrum</i> KAS5827	KY469043.1			
					<i>Penicillium glabrum</i> SFC10125	MF185992.1			
18	30	SE	GYP	375	<i>Penicillium glabrum</i> SYPF 6991	MH279474.1	Eurotiales	100	MH881457
					<i>Penicillium glabrum</i> KAS5827	KY469043.1			
					<i>Penicillium glabrum</i> SFC10125	MF185992.1			
19	31	SE	GYP	338	<i>Penicillium glabrum</i> SYPF 6991	MH279474.1	Eurotiales	100	MH881458
					<i>Penicillium brevicompactum</i> GIBI220	KX965655.1			
					<i>Penicillium</i> sp. M_FA_V8	MH137760.1			
20	32	FVE	PDM	366	<i>Penicillium brevicompactum</i>	MH047201.1	Eurotiales	100	MH881459
					<i>Penicillium brevicompactum</i> MERVA5	MF503895.1			
					<i>Penicillium brevicompactum</i>	MH047201.1			
21	33	FVE	PDM	318	<i>Penicillium brevicompactum</i> KAS5854	KY469047.1	Eurotiales	100	MH881460
					<i>Penicillium atrovenetum</i> bqW5	MF599167.1			

					<i>Penicillium atrovenetum</i> CBS 243.56	KP016835.1			
					<i>Penicillium</i> sp. MT152	MH109377.1			
22	34	FVE	GYP	468	<i>Penicillium atrovenetum</i> bqW5	MF599167.1	Eurotiales	100	MH881461
					<i>Penicillium coralligerum</i> YK-247	LC214562.1			
					<i>Penicillium antarcticum</i> SFC101809	MF186085.1			
23	35	FVE	GYP	323	<i>Cadophora malorum</i> M7	MG813381.1	Incertae sedis	100	MH881462
					<i>Cadophora malorum</i> VKM F-4744	MF494613.1			
					<i>Cadophora malorum</i> VKM F-4747	MF494620.1			
24*	37	FVE	GYP	304	<i>Emericellopsis</i> sp. SNT1-23	KY379579.1	Hypocreales	99	MH881463
					<i>Acremonium zonatum</i> CSR1-21	KY379556.1			
					<i>Sarocladium kiliense</i> 11-84	KX815337.1			
25	38	FVE	WM	328	<i>Penicillium biourgeianum</i> UWR031	KX426968.1	Eurotiales	100	MH881464
					<i>Penicillium bialowiezensc</i> SFC101475	MF186021.1			
					<i>Penicillium bialowiezensc</i> KAS5860	KY469051.1			
26	39	FVE	WM	224	<i>Penicillium brevicompactum</i> UWR031	KX426968.1	Eurotiales	100	MH881465
					<i>Penicillium bialowiezensc</i> KAS5860	KY469051.1			
					<i>Penicillium brevicompactum</i> 82	KY401133.1			
27	40	FVE	WM	347	<i>Penicillium</i> sp. 86	KY401137.1	Eurotiales	100	MH881466
					<i>Penicillium atrovenetum</i> BQW5	MF599167.1			
					<i>Penicillium</i> sp. 8	KY401130.1			
28	42	FVE	GYP	517	<i>Penicillium brevicompactum</i> F27-02	KX664363.1	Eurotiales	100	MH881467
					<i>Penicillium brevicompactum</i> KAS5854	KY469047.1			
					<i>Penicillium brevicompactum</i> KAS5812	KY469041.1			
29	43	SE	WM	228	<i>Penicillium</i> sp. L2-3C	MG813426.1	Eurotiales	100	MH881468
					<i>Penicillium</i> sp. UCD161305F	MG686509.1			
					<i>Penicillium thomii</i> MUT<ITA>:2257	MG813165.1			
30	44	SE	PDM	206	<i>Fusarium chlamydosporum</i> CFFSUR-22A	KY860655.1	Hypocreales	100	MH881469
					<i>Fusarium oxysporum</i> f. sp. momordicae GuangX26	MF445489.1			
					<i>Fusarium chlamydosporum</i> Ng30	MH141316.1			
31	46	SE	PDM	355	<i>Penicillium glabrum</i> KAS5827	KY469043.1	Eurotiales	100	MH881470
					<i>Penicillium glabrum</i> SFC101259	MF185992.1			
					<i>Penicillium glabrum</i> SFC101229	MF185985.1			
32	47	SE	PDM	372	<i>Penicillium glabrum</i> KAS5767	KY469033.1	Eurotiales	100	MH881471
					<i>Penicillium glabrum</i> SFC101259	MF185992.1			

33	48	SE	PDM	365	<i>Penicillium glabrum</i> PO6	KY463488.1	Eurotiales	100	MH881472
					<i>Penicillium jensenii</i> P6342	MH063657.1			
					<i>Penicillium</i> sp.1217_476	MG917754.1			
					<i>Penicillium canescens</i> 3S.106	KY458474.1			
34	49	SE	GYP	307	<i>Penicillium jensenii</i> P6342	MH063657.1	Eurotiales	100	MH881473
					<i>Penicillium</i> sp.1217_476	MG917754.1			
					<i>Penicillium canescens</i> 3S.106	KY458474.1			
					<i>Penicillium</i> sp. 86	KY401137.1			
35	50	FVE	PDM	507	<i>Penicillium sanguifluum</i> IG103	MG973279.1	Eurotiales	100	MH881474
					<i>Penicillium</i> sp. 8	KY401131.1			
					<i>Penicillium</i> sp. L2-3C	MG813426.1			
					<i>Penicillium</i> sp. UCD161305F	MG686509.1			
36	52	SE	WM	322	<i>Penicillium thomii</i> MUT<ITA>:2257	MG813165.1	Eurotiales	100	MH881475
					<i>Phoma</i> sp. MUT5465	KU314987.1			
					<i>Roussoellaceae</i> sp. MUT 4859	KR014355.1			
					<i>Phoma</i> sp. MUT 5462	KU314985.1			
37*	53	FVS	GYP	314	<i>Penicillium brevicompactum</i> F27-02	KX664363.1	Eurotiales	100	MH881477
					<i>Penicillium</i> sp. UCD160901G3	MG686505.1			
					<i>Penicillium brevicompactum</i> KAS5854	KY469047.1			
					<i>Penicillium glabrum</i> ND70	MG659664.1			
38	54	FVS	GCM	337	<i>Penicillium thomii</i> MUT<ITA>:2257	MG813165.1	Eurotiales	100	MH881478
					<i>Penicillium glabrum</i> SFC101229	MF185985.1			
					<i>Penicillium coralligerum</i> YK-247	LC214562.1			
					<i>Penicillium</i> sp. 86	KY401137.1			
39	55	FVE	PDM	300	<i>Penicillium</i> sp. 76	KY401126.1	Eurotiales	100	MH881479
					<i>Penicillium atrovenetum</i> FO.1	KT587349.1			
					<i>Penicillium antarcticum</i> SFC101809	MF186085.1			
					<i>Penicillium coralligerum</i> YK-247	LC214562.1			
40	56	FVE	WM	523	<i>Fusarium graminearum</i> WF1	KY985465.1	Hypocreales	96	MH881480
					<i>Fusarium graminearum</i> PGTU11	MF497390.1			
					<i>Fusarium graminearum</i> PGTU10	MF497389.1			
					<i>Gibellulopsis nigrescens</i> LG1402	KY459202.1			
41	57	FVE	GYP	331	<i>Plectosphaerella</i> sp. sedF4	KX359602.1	Glomerellales	100	MH881481
					Uncultured <i>Verticillium</i> JB40C25 (MOTU06)	HG935585.1			
					<i>Penicillium coralligerum</i> YK-247	LC214562.1			
42	58	FVE	WM	258			Eurotiales	100	MH881482
43*	59	FVE	WM	231			Eurotiales	100	MH881483
44	60	FVE	WM	310			Eurotiales	100	MH881483

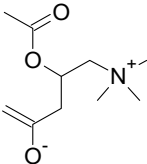
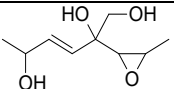
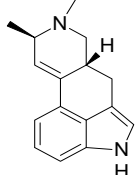
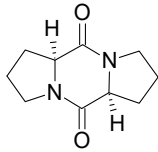
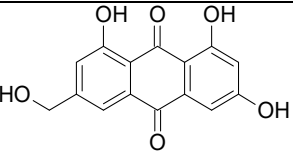
					<i>Penicillium atrovenetum</i> bqW5	MF599167.1			
					<i>Penicillium</i> sp. 86	KY401137.1			
45	61	FVE	PDM	514	<i>Penicillium brevicompactum</i> TCDFvLDB1814	MH71548.1	Eurotiales	100	MH881484
					<i>Penicillium brevicompactum</i> Asa3SNA1	KY558614.1			
					<i>Penicillium brevicompactum</i> KAS5854	KY469047.1			
46	62	FVE	PDM	324	<i>Penicillium brevicompactum</i> F27-02	KX664363.1	Eurotiales	100	MH881485
					<i>Penicillium brevicompactum</i> KAS5854	KY469047.1			
					<i>Penicillium brevicompactum</i> KAS5812	KY469041.1			
47	63	FVE	PDM	334	<i>Penicillium brevicompactum</i> F27-02	KX664363.1	Eurotiales	100	MH881486
					<i>Penicillium brevicompactum</i> KAS5854	KY469047.1			
					<i>Penicillium brevicompactum</i> KAS5812	KY469041.1			
48	64	FVE	PDM	341	<i>Penicillium brevicompactum</i> MERV5	MF503895.1	Eurotiales	100	MH881487
					<i>Penicillium brevicompactum</i> SFC102216	MF186137.1			
					<i>Penicillium brevicompactum</i> 2-Z-30	MH310820.1			
49	65	SA	PDM	247	<i>Candida</i> sp. KJS-2016	LC155354.1	Saccharomycetales	99	MH881488
					<i>Candida pseudolambica</i> yHRM77	KM384061.1			
					<i>Candida pseudolambica</i> yHRM67	KM384060.1			
50	66	SE	PDM	182	<i>Fusarium lateritium</i> 3821	MG066631.1	Hypocreales	100	MH881489
					<i>Fusarium tricinatum</i> SFC101814	MF186086.1			
					<i>Fusarium avenaceum</i> SFC101774	MF186082.1			
51	67	FVE	WM	250	<i>Gibellulopsis nigrescens</i> STAF302	KU214559.1	Glomerellales	100	MH881490
					<i>Gibellulopsis nigrescens</i> LG1401 GL11A	KX359602.1			
					<i>Gibellulopsis nigrescens</i> STAF302	KU314961.1			
52	68	FVE	WM	316	<i>Penicillium atrovenetum</i> bqW5	MF599167.1	Eurotiales	100	MH881491
					<i>Penicillium coralligerum</i> YK-247	LC214562.1			
					<i>Penicillium antarcticum</i> SFC101809	MF186085.1			
53	69	FVE	PDM	329	<i>Penicillium brevicompactum</i> MERV5	MF503895.1	Eurotiales	100	MH881492
					<i>Penicillium brevicompactum</i> SFC102216	MF186137.1			
					<i>Penicillium brevicompactum</i> 2-Z-30	MH310820.1			
54	72	FVE	WM	204	<i>Penicillium coralligerum</i> YK-247	LC214562.1	Eurotiales	100	MH881493
					<i>Penicillium atrovenetum</i> bqW5	MF599167.1			
					<i>Penicillium antarcticum</i> SFC101809	MF186085.1			
55	73	FVE	GYP	321	<i>Penicillium brevicompactum</i> MERV5	MF503895.1	Eurotiales	98	MH881494
					<i>Penicillium brevicompactum</i> SFC102216	MF186137.1			
					<i>Penicillium brevicompactum</i> 2-Z-30	MH310820.1			

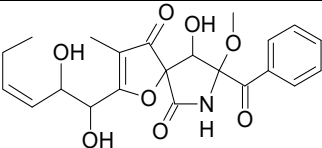
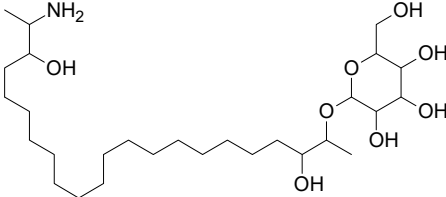
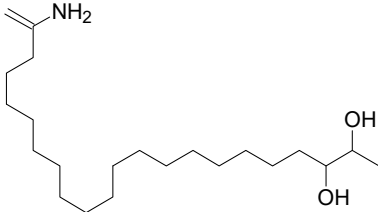
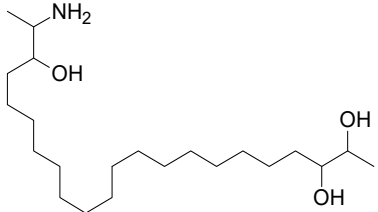
56	77	SE	PDM	249	<i>Penicillium</i> sp. L2-3C <i>Penicillium</i> sp. UCD161305F <i>Penicillium thomii</i> MUT:2257	MG813426.1 MG686509.1 MG813165.1	Eurotiales	100	MH881495
57	78	FVE	PDM	509	<i>Penicillium glabrum</i> DTO313-D4 <i>Penicillium glabrum</i> DTO313-C1 <i>Penicillium camemberti</i> ISSFR-016	MF803957.1 MF803952.1 KT832784.1	Eurotiales	100	MH881496
58	81	FVE	WM	227	<i>Wallemia muriae</i> KK18.3 <i>Wallemia muriae</i> KAS 6011 <i>Wallemia muriae</i> KAS 5869	KY322648.1 KX911859.1 KX911850.1	Wallemiales	100	MH881497
59	82	FVE	WM	328	<i>Emericellopsis terricola</i> CCF3815 <i>Emericellopsis minima</i> OUCMBII111121 Uncultured <i>Emericellopsis</i> 10J50C67 (MOTU75)	J430737.1 KT290876.1 HG936806.1	Hypocreales	99	MH881498
60*	84	FVE	WM	323	<i>Stilbella fimetaria</i> voucher AF3-097G <i>Emericellopsis salmosynnemata</i> CBS382.62 <i>Stilbella fimetaria</i> D99026	KX446764.1 AY632666.1 AY952467.1	Hypocreales	100	MH881499
61	85	SE	PDM	260	<i>Stereum hirsutum</i> P2A <i>Stereum hirsutum</i> gap67 <i>Stereum hirsutum</i> Wi-XI-1.1	KX838369.2 KX578081.1 MF476012.1	Russulales	100	MH881500
62	86	FVE	PDM	323	<i>Emericellopsis terricola</i> CCF3815 <i>Emericellopsis terricola</i> <i>Emericellopsis minima</i> A11	FJ430737.1 U57676.1 KY775297.1	Hypocreales	99	MH881501
63*	87	FVE	WM	279	<i>Phoma</i> sp. MUT 5465 <i>Pleosporales</i> sp. AT60 <i>Pyrenochaetopsis microspora</i> CBS 119739	KU314987.1 KX953409.1 LT623227.1	Pleosporales	99	MH881502
64	89	FVE	WM	395	<i>Trichoderma paraviridescens</i> <i>Trichoderma viride</i> IMF51186 <i>Trichoderma koningiopsis</i> ACCC32904	MG646337.1 LC317804.1 MF871558.1	Hypocreales	100	MH881503
65	91	FVE	GCM	473	<i>Penicillium spathulatum</i> AS3.15328 <i>Penicillium spathulatum</i> CBS 116977 <i>Penicillium</i> sp. DF-2	KC427190.1 JX313162.1 KT121500.1	Eurotiales	100	MH881504
66	92	FVS	PDM	330	<i>Penicillium coralligerum</i> YK-247 <i>Penicillium</i> sp. MT152 <i>Penicillium</i> sp. MT57	LC214562.1 MH109377.1 MH109376.1	Eurotiales	100	MH881505
67	95	FVE	PDM	350	<i>Penicillium coralligerum</i> YK-247	LC214562.1	Eurotiales	100	MH881506

