Electronic Supplementary Material (ESI) for Metallomics.

Supporting information

for

Metabolomic and proteomic changes induced by growth inhibitory concentrations of copper in the biofilm-forming marine bacterium *Pseudoalteromonas lipolytica*

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***Detailed description of the experimental protocol used for Cu chemical speciation*.**

Differential pulse anodic striping voltammetry (DPASV) measurements were performed to assess Cu chemical speciation in both VNSS and MB medium. All voltammetric measurements were performed using a PGSTAT12 potentiostat (EcoChemie, The Netherlands) equipped with a Metrohm 663 VA stand (Metrohm, Switzerland) on an Hg drop electrode. Analysis of the voltammetric peaks' (after 2nd derivative transformation) and construction of the pseudo-polarograms were performed automatically using ECDSoft software. The experimental procedure adapted from Nicolau *et al.* (2008) and Bravin *et al.* (2012) is explained briefly below. Pseudo-polarographic measurements (DPASV measurement with E_{dep} from -1.0 to 0.0V by steps of 100 mV, using a deposition time of 30s) were initially performed on UV-irradiated seawater (collected outside the Toulon bay: ambient Cu concentration of 2.5 nM) at pH < 2 (by adding HNO_3 Suprapur grade, Merck), to determine the deposition potential (E_{dep} -0.35V) corresponding to the electrochemically "labile" Cu fraction (sum of free Cu ions plus inorganically bound Cu) (Figure S2). Copper additions were then performed in order to determine the sensitivity of the method.

Then Cu additions (25 to 2500 nM) were performed in VNSS and MB medium 1000-fold diluted in UV-irradiated seawater at pH 8.0 ± 0.2 (using borate buffer, Suprapur, Merck). Pseudopolarograms were recorded, repeating DPASV measurement with E_{dep} from -1.5 to 0.0 V by steps of 50 mV, using a deposition time of 30s followed by a short conditioning time (1s) at a E_{dep} of −1.6 V to avoid any interference from organic surfactants. From the obtained pseudopolarograms, as previously defined (Feldmann et al., 2009; Nicolau et al., 2008), the additional fraction of Cu possibly measured at the most negative E_{dep} (leading to an additional wave on the pseudopolarograms) thus corresponds to the direct reduction of organic Cu complexes at the Hg drop electrode, electrochemically dissociable, hereafter referred to as the "dissociable" Cu fraction (Figure S2). The difference between the total Cu concentration and the sum of labile and dissociable Cu concentrations correspond to the presence of non-dissociable organic Cu complexes, hereafter referred to as the "inert" Cu fraction. Obtained pseudopolarograms on 1000-fold diluted VNSS and MB medium in presence of 500 nM of Cu at pH ~ 8 are depicted on Figure S2 and compared with the pseudopolarogram measured in seawater at pH < 2.

M. N. Bravin, C. Garnier, V. Lenoble, F. Gérard, Y. Dudal and P. Hinsinger, *Geochim. Cosmochim. Acta*, 2012, **84**, 256–268.

J. Feldmann, P. Salaün and E. Lombi, *Environ. Chem.*, 2009, **6**, 275–289.

R. Nicolau, Y. Louis, D. Omanović, C. Garnier, S. Mounier and I. Pižeta, *Anal. Chim. Acta*, 2008, **618**, 35–42.

TABLES

Table S1. Summary of the parameters for the assessment of quality and validity of the PLS-DA models used for the discrimination of controls and Cu-treated planktonic and biofilm cultures of *P. lipolytica* TC8 after metabolomic and proteomic analyses.

Study	Model type	Number of classes	N^a	$R^2X_{cum}{}^b$	$R^2Y_{cum}{}^c$	$Q^2Y_{cum}{}^d$	$R_{intercept}{}^e$	$Q_{intercept}{}^e$	P^f
Metabolomic	PLS-DA (#1)	6	7	0.727	0.960	0.799	0.576	-0.616	< 0.001
	PLS-DA (#2)	6	8	0.813	0.962	0.818	0.568	-0.809	< 0.001
	PLS-DA (#3)	6	9	0.880	0.963	0.825	0.553	-0.938	< 0.001
Proteomic	PLS-DA	2	4	0.748	0.988	0.980	0.294	-0.324	< 0.001
	OPLS-DA (#1)	2	1 + 2 + 0	0.899	0.995	0.988	-	-	< 0.001
	OPLS-DA (#2)	2	1 + 2 + 0	0.926	0.996	0.991	-	-	< 0.001

[a] Number of components of the model; [b] Cumulative modeled variation in X matrix; [c] Cumulative modeled variation in Y matrix; [d] Cumulative predicted variation in Y matrix; [e] R and Q intercepts obtained after permutation test (*n* = 150); [f] *p* value obtained from 7-fold cross validation ANOVA of PLS-DA.