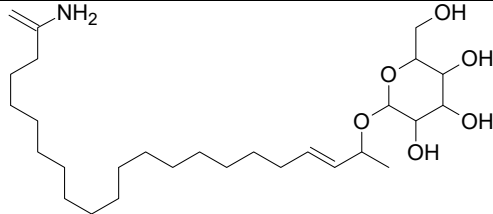
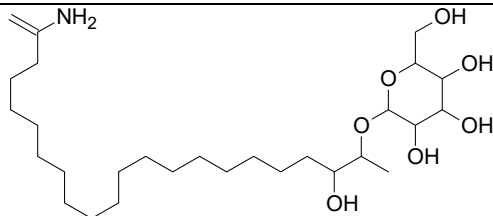
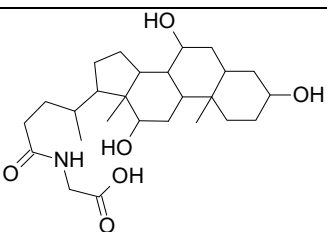
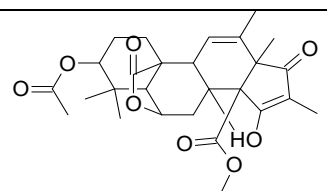
					<i>Penicillium</i> sp. MT152	MH109377.1			
					<i>Penicillium</i> sp. MT57	MH109376.1			
68	96	FVS	GYP	502	<i>Penicillium brevicompactum</i> BEOFB1102m	MH630035.1	Eurotiales	100	MH881507
					<i>Penicillium brevicompactum</i> TCDFvLDB1814	MH714548.1			
					<i>Penicillium brevicompactum</i> 1	MH047201.1			
69	97	SE	GYP	428	<i>Fusarium culmorum</i> S68	MH681156.1	Eurotiales	100	MH88150
					<i>Fusarium culmorum</i> F150	MH681154.1			8
					<i>Fusarium asiaticum</i> G84	MH681153.1			
70	99	FVS	GCM	315	<i>Penicillium brevicompactum</i> KAS5854	KY469047.1	Eurotiales	100	MH881509
					<i>Penicillium brevicompactum</i> KAS5812	KY469041.1			
					<i>Penicillium brevicompactum</i> KAS5776	KY469037.1			
71	101	FVE	GCM	326	<i>Penicillium brevicompactum</i> KG_6i	MG686505.1	Eurotiales	100	MH8815010
					<i>Penicillium brevicompactum</i> Asa3SNA1	KY558614.1			
					<i>Penicillium brevicompactum</i> Cch1SNA3	KY558611.1			
72	102	FVE	W	349	<i>Penicillium</i> sp. 86	MF599167.1	Eurotiales	100	MH881511
					<i>Penicillium atrovenetum</i> BQW5	KY401137.1			
					<i>Penicillium</i> sp. 8	MF599167.1			
73	104	FVS	WM-S	318	<i>Penicillium chrysogenum</i> DCMAF01BCI	KY401130.1	Eurotiales	100	MH881512
					<i>Penicillium brevicompactum</i> SFC102216	MF186137.1			
					<i>Penicillium brevicompactum</i> 2-Z-30	MH310820.1			
74	105	FVS	GCM	377	<i>Penicillium</i> sp. 86	KY401137.1	Eurotiales	100	MH881513
					<i>Penicillium atrovenetum</i> BQW5	MF599167.1			
					<i>Penicillium</i> sp. 8	KY401130.1			
75	107	FVE	PDM	415	<i>Penicillium</i> sp. 86	KY401137.1	Eurotiales	100	MH881514
					<i>Penicillium atrovenetum</i> BQW5	MF599167.1			
					<i>Penicillium</i> sp. 8	KY401130.1			
76	108	FVS	WM	305	<i>Penicillium</i> sp. 86	KY401137.1	Eurotiales	100	MH881515
					<i>Penicillium atrovenetum</i> BQW5	MF599167.1			
					<i>Penicillium</i> sp. 8	KY401130.1			
77	109	FVS	GCM	291	<i>Penicillium</i> sp. 86	KY401137.1	Eurotiales	100	MH881516
					<i>Penicillium atrovenetum</i> BQW5	MF599167.1			
					<i>Penicillium</i> sp. 8	KY401130.1			
78	111	FVE	GYP	312	<i>Penicillium</i> sp. 86	KY401137.1	Eurotiales	100	MH881517
					<i>Penicillium atrovenetum</i> BQW5	MF599167.1			
					<i>Penicillium</i> sp. 8	KY401130.1			

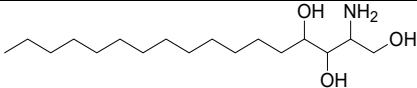
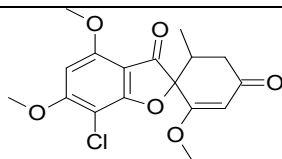
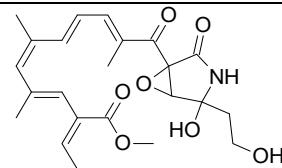
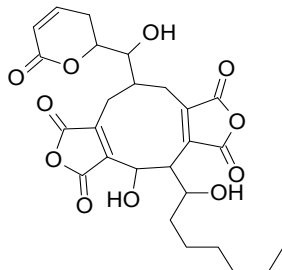
79	112	FVE	GCM	367	<i>Penicillium glabrum</i> R2EK05	KR091814.1	Eurotiales	100	MH881518
					<i>Penicillium glabrum</i> SFC101259	MF185992.1			
					<i>Penicillium glabrum</i> SFC101229	MF185985.1			
80*	113	SE	GCM	296	<i>Nectria inventa</i> MUT1135	KR709185.1	Hypocreales	100	MH881519
					<i>Acrostalagmus luteoalbus</i> P6424	MH063783.1			
					<i>Acrostalagmus luteoalbus</i> H35	KX375795.1			
81	114	FVS	PDM	300	<i>Penicillium brevicompactum</i> KAS5871	KY469055.1	Eurotiales	100	MH881520
					<i>Penicillium brevicompactum</i> SFC102216	MF186137.1			
					<i>Penicillium brevicompactum</i> 2-Z-30	MH310820.1			
82	115	SA	PDM	124	<i>Penicillium coralligerum</i> YK247	LC214562.1	Eurotiales	100	MH881521
					<i>Penicillium atrovenetum</i> bqW5	MF599167.1			
					<i>Penicillium</i> sp. 8	KY401130.1			
83	117	SE	PDM	434	<i>Phoma</i> sp. MUT 5465	KU314987.1	Pleosporales	100	MH881522
					<i>Phoma</i> sp. MUT 5462	KU314985.1			
					<i>Phoma</i> sp. MUT 5460	KU314983.1			
84	121	FVE	GCM	287	<i>Penicillium canescens</i> 3S.106	KY458474.1/	Eurotiales	100	MH881523
					<i>Penicillium murcianum</i> KK19.1	KY322566.1			
					<i>Penicillium jensenii</i> P6342	MH063657.1			
85	122	FVE	GCM	376	<i>Penicillium brevicompactum</i> KAS5871	KY469055.1	Eurotiales	100	MH881524
					<i>Penicillium brevicompactum</i> SFC102216	MF186137.1			
					<i>Penicillium brevicompactum</i> 2-Z-30	MH310820.1			
86	123	SE	GCM	102	<i>Penicillium denovo</i> 13735	KR266650.1	Eurotiales	100	MH881525
					<i>Penicillium</i> sp. SF1	KX011018.1			
					<i>Neosartorya</i> sp. BAB-4715	KU571518.1			
87	124	SE	GCM	309	<i>Penicillium coralligerum</i> YK247	LC214562.1	Eurotiales	100	MH881526
					<i>Penicillium atrovenetum</i> bqW5	MF599167.1			
					<i>Penicillium</i> sp. 8	KY401130.1			

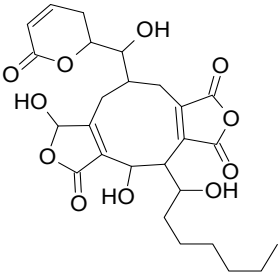
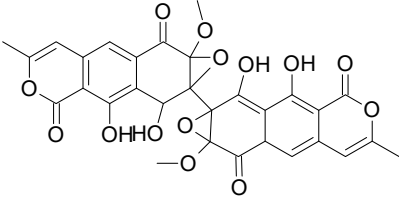
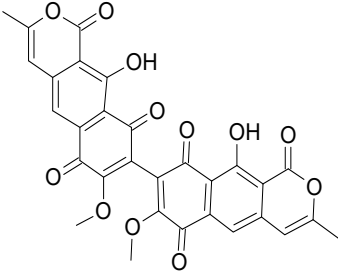
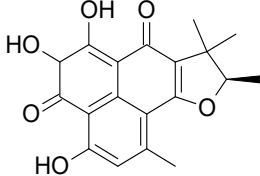
Table S2. Putatively identified compounds from 40 liquid culture extracts and 40 solid culture extracts. Dereplication of the compounds was based on GNPS, UNPD-ISDB, and manual dereplication by using several databases such as DNP, Scifinder and Chemspider.

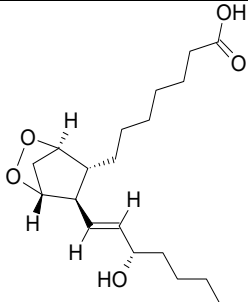
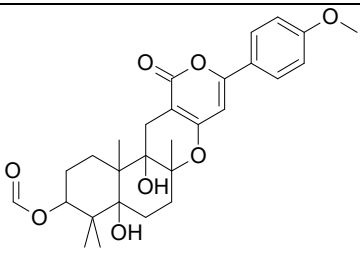
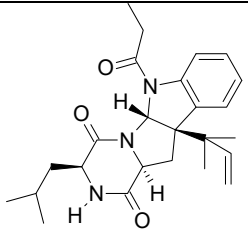
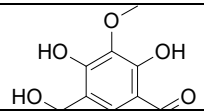
Comp. No.	tr (min)	Culture regime (medium)	Precursor <i>m/z</i>	Putative ID (chemical family)	Chemical structure	Molecular formula (change in Δ ppm)	MS/MS fragmentation	Strain number
1	0.70	Solid (SYM)	204.1113 [M+H] ⁺	Acetylcarnitine (amino acid derivative)		C ₉ H ₁₇ NO ₄ (-59.3)*	145.1231; 85.9665	1
2	1.66	Liquid (WM)	189.1130 [M+H] ⁺	Aspinonene (pentaketide)		C ₉ H ₁₆ O ₄ (0)	-	68
3	2.24	Solid (PDM, SYM, Cza, WM)	239.1592 [M+H] ⁺	Lysergine (indole alkaloid)		C ₁₆ H ₁₈ N ₂ (-7.5)	197.1551; 141.9877	37
4	3.04	Solid (Cza)	245.1508 [M+H] ⁺	Cyclo(L-Phe-D-Pro) (diketopiperazine)		C ₁₄ H ₁₆ N ₂ O ₂ (1.9)	217.1613; 154.1008; 120.1105	35
5	4.15	Liquid (PDM)	301.0852 [M+H] ⁺	Questinol (dihydroxyanthraquinone)		C ₁₆ H ₁₂ O ₆ (-0.5)	286.0602; 257.0612	50

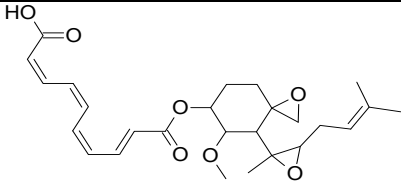
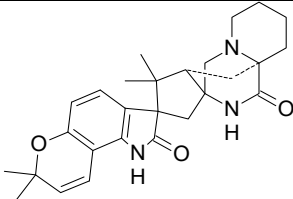
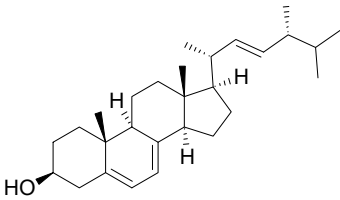
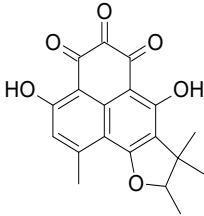
6	4.18	Solid (WM)	454.1482 [M+Na] ⁺	Pseurotin A (amide alkaloid)		C ₂₂ H ₂₅ NO ₈ (-0.9)	422.1124; 370.0889; 261.0882; 216.0832	78
		Liquid (SYM)						35
7	5.19	Liquid (Cza) Solid (Cza)	536.4123 [M+H] ⁺	2-(21-amino-3, 20- dihydroxydocosan-2-yl) oxy-6-(hydroxymethyl) oxane-3, 4, 5-triol (aminoglycolipid)		C ₂₈ H ₅₇ NO ₈ (-1.9)	518.4053; 500.3958; 482.3873; 374.3875; 338.3654; 320.3527	59
8	5.19	Liquid (Cza) Solid (Cza)	356.3711 [M+H] ⁺	21-aminodocos-21-ene- 2,3-diol (aminolipid)		C ₂₂ H ₄₅ NO ₂ (0.5)	338.3616; 320.3527	59
9	5.20	Liquid (Cza) Solid (Cza)	374.3796 [M+H] ⁺	21-aminodocosane- 2,3,20-triol (aminolipid)		C ₂₂ H ₄₇ NO ₃ (42.2) *	356.3704; 338.3615; 320.3528	59

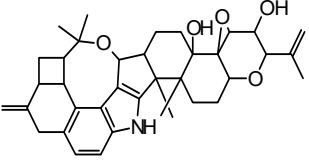
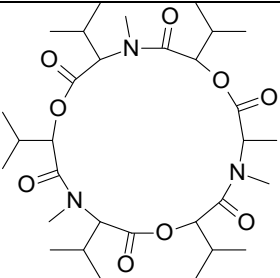
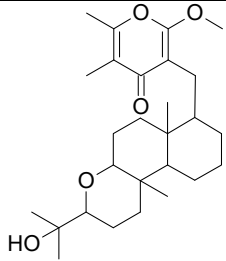
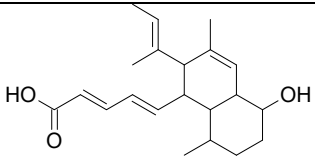
10	5.21	Liquid (Cza) Solid (Cza)	500.3968 [M+H] ⁺	(E)-2-((21-aminodocosa-3,21-dien-2-yl)oxy)-6-(hydroxymethyl)tetrahydro-2H-pyran-3, 4, 5-triol (aminolipid)		C ₂₈ H ₅₃ NO ₆ (3.2)	482.3876; 374.3875; 356.3695; 338.3606; 320.3527	59
11	5.23	Liquid (Cza) Solid (Cza)	518.4051 [M+H] ⁺	2-(21-amino-3-hydroxydocos-21-en-2-yl)oxy)-6-(hydroxymethyl)tetrahydro-2H-pyran-3, 4, 5-triol (aminoglycolipid)		C ₂₈ H ₅₅ NO ₇ (-1.7)	500.3958; 482.3873; 356.3700; 338.3612; 320.3526	59
12	5.47	Solid (WM)	466.3 170 [M+H] ⁺ 488.2 957 [M+Na] ⁺	Glycocholic acid (bile acid)		C ₂₆ H ₄₄ NO ₆ (0.2)	412.2906; 337.2691; 319.2593; 227.1693 470.2871; 412.2914	59
13	6.32	Liquid (Cza, SYM) Solid (SYM, WM, PDM)	501.2903 [M+H] ⁺	Citreohybridonol (sesterterpenoid)		C ₂₈ H ₃₆ O ₈ (-0.3)	486.2682; 409.2138; 381.2216; 363.2131; 335.2205; 217.1520; 179.1021	68

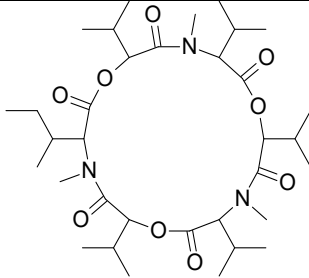
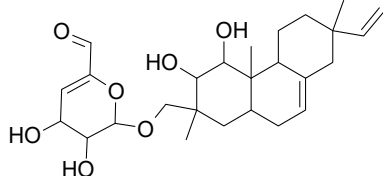
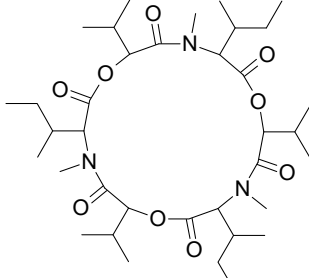
14	6.45	Solid (SYM)	318.3213 [M+H] ⁺	Phytosphingosine (sphingolipid)		C ₁₈ H ₃₉ NO ₃ (6.5)	300.3127; 282.3036; 270.3043; 264.2945; 240.2946;	56
15	6.52	Liquid (WM)	353.0795 [M+H] ⁺	Griseofulvin (tetrahydrofuranone polyketide)		C ₁₇ H ₁₇ ClO ₆ (0.8)	285.0648; 215.0305; 165.0792	68
16	6.70	Liquid (Cza) Solid (WM)	454.1801 [M+Na] ⁺	Fusarin C (polyene)		C ₂₃ H ₂₉ NO ₇ (-10.4)	413.2605; 335.1281; 290.1098	58
17	6.78	Liquid (Cza, PDM)	519.1832 [M+H] ⁺	Rubratoxin B (bis-anhydride)		C ₂₆ H ₃₀ O ₁₁ (-4.0)	501.1757; 451.1306; 271.1122	50

18	6.99	Liquid (Cza, PDM)	521.1890 [M+H] ⁺	Rubratoxin A (bis-anhydride)		C ₂₆ H ₃₂ O ₁₁ (-5.0)	503.1911; 435.1422; 283.1126; 271.1121	50
19	7.14	Liquid (PDM)	589.0890 [M+H- H ₂ O] ⁺	Xanthoepocin (binaphthoquinone)		C ₃₀ H ₂₂ O ₁₄ (-10.6)	571.0801; 483.0744; 470.0672; 441.0686; 413.0764; 313.0562	59
20	7.16	Liquid (PDM)	571.0803 [M+H] ⁺	Bisdehydroxanthomegn in (binaphthoquinone)		C ₃₀ H ₁₈ O ₁₂ (-12.6)	511.0682; 483.0735; 469.0599; 286.0680; 257.0700	59
21	7.46	Liquid (SYM, PDM, Cza)	343.1276 [M+H] ⁺	Atrovenetin (aromatic polyketide)		C ₁₉ H ₁₈ O ₆ (24.30)	287.0714; 255.0495	68

22	7.55	Solid (SYM, Cza)	337.2900 [M+H- H ₂ O] ⁺	Prostaglandin H ₁ (fatty acid derivative)		C ₂₀ H ₃₄ O ₅ (8.6)	263.2607; 123.1482; 109.1327	78
23	7.58	Solid (WM, Cza)	513.2470 [M+H] ⁺	Arisugacin D (dihydroxanthone derivative)		C ₂₉ H ₃₆ O ₈ (-3.9)	495.2372; 395.1965; 209.1114	50
24	7.67	Solid (SYM, Cza)	446.2421 [M+Na] ⁺	Brevicompanine E (diketopiperazine alkaloid)		C ₂₅ H ₃₃ N ₃ O ₃ (-0.4)	386.2237; 328.1892; 130.0972; 358.1982	68
25	8.05	Solid (WM, SYM, PDM, Cza)	357.1544 [M+H] ⁺	Deoxyherquenone (aromatic polyketide)		C ₂₀ H ₂₀ O ₆ (5.4)	342.1268; 327.1049; 301.0910	50

		Liquid (SYM, PDM, Cza, WM)					68	
26	8.12	Liquid (SYM)	481.2016 [M+Na] ⁺	Fumagillin (meroterpenoid)		C ₂₆ H ₃₄ O ₇ (-3.8)	329.2926	35
27	8.88	Solid (SYM)	448.2588 [M+H] ⁺	Marcfortine C (indole alkaloid)		C ₂₇ H ₃₃ N ₃ O ₃ (-2.7)	406.2837; 330.2077; 182.1254	68
28	9.16	Liquid (SYM)	379.3 329 [M+H- H ₂ O] ⁺	Ergosterol (steroid)		C ₂₈ H ₄₄ O (-9.3)	309.2665; 295.2521; 253.2106; 213.1840; 199.1696; 159.1414	35
29	9.35	Liquid (WM, Cza, PDM)	341.1123 [M+H] ⁺	Atrovenetinone (aromatic polyketide)		C ₁₉ H ₁₆ O ₆ (27.9)	313.7212; 287.0724	68

30	9.78	Solid (SYM)	584.3291 [M+H] ⁺	Penitrem B (indole diterpenoid)		C ₃₇ H ₄₆ NO ₅ (-14.2)	566.3217; 514.2602; 497.2591; 480.2563; 478.2471 304.1931; 260.1345	68
31	10.16	Liquid (PDM, Cza)	640.3732 [M+H] ⁺	Enniatin B (cyclic depsipeptide)		C ₃₃ H ₅₇ N ₃ O ₉ (-53.4) *	527.3075; 427.2713; 314.2042; 214.1643; 195.1562; 186.1716 549.2864; 336.1829	35
32	10.30	Solid (Cza)	481.2922 [M+Na] ⁺	Candelalide C (diterpenoid pyrone)		C ₂₈ H ₄₂ O ₅ (-1.7)	355.2387; 283.2012; 240.2581; 133.1116	50
33	10.61	Liquid (SYM)	331.2302 [M+H] ⁺	Phomopsidin (trimethylated nonaketide)		C ₂₁ H ₃₀ O ₃ (6.5)	293.0333; 273.8689; 250.8805' 192.8811; 165.0659	87

34	10.66	Liquid (WM, PDM)	654.3968 [M+H] ⁺	Enniatin B ₁ (cyclic depsipeptide)		C ₃₄ H ₅₉ N ₃ O ₉ (-55.3) *	541.3203; 441.2848; 328.2178; 314.2042; 210.1696; 196.1553	35
		Liquid (WM, PDM, Cza, SYM)	676.3968 [M+Na] ⁺				563.2997	
35	10.95	Liquid (PDM, Cza, WM)	463.2682 [M+H] ⁺	Viresenoside E (diterpene glycoside)		C ₂₆ H ₃₈ O ₇ (-5.2)	355.2312	1
36	11.67	Liquid (PDM, WM)	704.3914 [M+Na] ⁺	Enniatin A (cyclic depsipeptide)		C ₃₆ H ₆₃ N ₃ O ₉ (48.5) *	577.3101	35

*Peak ions of low intensity (molecular formula prediction with high Δ ppm).

Supplementary Figures

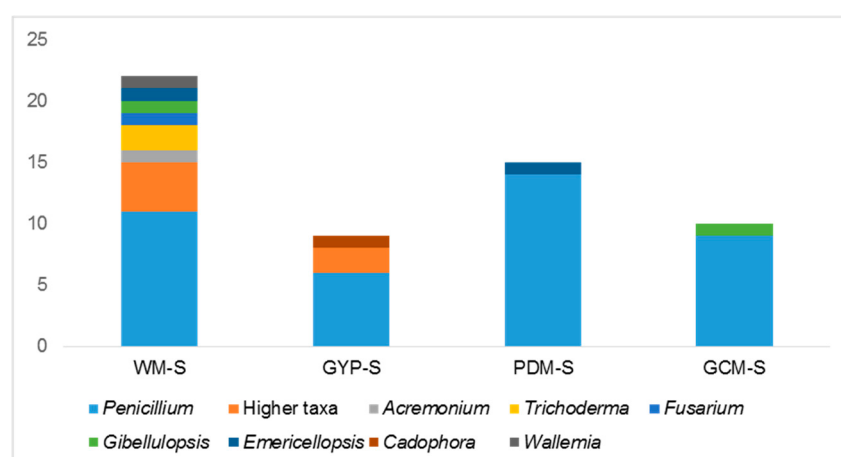


Figure S1. Comparison of 55 *F. vesiculosus* – derived fungi in diversity and distribution according to solid (S) isolation media. WM-S = modified Wickerham medium, PDM-S = Potato Dextrose medium, GCM-S = Glucose Casein medium, GYP-S = Glucose Yeast Peptone medium. Height of the column represents the total number of isolates derived from each media – WM-S: 21 isolates; PDM-S: 15 isolates, GCM-S: 10 isolates. GYP-S: 9 isolates.

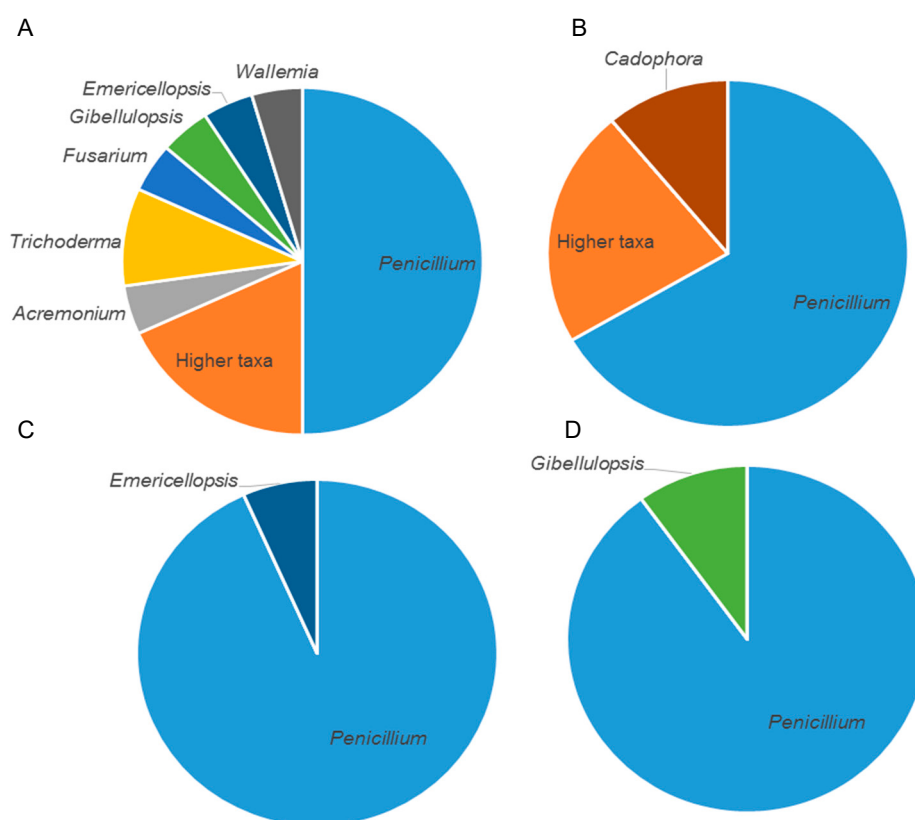


Figure S2. Pie chart showing the diversity of 55 *Fucus vesiculosus* – derived fungal community obtained by different isolation media. Strains that could not be identified to genus level are indicated as 'Higher taxa'. (A). Fungal isolates obtained from the WM-S medium that were identified as 10 *Penicillium* sp., 1 *Emericellopsis* sp., 1 *Gibellulopsis* sp., 1 *Fusarium* sp., 2 *Trichoderma* sp., 1 *Acremonium* sp., 1 *Wallemia* sp. and 4 'Higher taxa'. (B). Fungal isolates obtained from the GYP-S medium that were identified as 6 *Penicillium* sp., 2 'Higher taxa', and 1 *Cadophora* sp. (C). Fungal

isolates obtained from the PDM-S medium that were identified as 14 *Penicillium* sp. and 1 *Emericlesia* sp. (D). Fungal isolates obtained from the GCM-S medium that were identified as 9 *Penicillium* sp. and 1 *Gibellulopsis* sp.

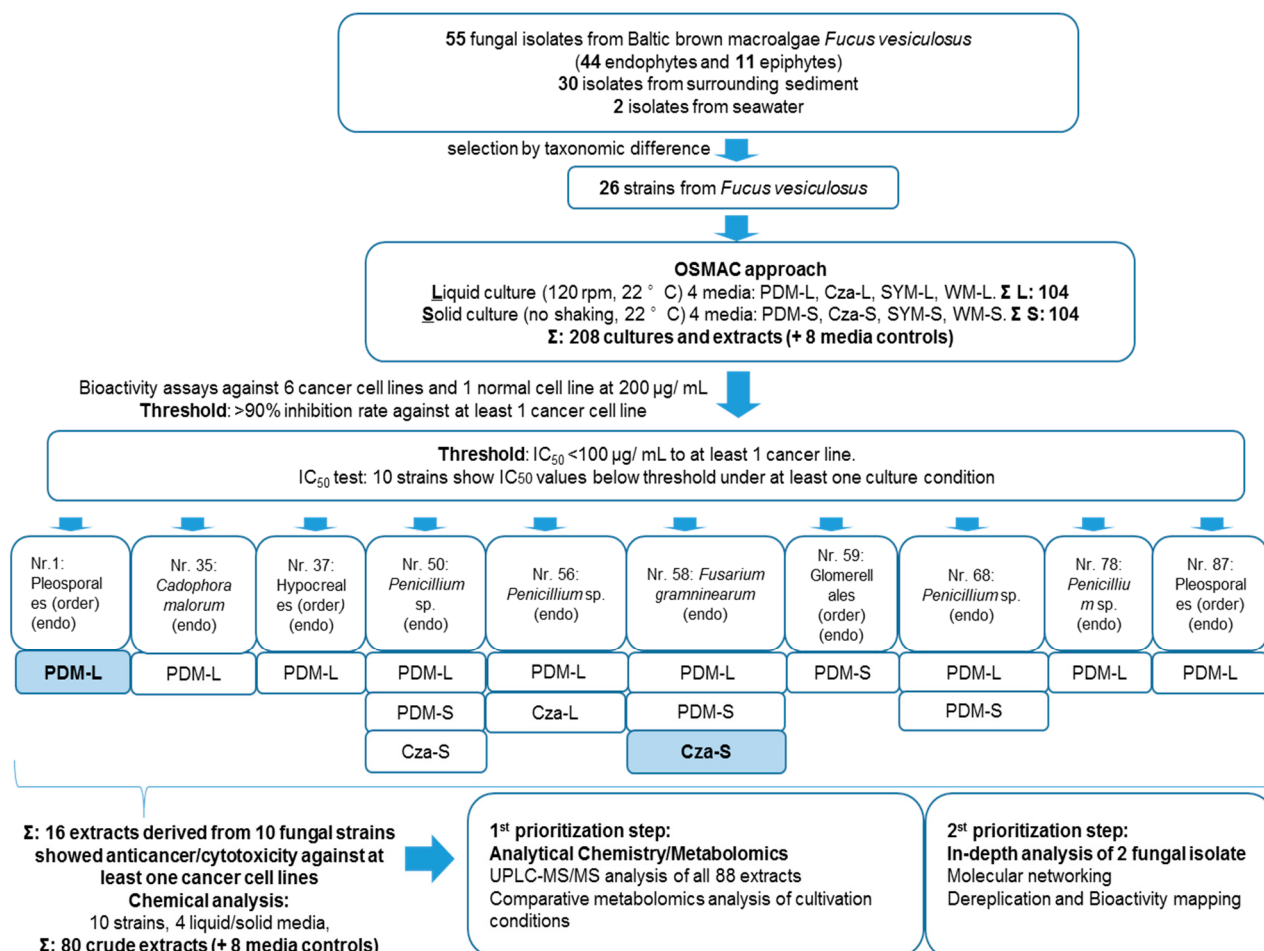


Figure S3. Workflow for the OSMAC study based on the 55 fungal isolates derived from *F. vesiculosus*. 26 isolates were selected for small-scale fermentation. The OSMAC approach was designed using 4 different media and 2 culture regimes. In total 208 culture extracts were tested for anticancer activity and the bioactive samples were further tested for IC₅₀ determination. 10 strains showed IC₅₀ values below 100 µg/mL against at least one cancer cell line. In the end, all 80 culture extracts derived from 10 strains were analysed by an integrated metabolomics approach.