Table S2: List of the characteristic biomarkers (VIP value > 1, identified by UPLC-HRMS) of the six-class PLS-DA model (#3) discriminating planktonic (Pl) and biofilm (Bf) samples of *P. lipolytica* TC8 cultured without (Control) and with Cu supplement (1000 μM: Cu-1000 and 1400 μM: Cu-1400).

Culture conditions	VIP number	*m/z*	RT (s)	Formula	Mass error (ppm)	mσ[a]	Main MS/MS fragment ions (relative abundance in %)	Putative identification
Pl Cu-1000 (over-expressed compounds)	7	347.2200	360	$C_{21}H_{31}O_4$	1.6	4.7	329.2111 $[M - H_2O + H]^+$ (3), 319.2249 $[M - H_2O - CO + H]^+$ (10), 275.1710 $[M - C_4H_8O + H]^+$ (100), 257.1599 $[M - C_4H_8O - H_2O + H]^+$ (59), 239.1499 $[M - C_4H_8O - 2H_2O + H]^+$ (62), 221.1387 $[M - C_4H_8O - 3H_2O + H]^+$ (67)	-
	8	147.0557	65	$C_8H_7N_2O$	3.1	0.7	130.0290 $[M - NH_3 + H]^+$ (100), 129.0450 $[M - H_2O + H]^+$ (27), 120.0446 $[C_7H_6NO]^+$ (65), 119.0608 $[C_7H_7N_2]^+$ (7), 104.0497 $[C_7H_6N]^+$ (56), 92.0495 $[C_6H_6N]^+$ (65), 84.0808 $[C_5H_{10}N]^+$ (31)	-
	9	120.0449	297	C_7H_6NO	0.5	4.6	92.0498 $[C_6H_6N]^+$ (100), 65.0386 $[C_5H_5]^+$ (69)	-
Pl Cu-1400 (over-expressed compounds)	11	688.4909	491	$C_{37}H_{71}NO_8P$	0.3	11.7	547.4667 $[M - C_2H_8NO_4P + H]^+$ (100)	PE (C16:1, C16:1)
	12	702.5067	505	$C_{38}H_{73}NO_8P$	0.5	3.5	561.4824 $[M - C_2H_8NO_4P + H]^+$ (100)	PE (C17:1, C16:0)
	28	325.2688	412	$C_{20}H_{37}O_3$	0.8	4.2	n.f.[b]	
	34	676.4911	498	$C_{36}H_{71}NO_8P$	0.2	6.1	535.4673 $[M - C_2H_8NO_4P + H]^+$ (100)	PE (C16:1, C15:0)
	35	663.5662	424	$C_{40}H_{75}N_2O_5$	1.3	1.8	645.5588 $[M - H_2O + H]^+$ (2), 413.3382 $[M - C_{17}H_{31}O + H]^+$ (13), 395.3274 $[M - H_2O - C_{17}H_{31}O + H]^+$ (46), 377.3168 $[M - 2\ H_2O - C_{17}H_{31}O + H]^+$ (46), 159.0767 $[C_6H_{11}N_2O_3]^+$ (5)[c], 141.0661 $[C_6H_9N_2O_2]^+$ (3)[c], 133.0976 $[C_5H_{13}N_2O_2]^+$ (5)[c], 115.0870 $[C_5H_{11}N_2O]^+$ (100)[c], 70.0651 $[C_4H_8N]^+$ (34)[c]	OL (C18:1, C17:1)