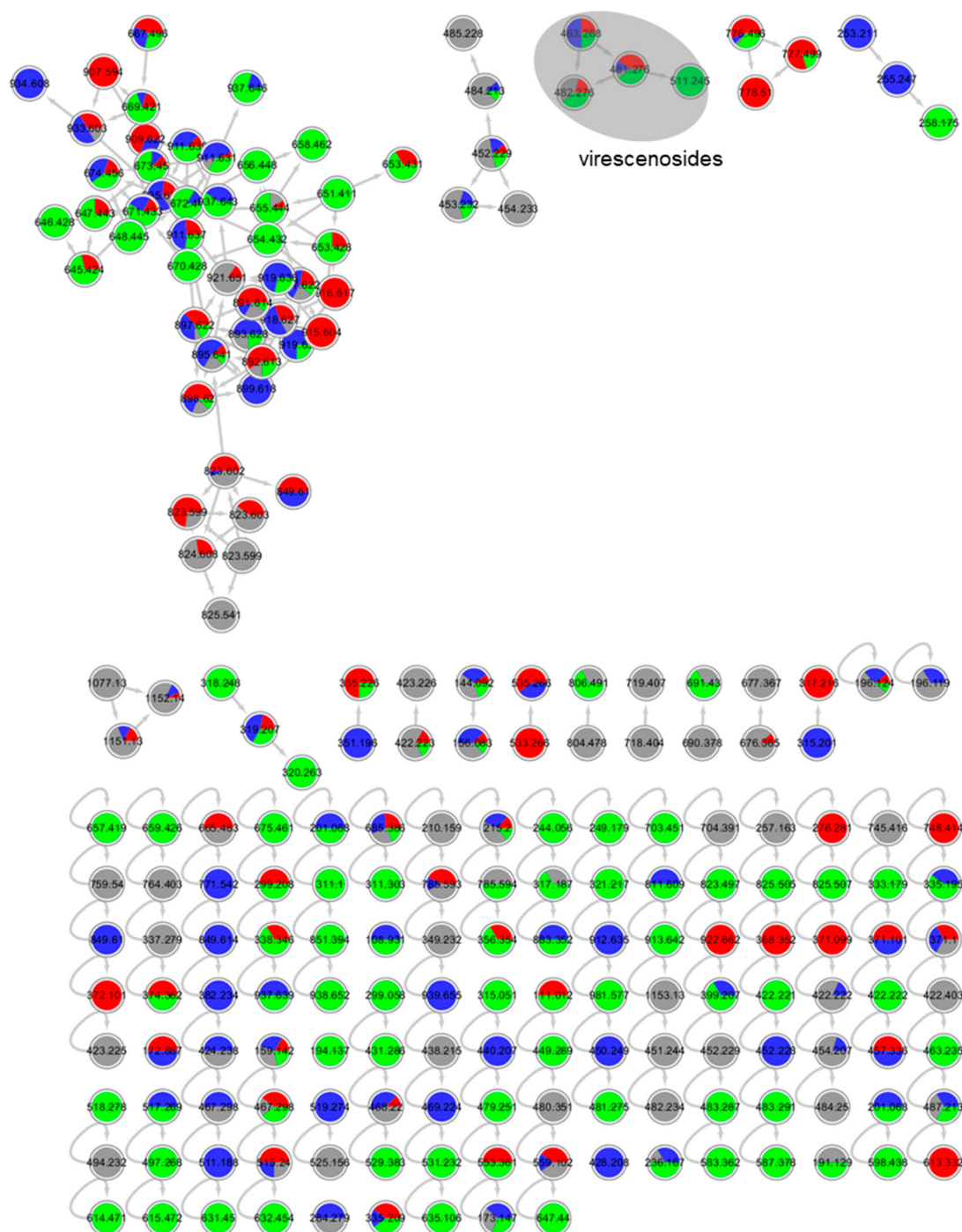


Figure S4. Molecular network for strain 1 (order Pleosporales) liquid culture extracts in PDM-L (blue), Cza-L (red), SYM-L (green), WM-L (grey). Annotated peak ions of putatively known compounds are highlighted by a grey loop.

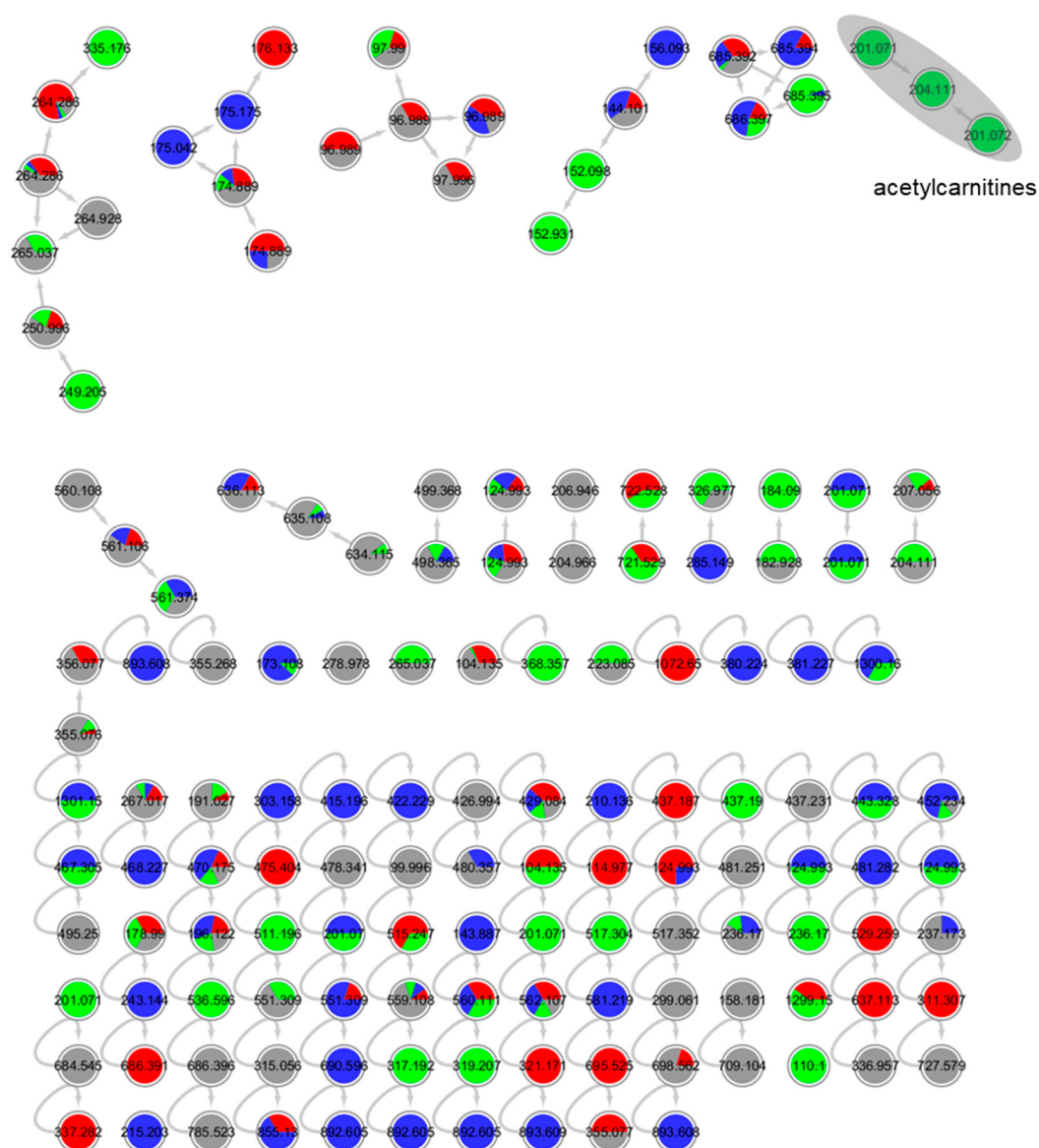
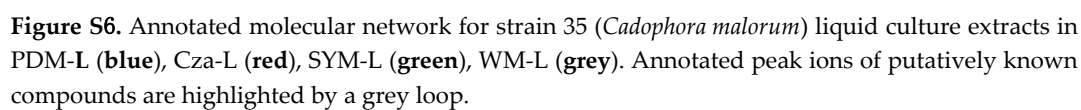


Figure S5. Annotated molecular network for strain 1 (order Pleosporales) solid culture extracts in PDM-S (blue), Cza-S (red), SYM-S (green), WM-S (grey). Annotated peak ions of putatively known compounds are highlighted by a grey loop.



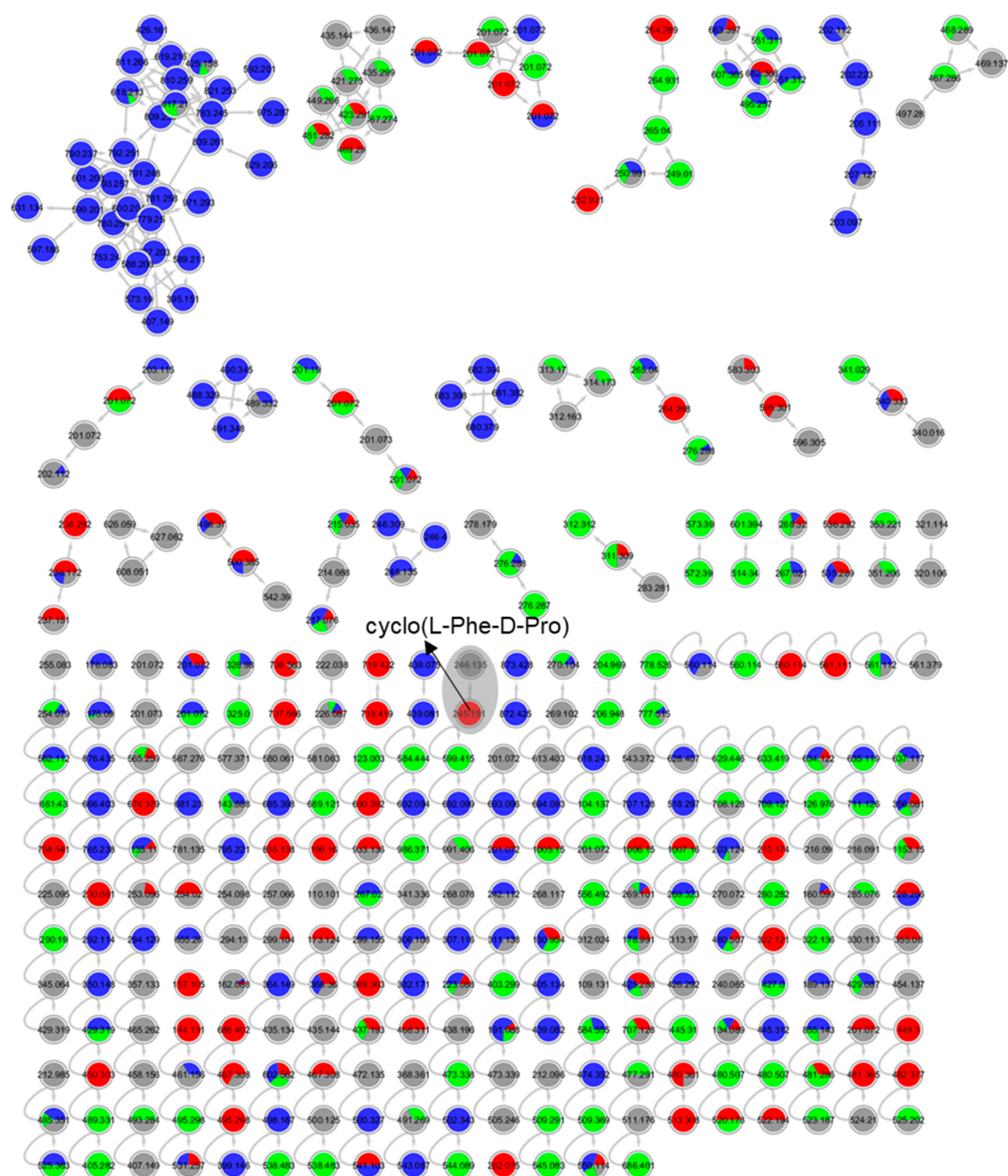


Figure S7. Annotated molecular network for strain 35 (*Cadophora malorum*) solid culture extracts in PDM-S (blue), Cza-S (red), SYM-S (green), WM-S (grey). Annotated peak ions of putatively known compounds are highlighted by a grey loop.

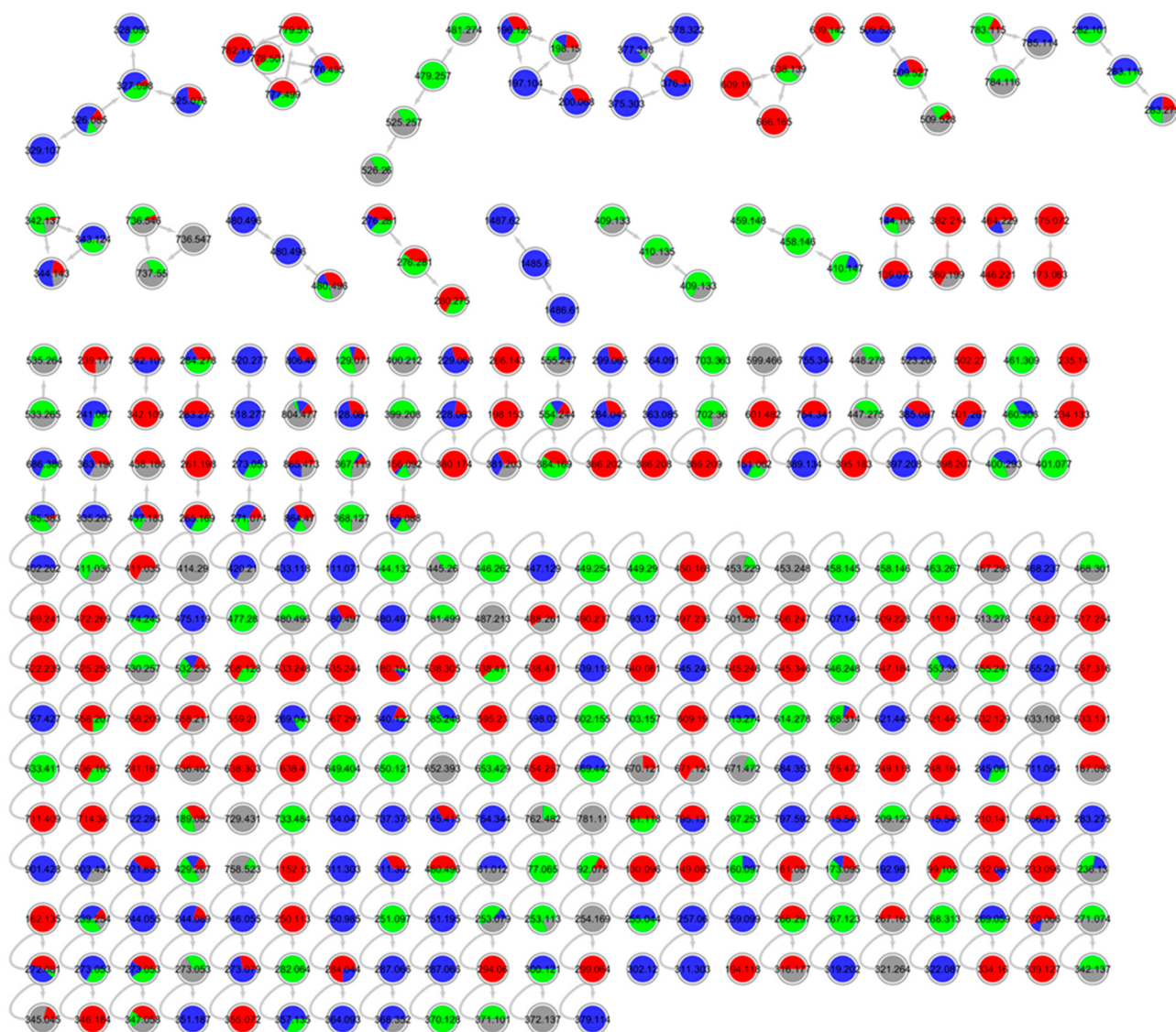


Figure S8. Annotated molecular network for strain 37 (order Hypocreales) liquid culture extracts in PDM-L (**blue**), Cza-L (**red**), SYM-L (**green**), WM-L (**grey**).

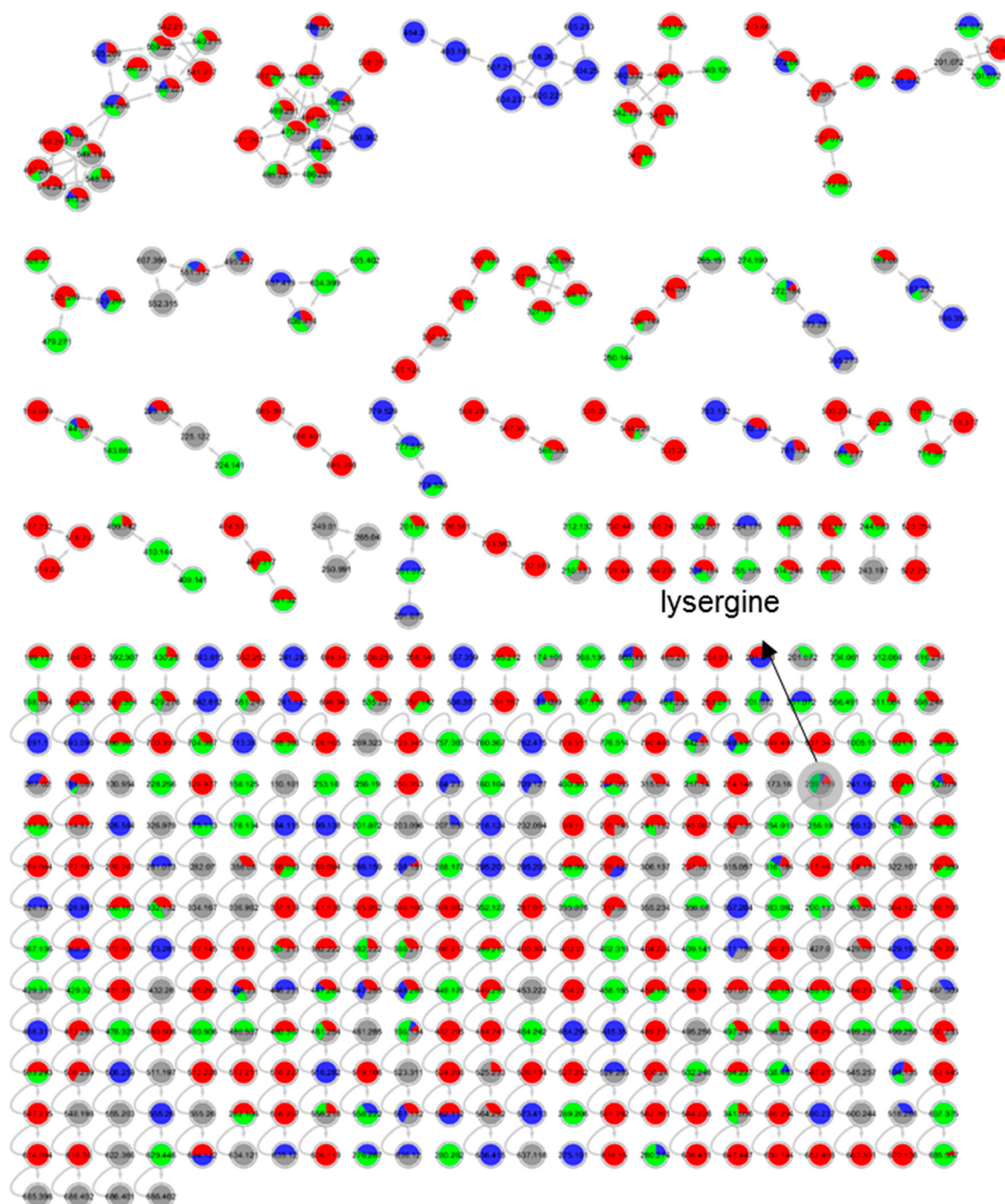


Figure S9. Annotated molecular network for strain 37 (order Hypocreales) solid culture extracts in PDM-S (blue), Cza-S (red), SYM-S (green), WM-S (grey). Annotated peak ions of putatively known compounds are highlighted by a grey loop.

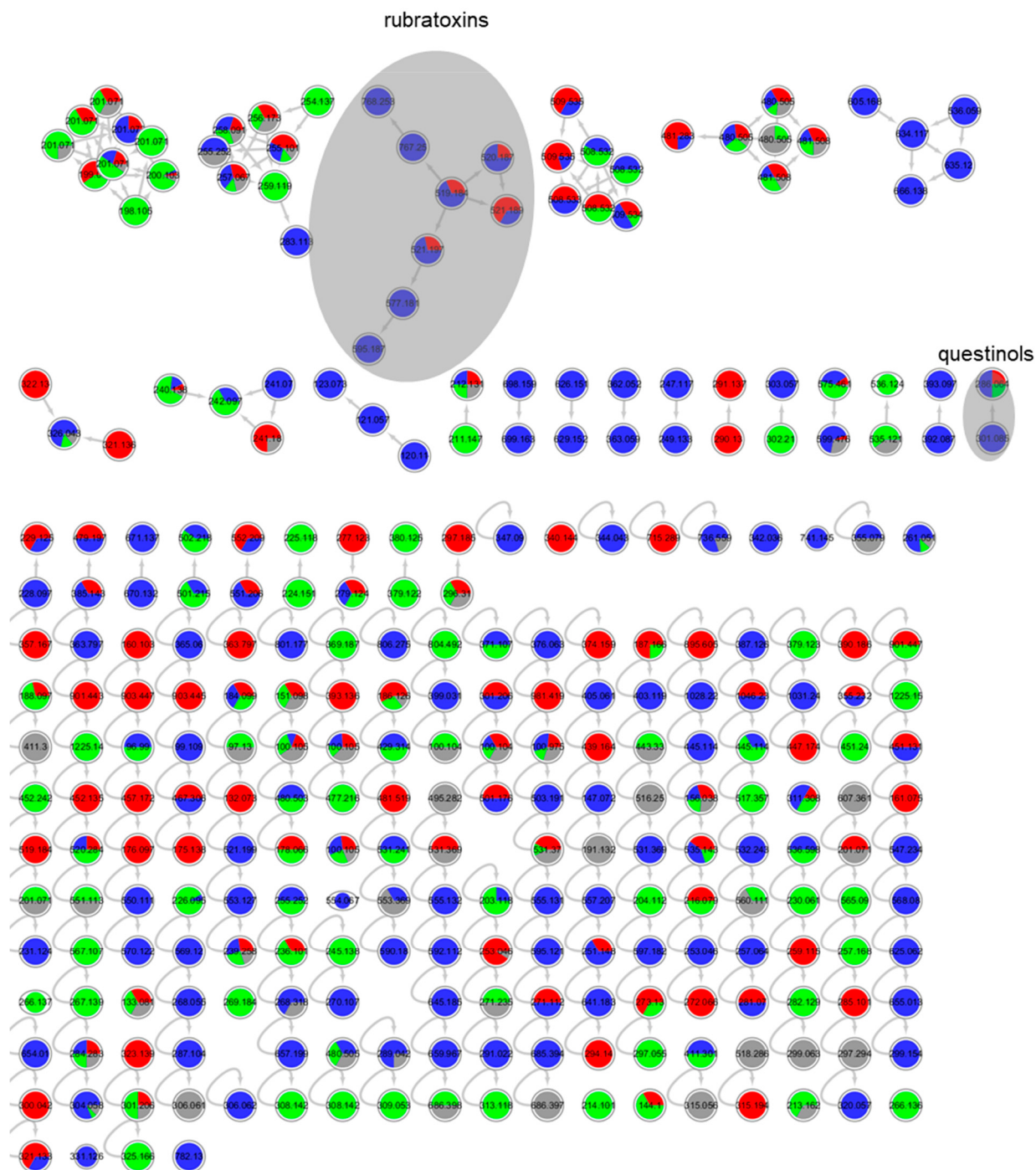


Figure S10. Annotated molecular network for strain 50 (*Penicillium* sp.) liquid culture extracts in PDM-L (blue), Cza-L (red), SYM-L (green), WM-L (grey). Annotated peak ions of putatively known compounds are highlighted by a grey loop.

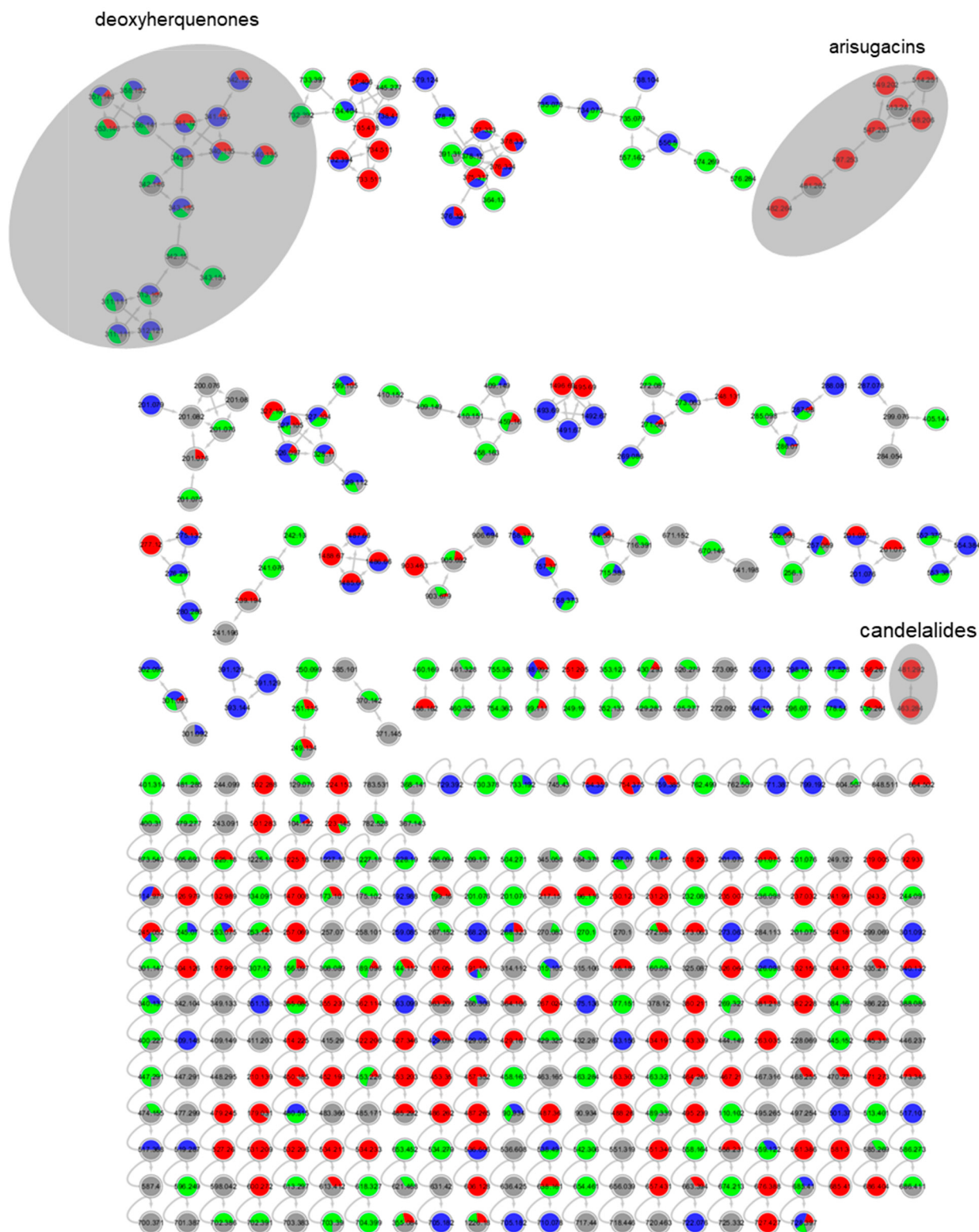


Figure S11. Annotated molecular network for strain 50 (*Penicillium* sp.) solid culture extracts in PDM-S (blue), Cza-S (red), SYM-S (green), WM-S (grey). Annotated peak ions of putatively known compounds are highlighted by a grey loop.