Pl Cu-1400 (under-expressed compounds)	16	413.3376	301	$C_{24}H_{45}N_2O_4$	3.0	12.4	395.3273 $[M - H_2O + H]^+$ (3), 377.3166 $[M - 2H_2O + H]^+$ (5), 359.3006 $[M - 3H_2O + H]^+$ (4), 159.0768 $[C_6H_{11}N_2O_3]^+$ (1)[c], 141.0661 $[C_6H_9N_2O_2]^+$ (3)[c], 133.0976 $[C_5H_{13}N_2O_2]^+$ (7)[c], 115.0870 $[C_5H_{11}N_2O]^+$ (100)[c], 70.0650 $[C_4H_8N]^+$ (54)[c]	LOL (C18:1)
	17	621.5194	404	$C_{37}H_{69}N_2O_5$	1.1	0.3	603.5105 $[M - H_2O + H]^+$ (2), 385.3061 $[M - C_{16}H_{29}O + H]^+$ (11), 367.2956 $[M - H_2O - C_{16}H_{29}O + H]^+$ (38), 349.2851 $[M - 2H_2O - C_{16}H_{29}O + H]^+$ (37), 159.0767 $[C_6H_{11}N_2O_3]^+$ (4)[c], 141.0660 $[C_6H_9N_2O_2]^+$ (3)[c], 133.0976 $[C_5H_{13}N_2O_2]^+$ (5)[c], 115.0870 $[C_5H_{11}N_2O]^+$ (100)[c], 70.0650 $[C_4H_8N]^+$ (28)[c]	OL (C16:1, C16:1)
	18	597.5147	409	$C_{35}H_{69}N_2O_5$	1.5	1.8	579.5110 $[M - H_2O + H]^+$ (2), 359.2908 $[M - C_{16}H_{31}O + H]^+$ (8), 341.2803 $[M - H_2O - C_{16}H_{31}O + H]^+$ (29), 323.2697 $[M - 2H_2O - C_{16}H_{31}O + H]^+$ (32), 159.0767 $[C_6H_{11}N_2O_3]^+$ (3)[c], 141.0661 $[C_6H_9N_2O_2]^+$ (2)[c], 133.0975 $[C_5H_{13}N_2O_2]^+$ (4)[c], 115.0870 $[C_5H_{11}N_2O]^+$ (100)[c], 70.0650 $[C_4H_8N]^+$ (26)[c]	OL (C14:0, C16:0)
	19	677.5825	434	$C_{41}H_{77}N_2O_5$	0.2	4.4	659.5738 $[M - H_2O + H]^+$ (3), 413.3377 $[M - C_{18}H_{33}O + H]^+$ (18), 395.3271 $[M - H_2O - C_{18}H_{33}O + H]^+$ (68), 377.3165 $[M - 2H_2O - C_{18}H_{33}O + H]^+$ (68), 159.0767 $[C_6H_{11}N_2O_3]^+$ (5)[c], 141.0662 $[C_6H_9N_2O_2]^+$ (3)[c], 133.0977 $[C_5H_{13}N_2O_2]^+$ (5)[c], 115.0870 $[C_5H_{11}N_2O]^+$ (100)[c], 70.0651 $[C_4H_8N]^+$ (27)[c]	OL (C18:1, C18:1)

	24	595.5035	400	$C_{35}H_{67}N_2O_5$	1.8	1.6	577.4956 $[M - H_2O + H]^+$ (2), 359.2910 $[M - C_{16}H_{29}O + H]^+$ (6), 341.2802 $[M - H_2O - C_{16}H_{29}O + H]^+$ (21), 323.2697 $[M - 2H_2O - C_{16}H_{29}O + H]^+$ (23), 159.0766 $[C_6H_{11}N_2O_3]^+$ (4)[c], 141.0661 $[C_6H_9N_2O_2]^+$ (3)[c], 133.0976 $[C_5H_{13}N_2O_2]^+$ (5)[c], 115.0870 $[C_5H_{11}N_2O]^+$ (100)[c], 70.0650 $[C_4H_8N]^+$ (38)[c]	OL (C14:0, C16:1)
	30	625.5513	424	$C_{37}H_{73}N_2O_5$	0.4	2.0	607.5420 $[M - H_2O + H]^+$ (2), 387.3222 $[M - C_{16}H_{31}O + H]^+$ (11), 369.3116 $[M - H_2O - C_{16}H_{31}O + H]^+$ (41), 351.3010 $[M - 2H_2O - C_{16}H_{31}O + H]^+$ (44), 159.0767 $[C_6H_{11}N_2O_3]^+$ (6)[c], 141.0662 $[C_6H_9N_2O_2]^+$ (3)[c], 133.0976 $[C_5H_{13}N_2O_2]^+$ (5)[c], 115.0870 $[C_5H_{11}N_2O]^+$ (100)[c], 70.0651 $[C_4H_8N]^+$ (24)[c]	OL (C16:0, C16:0)
	36	329.2690	401	$C_{19}H_{37}O_4$	3.1	4.3	311.2560 $[M - H_2O + H]^+$ (9), 237.2189 $[C_{16}H_{29}O]^+$ (29), 219.2089 $[C_{16}H_{27}]^+$ (30), 135.1154 $[C_{10}H_{15}]^+$ (34), 121.0999 $[C_9H_{13}]^+$ (40), 95.0846 $[C_7H_{11}]^+$ (57), 83.0853 $[C_6H_{11}]^+$ (83), 81.0690 $[C_6H_9]^+$ (100), 69.0690 $[C_5H_9]^+$ (86), 67.0540 $[C_5H_7]^+$ (50), 57.0693 $[C_4H_9]^+$ (28), 55.0535 $[C_4H_7]^+$ (51)	MAG (C16:1)
Bf Cu-1000 (over-expressed compounds)	5	285.0848	123	$C_{15}H_{13}N_2O_4$	3.0	2.7	195.0767 $[C_9H_{11}N_2O_3]^+$ (14), 130.0651 $[C_9H_8N]^+$ (100)	-
	23	223.0692	62	$C_{10}H_{11}N_2O_4$	9.5	4.2	n.f.[b]	-
Bf Cu-1000 and Cu-1400 & Pl Cu-1000 (over-expressed compounds)	1	375.1455	202	$C_{21}H_{19}N_4O_3$	-1.0	2.7	201.1024 $[C_{12}H_{13}N_2O: M - C_9H_6N_2O_2 + H]^+$ (100), 132.0448 $[C_8H_6NO]^+$ (0.5)	-
	2	391.1397	103	$C_{21}H_{19}N_4O_4$	1.1	0.6	217.0971 $[C_{12}H_{13}N_2O_2: M - C_9H_6N_2O_2 + H]^+$ (100), 132.0444 $[C_8H_6NO]^+$ (0.5)	-
	4	435.1276	74	$C_{22}H_{19}N_4O_6$	2.2	3.2	229.0588 $[C_{12}H_9N_2O_3: M - C_{10}H_{10}N_2O_3]^+$ (100)	-
	29	147.0557	74	$C_8H_7N_2O$	3.2	5.0	n.f.[b]	-