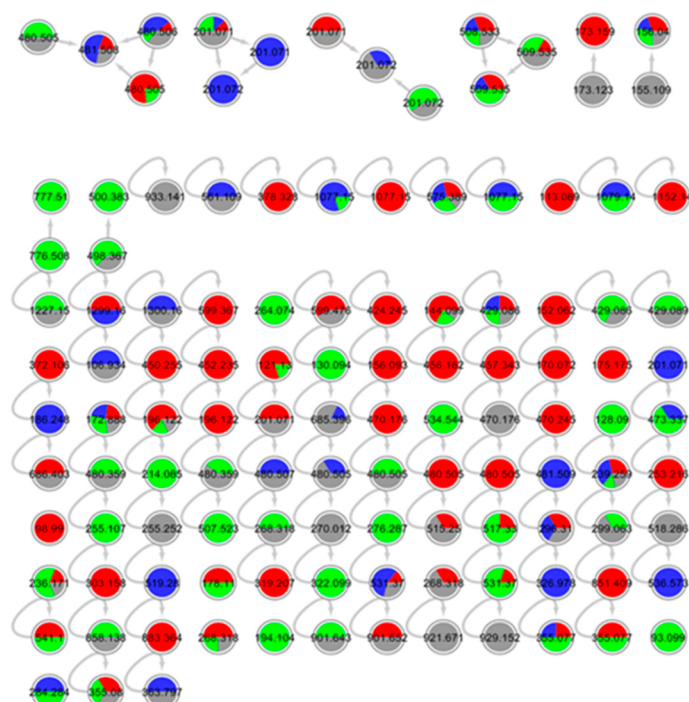


Figure S12. Annotated molecular network for strain 56 (*Penicillium* sp.) liquid culture extracts in PDM-L (blue), Cza-L (red), SYM-L (green), WM-L (grey).

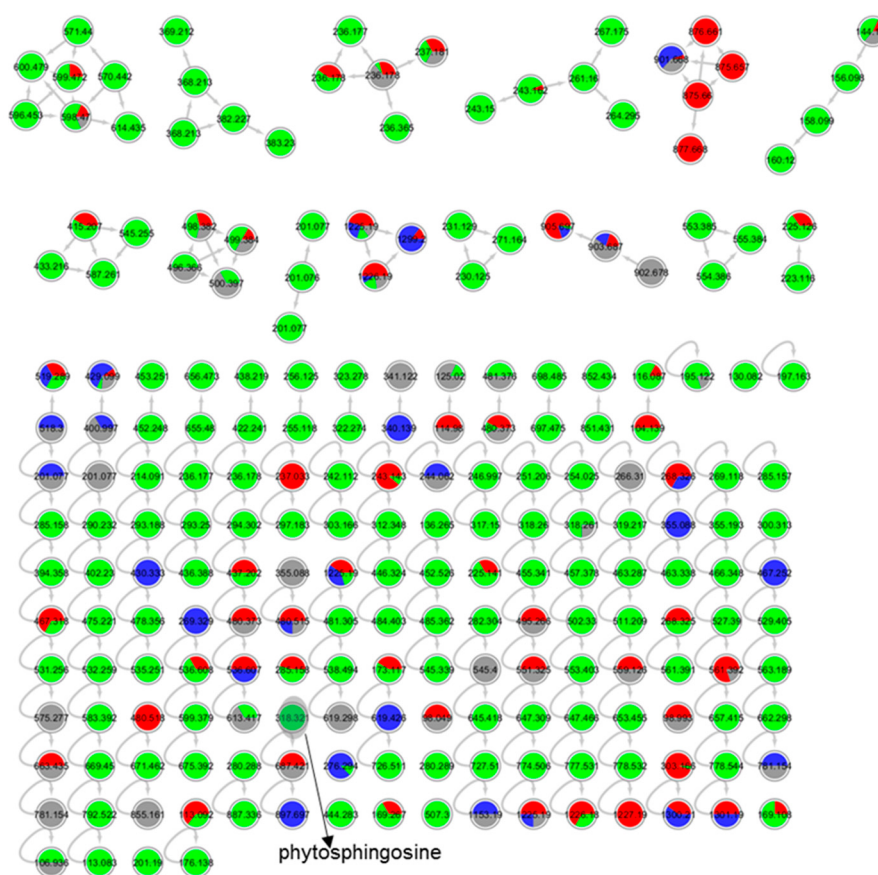


Figure S13. Annotated molecular network for strain 56 (*Penicillium* sp.) solid culture extracts in PDM-S (blue), Cza-S (red), SYM-S (green), WM-S (grey). Annotated peak ions of putatively known compounds are highlighted by a grey loop.

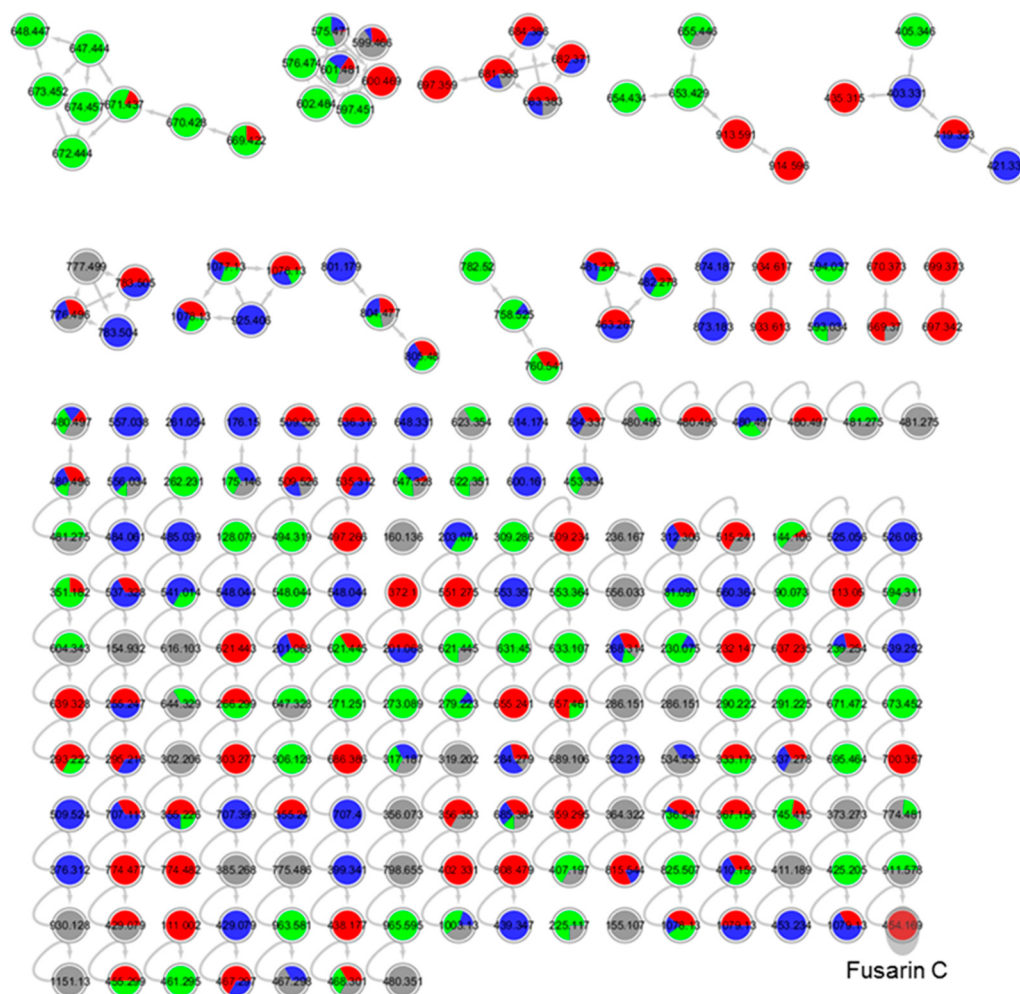


Figure S14. Annotated molecular network for strain 58 (*Fusarium graminearum*) liquid culture extracts in PDM-L (blue), Cza-L (red), SYM-L (green), WM-L (grey). Annotated peak ions of putatively known compounds are highlighted by a grey loop.

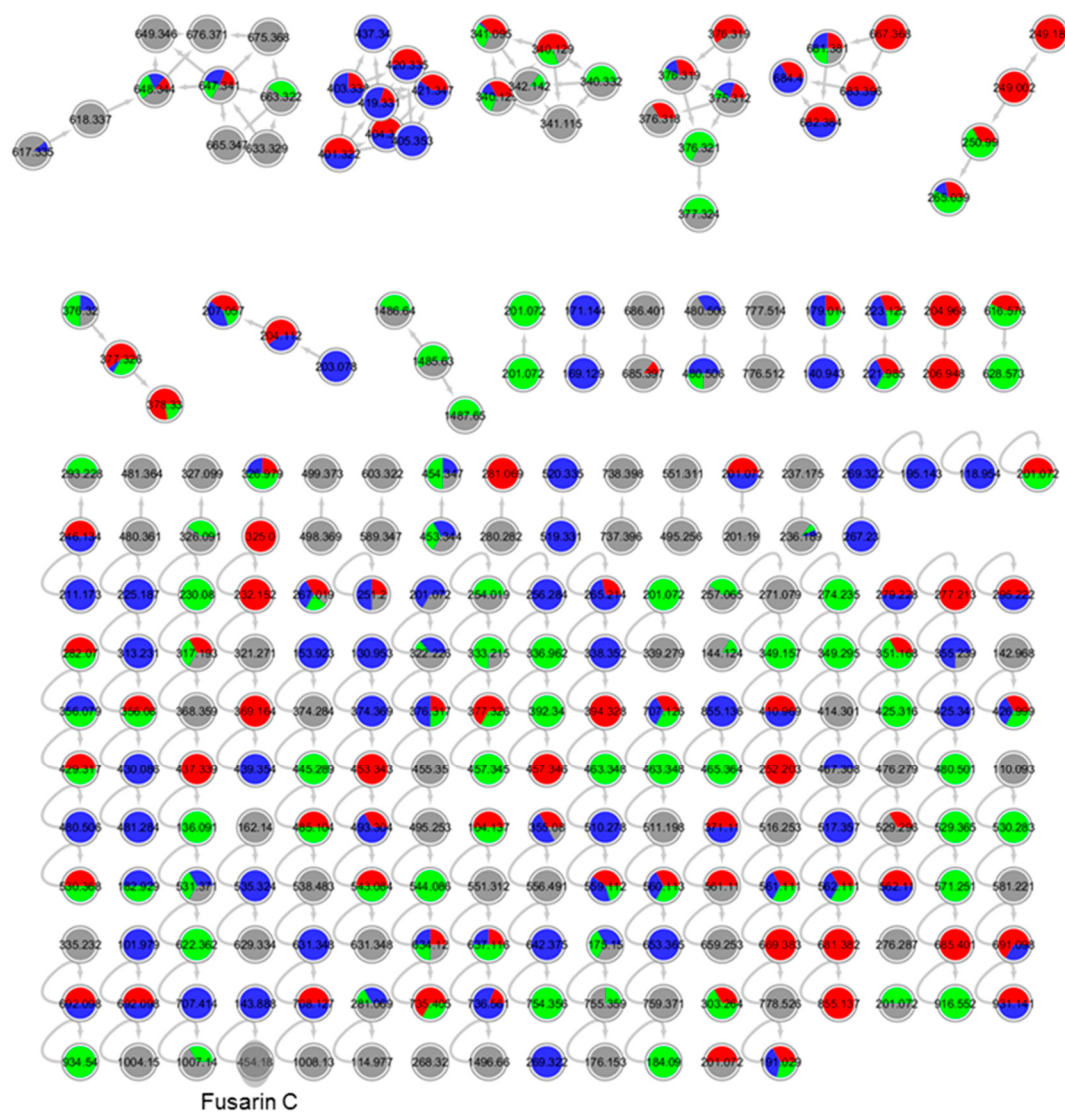


Figure S15. Annotated molecular network for strain 58 (*Fusarium graminearum*) solid culture extracts in PDM-S (blue), Cza-S (red), SYM-S (green), WM-S (grey). Annotated peak ions of putatively known compounds are highlighted by a grey loop.

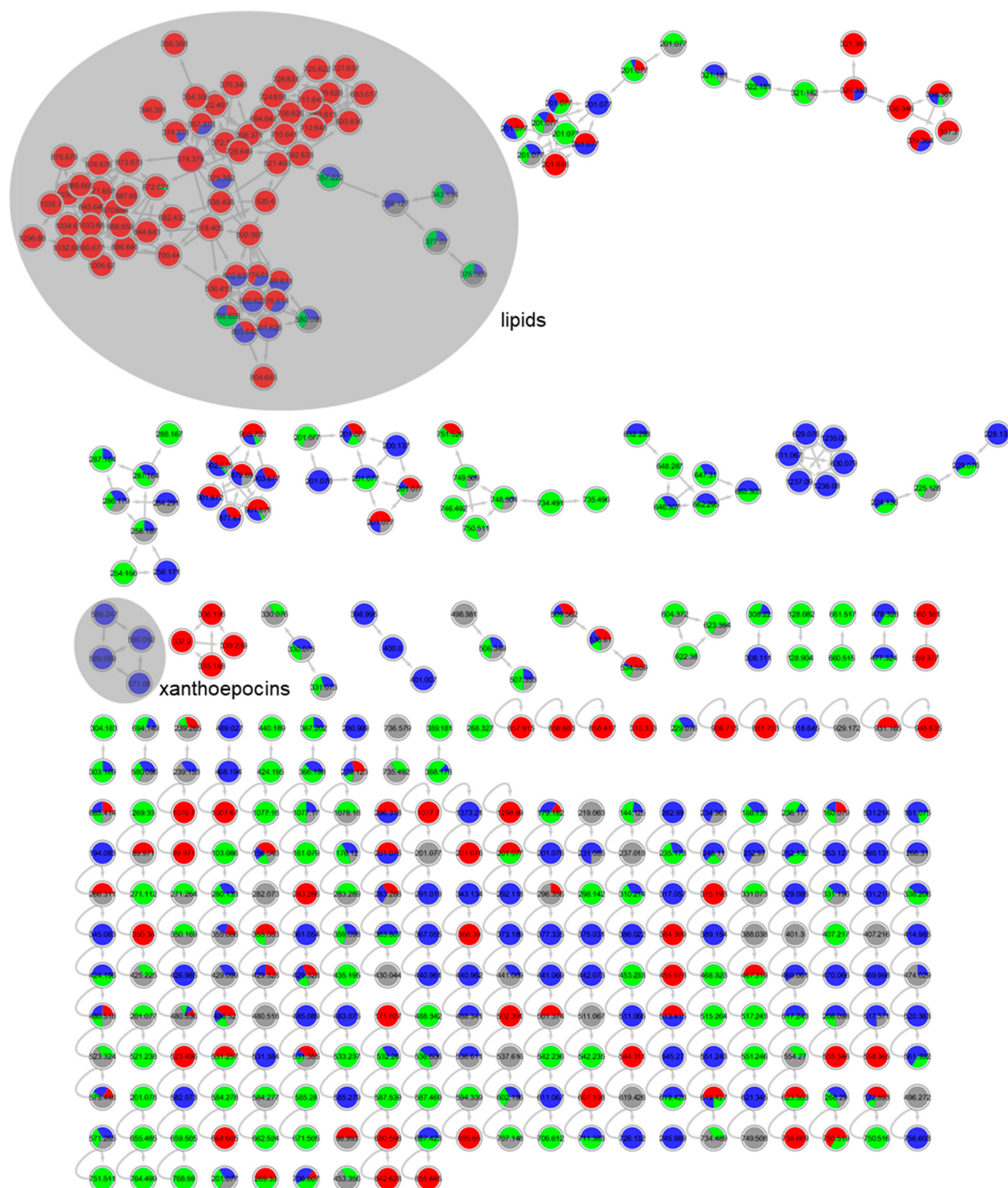


Figure S16. Annotated molecular network for strain 59 (order Glomerellales) liquid culture extracts in PDM-L (blue), Cza-L (red), SYM-L (green), WM-L (grey). Annotated peak ions of putatively known compounds are highlighted by a grey loop.