[a] Constructor statistical match factor obtained by comparison of the theoretical and observed isotopic pattern; [b] Not fragmented; [c] Typical OL ion fragments. Abbreviations: PE: Phosphatidylethanolamine, OL: Ornithine lipid, LOL: *Lyso*-ornithine lipid MAG: Monoacylglycerol.

Table S3. Subset of proteins differentially expressed when *P. lipolytica* TC8 was cultured in biofilm and treated with copper (Cu-treated) in comparison with controls (Ctrl).^{a}

Protein ID^b	Protein Name	Molecular weight (kDa)	Fold-Change Cu-treated/Ctrl	*p*-value
Z5XVI2	Succinate-semialdehyde dehydrogenase	50.3	438.3	0.0007
A0A0P7E5B7	ATP-dependent zinc metalloprotease FtsH	70.8	247.4	0.0034
Z5XQS7	Flagellar hook-length control protein Flg	79.2	150.6	0.0001
Z5XKK6	Glyoxalase	16.1	129.9	0.0000
Z5XQF9	Uncharacterized protein	19.1	115.5	0.0000
Z5XQ22	Transporter	48.8	104.1	0.0099
Z5XNW4	Copper resistance protein CopC	15.1	89.6	0.0010
Z5XTP5	Cell division protein FtsZ	42.9	43.5	0.0022
Z5XMG6	Pilus assembly protein PilM	39.2	37.7	0.0099
Z5XN79	Hemolysin D	54.0	37.2	0.0077
Z5XMF1	RND transporter	41.6	31.9	0.0015
Z5XT39	30S ribosomal protein S20	9.5	29.9	0.0064
Z5XUW8	Membrane protein	26.4	27.6	0.0049
Z5XLV2	Transporter	20.2	25.3	0.0002
Z5XSD9	UPF0276 protein	32.3	25.0	0.0009
Z5XM32	Isocitrate lyase	59.4	22.3	0.0010
Z5XPK6	Transporter	42.1	22.1	0.0017
Z5XLV1	Uncharacterized protein	17.81	21.1	0.0000
Z5XQ55	Uncharacterized protein	9.96	19.2	0.0057
Z5XP26	Nitrate reductase	140.29	17.6	0.0009
Z5XN71	Phosphate transport regulator	26.04	17.4	0.0018
Z5XLJ3	Copper resistance protein CopA	67.56	16.9	0.0001
Z5XPF0	Energy transducer TonB	27.93	16.7	0.0018
Z5XSH7	Flagellar P-ring protein	38.24	16.4	0.0001
Z5XY20	Uncharacterized protein	10.58	15.3	0.0022
Z5XPK0	Transcriptional regulator MraZ	17.68	15.1	0.0003
A0A0P7DX95	Hemolysin D	40.90	14.3	0.0041
Z5XSY6	Nucleoid-associated protein AOG27_03100	12.00	13.6	0.0002
Z5XL47	ATP-dependent protease ATPase subunit HslU	49.94	12.1	0.0000
Z5XQ66	Uncharacterized protein	27.09	11.5	0.0005
Z5XT07	Uncharacterized protein	17.20	11.5	0.0098
Z5XL96	Peptidase	77.78	11.5	0.0004
Z5XS22	Alkyl hydroperoxide reductase	21.05	11.4	0.0001
Z5XLL2	Uncharacterized protein	17.95	11.4	0.0073
Z5XSC5	Transcriptional regulator	25.83	11.2	0.0001
Z5XLS9	Ribonuclease P protein component	16.24	10.5	0.0028
A0A0P7E5L0	FMN reductase	17.90	10.5	0.0000
Z5XUB1	Flagellar L-ring protein	24.55	10.2	0.0001
A0A0P7EJ82	Protein phosphatase CheZ	28.4	9.7	0.0011
Z5XP53	Replicative DNA helicase	50.8	9.7	0.0001
Z5XUU7	NADH:flavin oxidoreductase	38.1	9.6	0.0001
Z5XSE7	GCN5 family acetyltransferase	22.2	9.6	0.0002
Z5XNF6	50S ribosomal protein L15	15.1	9.6	0.0095
Z5XNM8	Succinylglutamate desuccinylase	41.1	9.1	0.0021
Z5XW52	6,7-dimethyl-8-ribityllumazine synthase	16.1	9.0	0.0000
Z5XQM7	Protein BatD	60.4	9.0	0.0001
Z5XR12	Nitrate reductase	58.3	8.8	0.0002
Z5XQF6	Phage shock protein A	24.9	8.7	0.0035
A0A0P7DZT8	Trigger factor	47.7	8.6	0.0001
Z5XWM9	Uncharacterized protein	19.7	8.1	0.0041
Z5XNH0	Uncharacterized protein	14.5	8.0	0.0078
Z5XLX6	50S ribosomal protein L17	14.9	8.0	0.0037
Z5XSY9	Uncharacterized protein	14.8	7.9	0.0050
Z5XLZ4	50S ribosomal protein L14	13.4	7.9	0.0002
Z5XNU8	Uncharacterized protein	94.8	7.9	0.0000
Z5XLZ5	Extracelullar DNA degradation protein, EddB	97.2	7.6	0.0018
Z5XQ92	Protein phosphatase CheZ	28.5	7.5	0.0042
Z5XQG2	Uncharacterized protein	28.8	7.4	0.0002
Z5XLT6	Cobalamin biosynthesis protein CobQ	28.5	7.3	0.0034
A0A0P7E9Z8	50S ribosomal protein L19	13.4	7.3	0.0037
Z5XTV4	Phenylalanine 4-monooxygenase	30.4	7.2	0.0001
Z5XM20	Cold-shock protein	7.5	7.2	0.0002
Z5XKT4	50S ribosomal protein L5	20.2	7.1	0.0006
Z5XTT9	Anti-sigma B factor antagonist	11.2	7.1	0.0030
Z5XUK1	GTP cyclohydrolase FolE2	34.0	7.0	0.0003

Z5XMS0	Nucleoid occlusion factor SlmA	22.5	6.9	0.0029
Z5XTL2	Probable cytosol aminopeptidase	54.8	6.8	0.0002
Z5XSE8	Flagellar motor switch protein FliM	41.2	6.7	0.0002
Z5XLG5	Peptidase M13	77.3	6.5	0.0001
Z5XRT2	50S ribosomal protein L7/L12	12.1	6.5	0.0002
Z5XUH2	RNA polymerase subunit sigma	21.6	6.5	0.0041
Z5XP56	Long-chain fatty acid--CoA ligase	79.7	6.4	0.0002
Z5XLU5	FMN reductase	19.9	6.4	0.0025
A0A0P7DXG1	Nucleotide-binding protein AT00_11605	32.2	6.4	0.0098
Z5XQV5	Flagellar basal-body rod protein FlgG	28.0	6.4	0.0008
Z5XQ72	50S ribosomal protein L1	24.8	6.3	0.0001
Z5XSD6	RNA polymerase sigma factor FliA	27.2	6.2	0.0060
Z5XNR9	50S ribosomal protein L22	12.0	6.2	0.0037
A0A0P7E7H0	Uncharacterized protein	23.2	6.2	0.0000
Z5XM39	60 kDa chaperonin	57.3	6.1	0.0001
Z5XQ95	Agmatinase	33.7	6.1	0.0047
Z5XME0	Xaa-Pro dipeptidase	47.1	6.0	0.0025
Z5XMC9	Delta-aminolevulinic acid dehydratase	37.1	5.9	0.0015
Z5XNE9	Flagellar motor switch protein FliN	14.6	5.9	0.0055
Z5XMZ8	ATP synthase subunit beta	49.7	5.8	0.0001
Z5XSH6	Protein GrpE	22.6	5.8	0.0000
Z5XSN1	Dipeptidyl carboxypeptidase	80.9	5.6	0.0001
Z5XM80	50S ribosomal protein L4	21.9	5.6	0.0001
A0A0P7DT01	Urocanate hydratase	74.2	5.5	0.0031
Z5XPZ1	RND transporter	38.4	5.5	0.0003
Z5XW68	Uncharacterized protein	101.4	5.5	0.0055
Z5XPE5	Uncharacterized protein	49.0	5.4	0.0086
Z5XW70	Glyceraldehyde-3-phosphate dehydrogenase	53.1	5.4	0.0001
Z5XTR1	Enoyl-CoA hydratase	27.5	5.4	0.0022
A0A0P7E7U6	Peptidase S9	85.0	5.4	0.0035
Z5XN54	Trigger factor	47.7	5.3	0.0001
Z5XMC5	Oxidoreductase	36.3	5.2	0.0020
Z5XL85	30S ribosomal protein S19	10.5	5.1	0.0000
Z5XTL0	Keto-deoxy-phosphogluconate aldolase	21.6	5.1	0.0002
Z5XKY3	50S ribosomal protein L2	29.9	5.1	0.0001
Z5XLQ8	Chemotaxis protein	58.2	5.0	0.0004
Z5XNS7	50S ribosomal protein L3	22.2	5.0	0.0003
A0A0P7DWQ0	Uncharacterized protein	23.7	4.9	0.0001
Z5XQN4	Membrane protein TolA	35.4	4.6	0.0074
Z5XRF7	Ribonucleotide-diphosphate reductase subunit beta	43.2	4.6	0.0001
Z5XNR3	Uronate isomerase	54.4	4.6	0.0006
Z5XU35	Uncharacterized protein	69.4	4.6	0.0060
Z5XPM7	Cytochrome C oxidase subunit II	49.5	4.6	0.0000
Z5XPU0	Putative beta-barrel assembly-enhancing protease	54.3	4.5	0.0026
Z5XS30	Transcriptional regulator HU subunit alpha	9.2	4.5	0.0004
Z5XKE1	50S ribosomal protein L23	11.2	4.5	0.0039
Z5XTW0	Uncharacterized protein	23.3	4.5	0.0003
A0A0P7E5J5	Aldehyde dehydrogenase	55.4	4.5	0.0002
Z5XPC8	Uncharacterized protein	36.4	4.4	0.0012
Z5XU73	Glyceraldehyde-3-phosphate dehydrogenase	36.0	4.4	0.0000
Z5XRJ9	50S ribosomal protein L13	15.9	4.4	0.0035
Z5XV43	Protein RecA	37.5	4.4	0.0012
Z5XQM3	AAA family ATPase	35.1	4.4	0.0000
Z5XT54	Lactoylglutathione lyase	20.2	4.3	0.0061
Z5XQI4	Polyribonucleotide nucleotidyltransferase	76.2	4.3	0.0000
Z5XU48	Membrane protein	33.1	4.3	0.0069
Z5XV64	50S ribosomal protein L20	13.5	4.2	0.0021
Z5XU64	Chemotaxis protein CheW	18.2	4.2	0.0040
Z5XS56	Ribosome-binding factor A	15.3	4.2	0.0039
Z5XM26	Gamma-glutamyl phosphate reductase	44.6	4.1	0.0055
A0A0P7DP76	Amidohydrolase	42.5	4.0	0.0067
A0A0P7E746	Polyribonucleotide nucleotidyltransferase	75.9	4.0	0.0014
Z5XL22	50S ribosomal protein L28	9.0	3.9	0.0008
Z5XRF5	Aminopeptidase B	45.8	3.9	0.0000
Z5XL21	30S ribosomal protein S4	23.5	3.9	0.0010
Z5XLY7	50S ribosomal protein L6	19.2	3.9	0.0000
Z5XP62	50S ribosomal protein L9	15.7	3.8	0.0003
Z5XSB3	Energy transducer TonB	28.8	3.8	0.0049
Z5XQ90	Peptidase M14	94.9	3.8	0.0004
Z5XR76	Single-stranded DNA-binding protein	24.8	3.8	0.0003
Z5XR42	5-nucleotidase SurE	26.8	3.8	0.0000