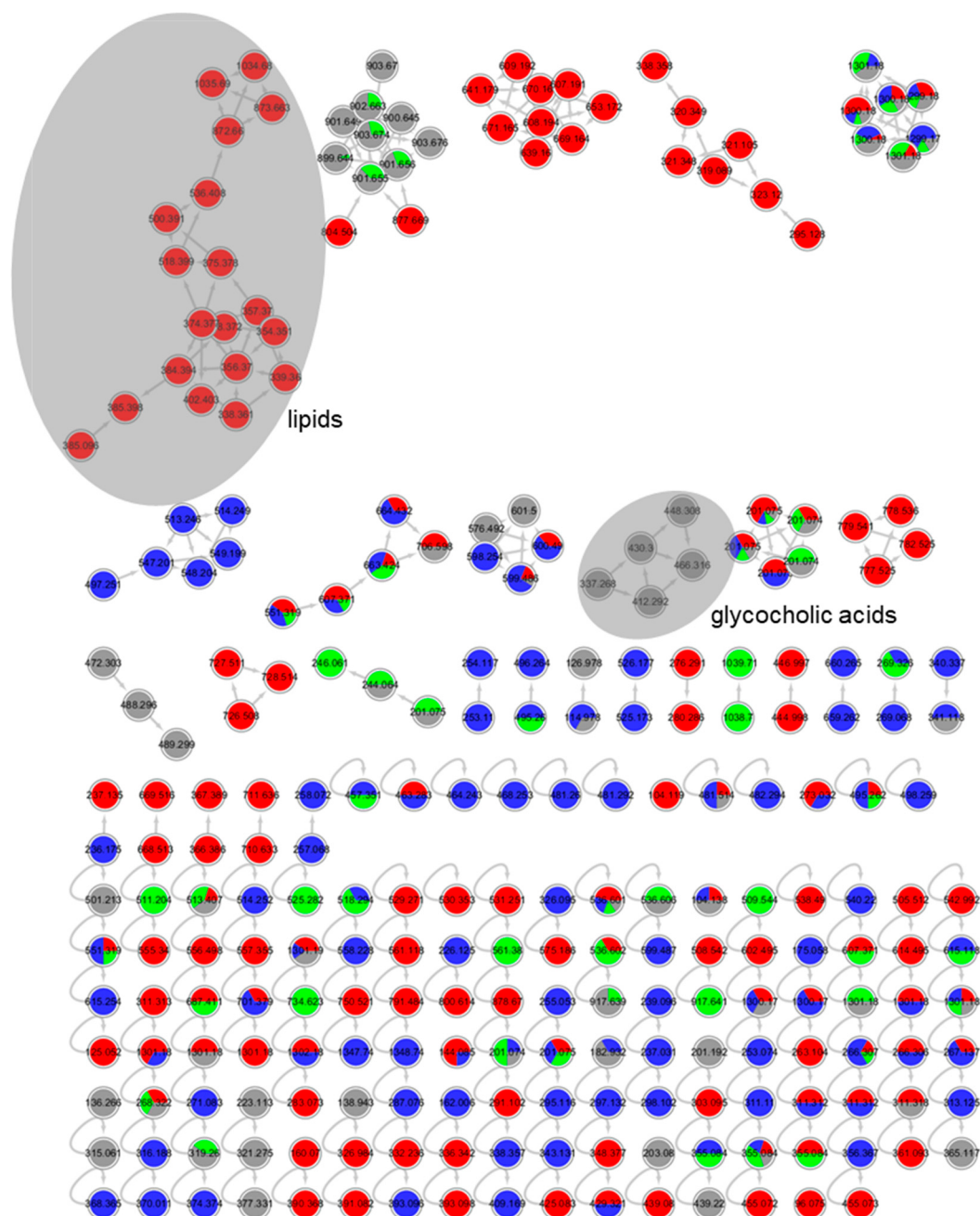


Figure S17. Annotated molecular network for strain 59 (order Glomerellales) solid culture extracts in PDM-S (blue), Cza-S (red), SYM-S (green), WM-S (grey). Annotated peak ions of putatively known compounds are highlighted by a grey loop.

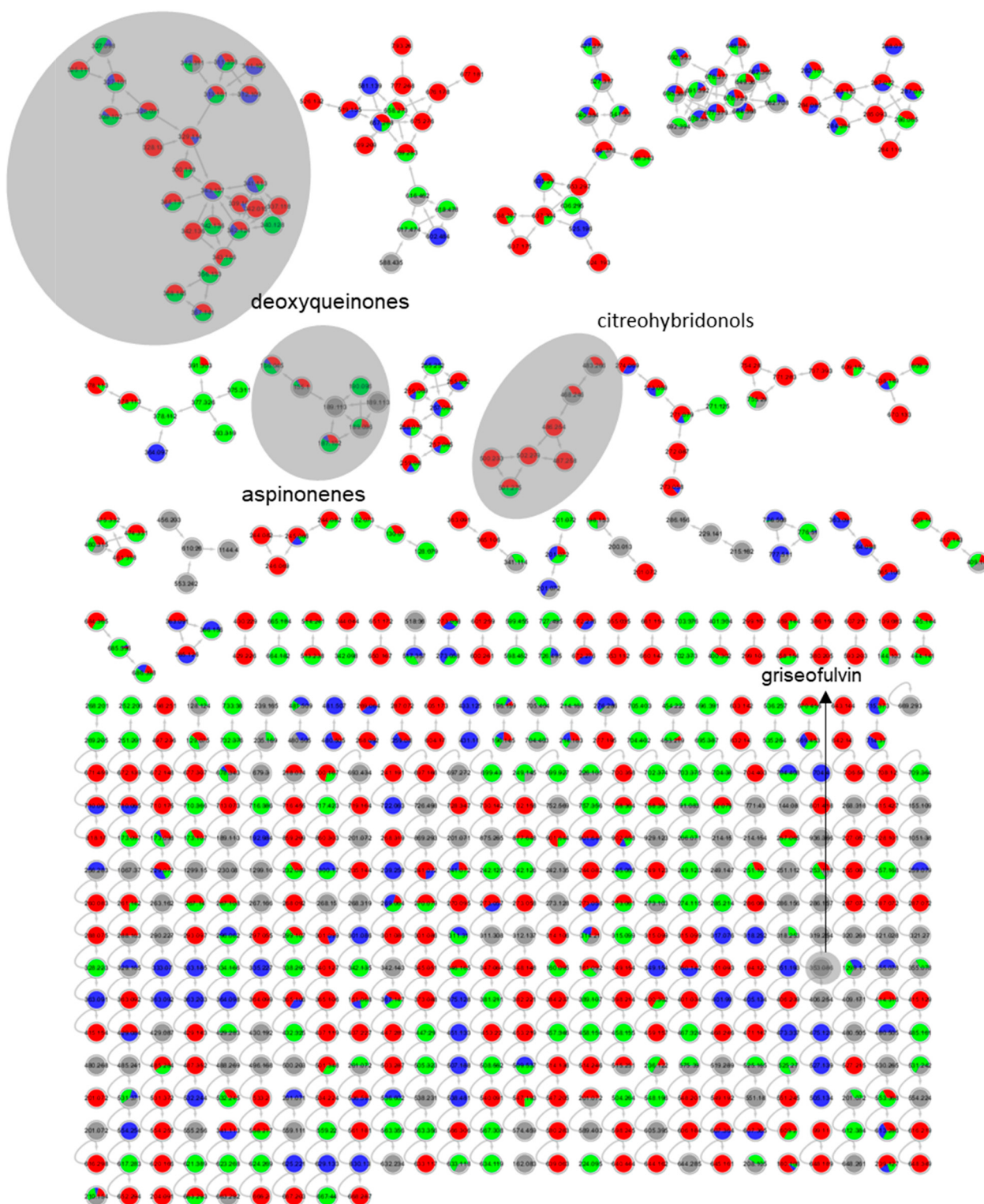


Figure S18. Annotated molecular network for strain 68 (*Penicillium* sp.) liquid culture extracts in PDM-L (blue), Cza-L (red), SYM-L (green), WM-L (grey). Annotated peak ions of putatively known compounds are highlighted by a grey loop.

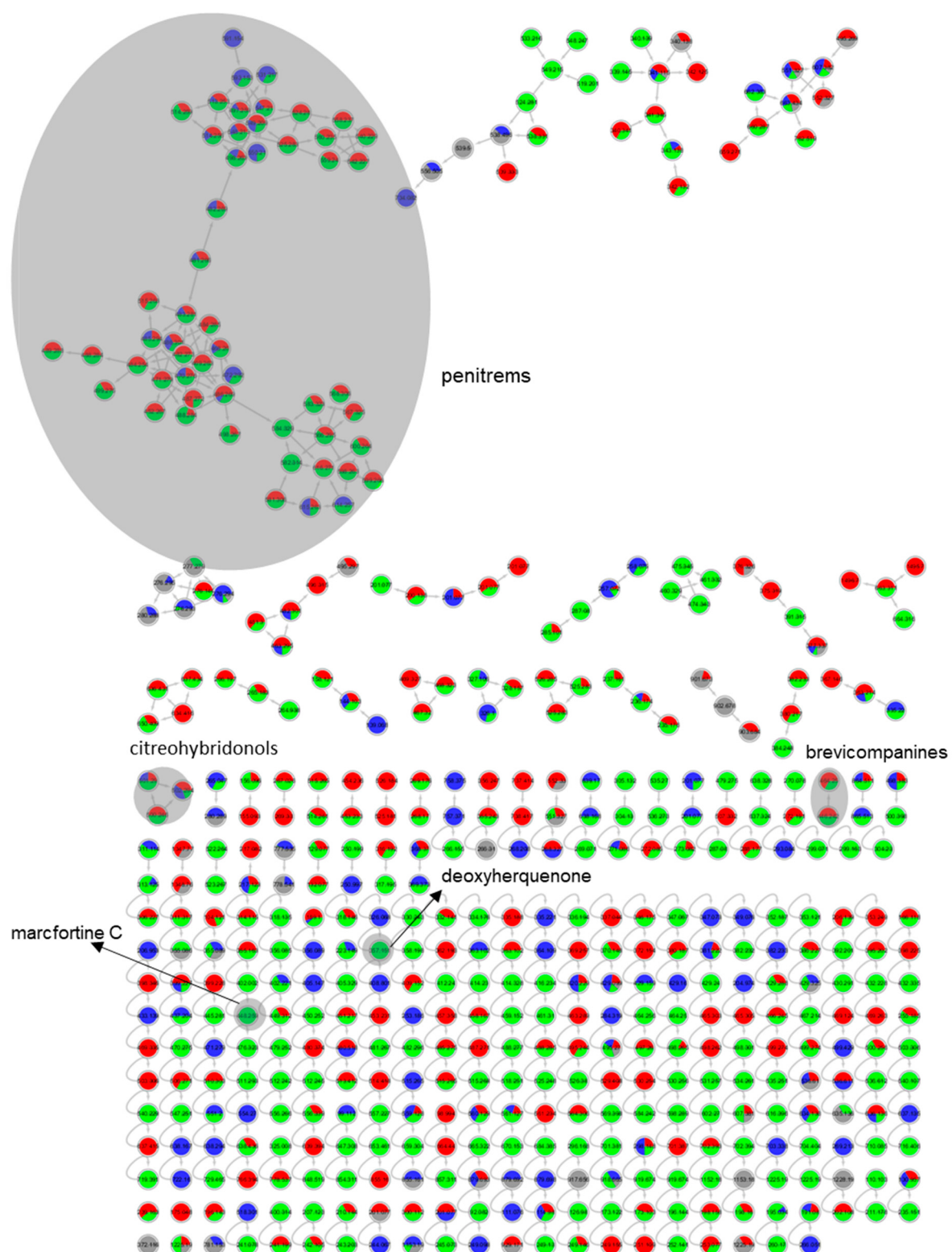
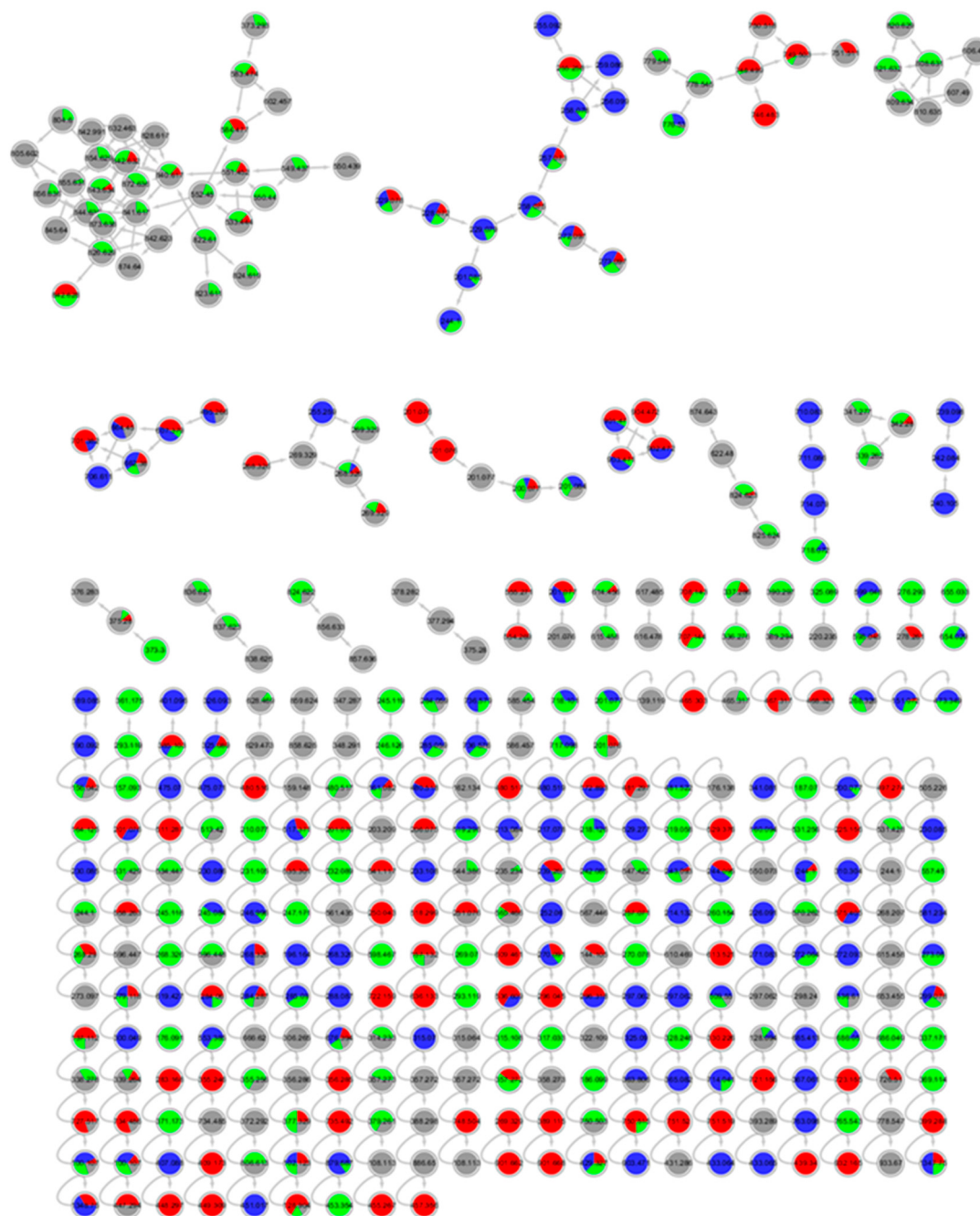


Figure S19. Annotated molecular network for strain 68 (*Penicillium* sp.) solid culture extracts in PDM-S (blue), Cza-S (red), SYM-S (green), WM-S (grey). Annotated peak ions of putatively known compounds are highlighted by a grey loop.