Z5XTD8	Protein-export protein SecB	18.0	3.7	0.0044
Z5XVH8	Phosphoribulokinase	33.8	3.6	0.0008
A0A0P7EE63	RNA polymerase sigma factor FliA	26.3	3.6	0.0082
Z5XTM1	50S ribosomal protein L10	17.2	3.6	0.0078
Z5XPU4	ATP synthase epsilon chain	15.1	3.6	0.0000
A0A0P7E7V7	LacI family transcriptional regulator	37.0	3.6	0.0018
Z5XKC4	50S ribosomal protein L24	11.3	3.6	0.0081
Z5XY08	Tryptophan synthase beta chain	42.5	3.6	0.0001
Z5XXU7	Peptidase M17	54.3	3.6	0.0000
Z5XXN8	Beta-ketoacyl synthase	68.3	3.6	0.0003
Z5XQR9	Malate synthase G	79.9	3.6	0.0000
Z5XPY8	30S ribosomal protein S2	26.9	3.6	0.0003
Z5XRC4	Peptide methionine sulfoxide reductase	47.5	3.5	0.0014
Z5XX38	3-methyl-2-oxobutanoate dehydrogenase	44.9	3.5	0.0019
Z5XR31	Ribosomal protein S6 modification protein	16.0	3.4	0.0077
Z5XXK3	50S ribosomal protein L27	9.1	3.4	0.0075
Z5XNG1	30S ribosomal protein S8	14.0	3.4	0.0024
Z5XMD5	Uncharacterized protein	9.4	3.4	0.0028
Z5XTC2	General secretion pathway protein GspB	40.3	3.4	0.0026
Z5XQJ1	DNA mismatch repair protein MutH	25.0	3.4	0.0027
Z5XNH8	Flagellar hook protein FlgE	47.0	3.3	0.0000
Z5XRB7	30S ribosomal protein S21	8.6	3.3	0.0098
Z5XKE6	Alkyl hydroperoxide reductase	22.6	3.3	0.0014
Z5XP68	30S ribosomal protein S30	13.2	3.3	0.0009
Z5XKU0	Uncharacterized protein	93.4	3.2	0.0001
Z5XLL9	Type II secretion system protein GspC	34.9	3.2	0.0002
Z5XTC3	Dihydrolipoyllysine-residue succinyl	54.0	3.2	0.0000
Z5XL24	50S ribosomal protein L30	6.7	3.2	0.0087
Z5XTL5	30S ribosomal protein S7	17.5	3.2	0.0012
Z5XVI3	Cell division protein FtsA	44.4	3.1	0.0013
Z5XKQ2	Aldehyde reductase	42.0	3.1	0.0009
Z5XNE1	AMP-dependent synthetase	51.2	3.1	0.0039
Z5XRU5	3-5-bisphosphate nucleotidase	28.0	3.0	0.0002
Z5XP80	Glutathione reductase	49.0	3.0	0.0004
Z5XKA4	Phage-shock protein	25.1	3.0	0.0031
Z5XQ38	Aldolase	28.4	3.0	0.0000
Z5XST6	Amidohydrolase	117.8	2.9	0.0009
Z5XTG0	50S ribosomal protein L21	11.5	2.9	0.0083