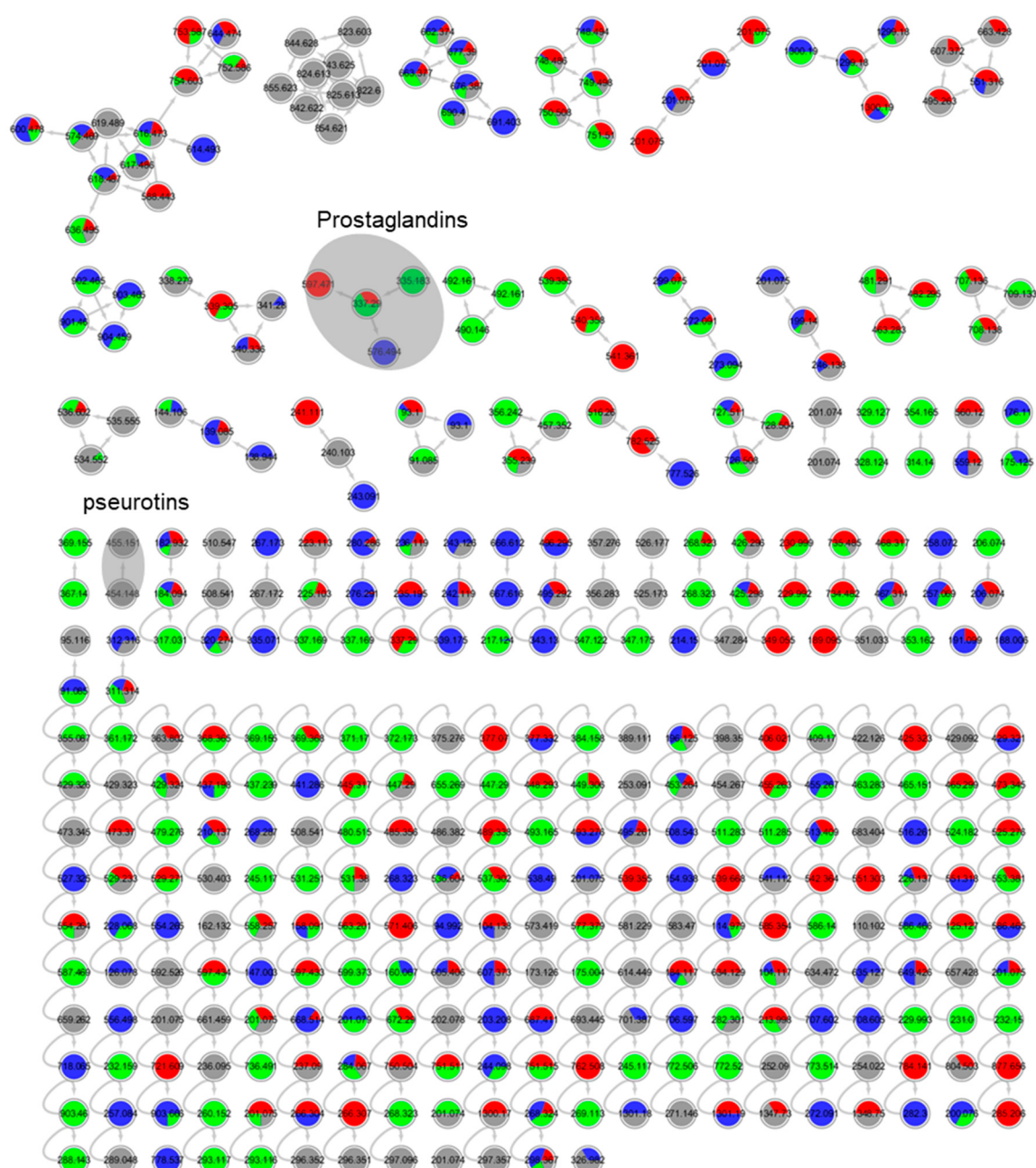


Figure S21. Annotated molecular network for strain 78 (*Penicillium* sp.) solid culture extracts in PDM-S (blue), Cza-S (red), SYM-S (green), WM-S (grey). Annotated peak ions of putatively known compounds are highlighted by a grey loop.

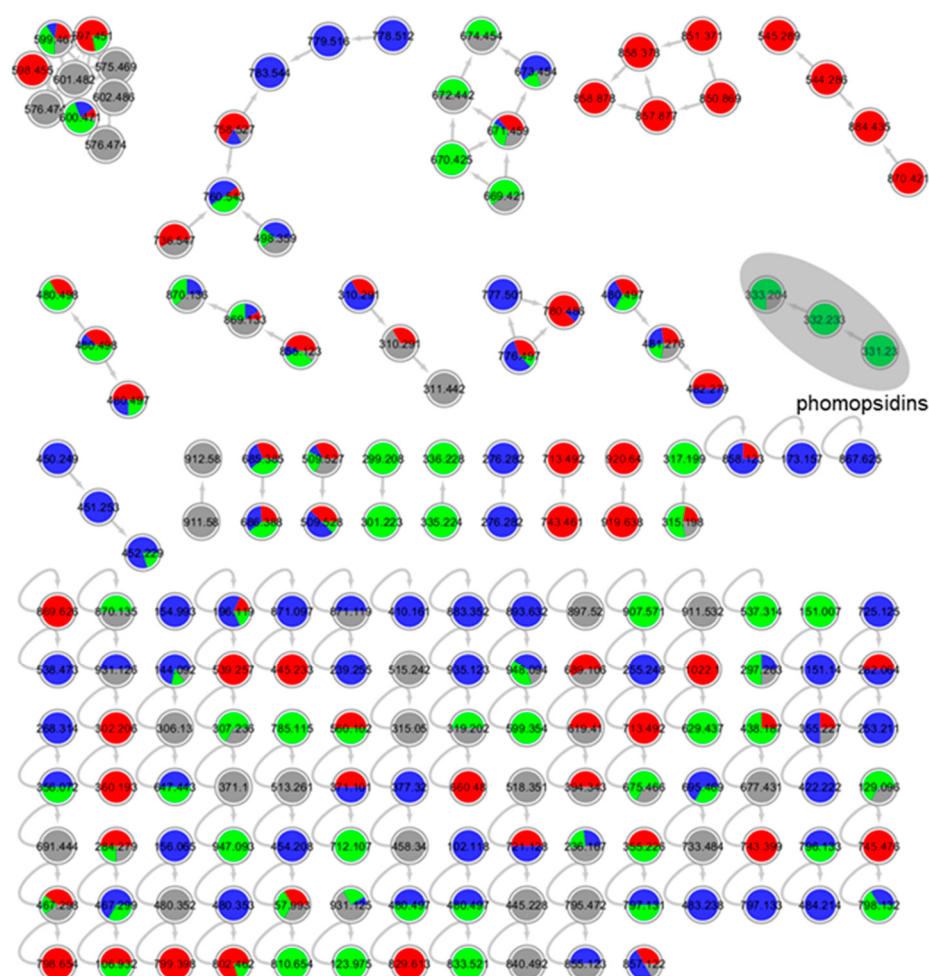
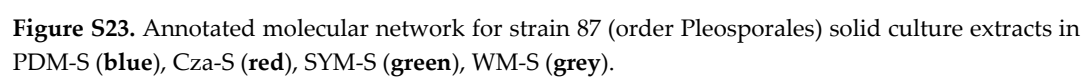


Figure S22. Annotated molecular network for strain 87 (order Pleosporales) liquid culture extracts in PDM-L (blue), Cza-L (red), SYM-L (green), WM-L (grey). Annotated peak ions of putatively known compounds are highlighted by a grey loop.



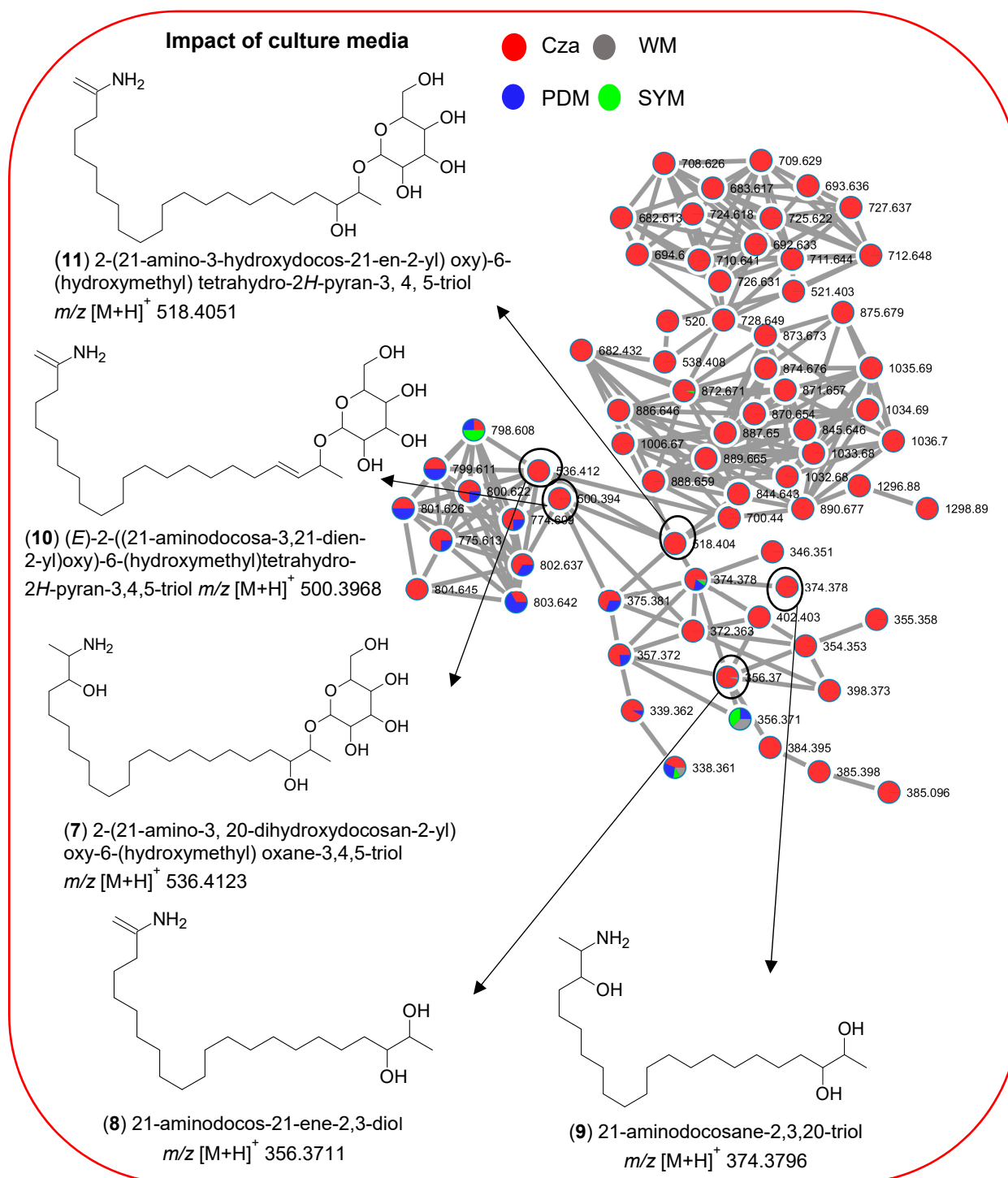


Figure S24. Molecular network of the aminolipid family detected in strain 59 (order Glomerellales) extracts. **Red nodes:** Ions detected in Cza extracts. **Blue nodes:** Ions detected in PDM extracts. **Green nodes:** Ions detected in SYM extracts. **Grey nodes:** Ions detected in WM extracts.

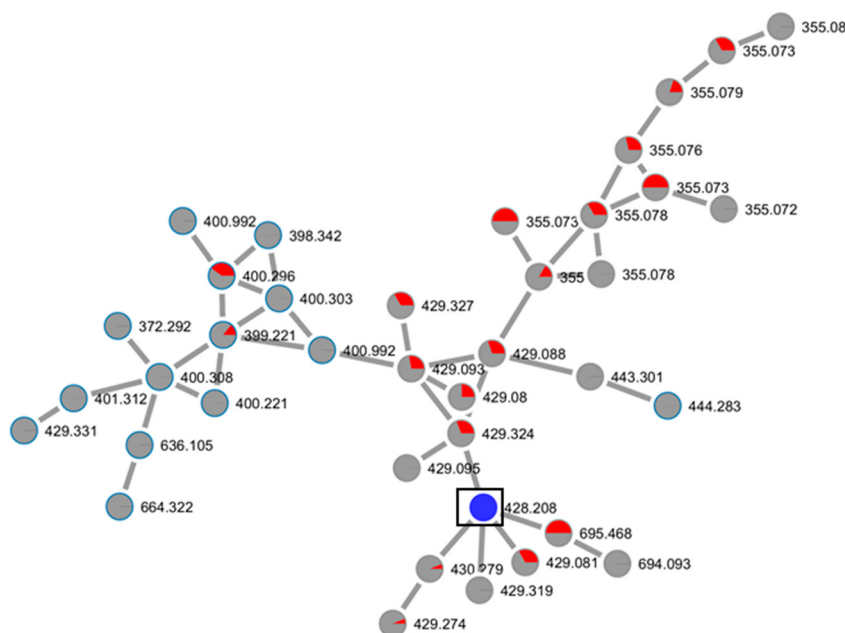


Figure S25. Molecular network of an unannotated cluster containing specific node (m/z $[M+H]^+$ 428.2081) generated from the global MN (Figure 7A). **Black square:** node exclusive to the bioactive 1PDM-L extract. **Red nodes:** Ions detected in toxic samples. **Grey nodes:** Ions detected in inactive samples. **Blue nodes:** Ions detected in bioactive samples.

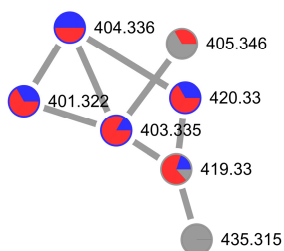


Figure S26. Molecular network of an unannotated cluster containing 3 specific nodes (m/z $[M+H]^+$ 401.3221, $[M+H]^+$ 403.3355, $[M+H]^+$ 419.3300) generated from the global MN (Figure 7A). **Red nodes:** Ions detected in toxic samples. **Grey nodes:** Ions detected in inactive samples. **Blue nodes:** Ions detected in bioactive samples.