Z5XVQ5	Dihydroorotate dehydrogenase (quinone)	36.8	2.8	0.0005
Z5XUF0	Ribose-phosphate pyrophosphokinase	34.4	2.8	0.0001
Z5XKB0	Serine protease	127.5	2.8	0.0012
Z5XKL6	Iron-sulfur cluster assembly scaffold protein IscU	13.4	2.8	0.0004
Z5XS53	Hemin receptor	17.2	2.8	0.0044
Z5XKM9	Uncharacterized protein	41.2	2.8	0.0054
Z5XSD8	Lipoprotein	69.0	2.7	0.0045
Z5XS31	Uncharacterized protein	42.6	2.7	0.0052
Z5XKP2	Uncharacterized protein	15.2	2.7	0.0039
Z5XLS2	Aldehyde dehydrogenase	55.3	2.7	0.0029
Z5XPF3	Peptidase M16	108.7	2.7	0.0070
Z5XQ65	Lactoylglutathione lyase	15.0	2.7	0.0013
Z5XVC3	4-hydroxythreonine-4-phosphate dehydrogenase	35.2	2.7	0.0012
Z5XKE0	50S ribosomal protein L16	15.7	2.7	0.0033
Z5XKC8	Alkaline phosphatase	65.2	2.7	0.0005
Z5XVF0	4-hydroxyphenylpyruvate dioxygenase	39.8	2.7	0.0000
Z5XRR3	Phosphoheptose isomerase	21.3	2.6	0.0004
Z5XRG1	Probable septum site-determining protein MinC	25.2	2.6	0.0014
Z5XL33	Rod shape-determining protein MreB	37.0	2.6	0.0043
Z5XXJ8	Dihydrolipoyl dehydrogenase	50.3	2.6	0.0000
Z5XVG7	3-ketoacyl-ACP reductase	26.7	2.6	0.0005
Z5XQ56	Acetyl-CoA carboxylase biotin carboxyl carrier protein subunit	16.1	2.5	0.0038
Z5XQ01	2OG-Fe(II) oxygenase	31.5	2.5	0.0002
Z5XNM4	Uncharacterized protein	24.7	2.5	0.0007
Z5XM74	30S ribosomal protein S3	25.7	2.5	0.0085
A0A0P7EG17	DNA degradation protein EddB	98.7	2.5	0.0001
Z5XW40	Peptidase S9	85.0	2.5	0.0003
A0A0P7DTD4	30S ribosomal protein S9	14.6	2.5	0.0000
Z5XQR5	Acyltransferase	33.2	2.5	0.0000
Z5XS25	3-deoxy-D-manno-octulosonate 8-phosphate phosphatase	17.8	2.5	0.0022
Z5XKK3	ATP synthase gamma chain	31.4	2.5	0.0013
Z5XMT9	Ribulose-phosphate 3-epimerase	23.8	2.5	0.0020
Z5XXF5	30S ribosomal protein S1	61.0	2.5	0.0007

Z5XT62	Acyl-CoA dehydrogenase	41.8	2.5	0.0000
Z5XSD5	Magnesium transporter	33.1	2.4	0.0003
Z5XSC3	UPF0250 protein AOG27_03855	10.4	2.4	0.0018
Z5XMA8	Transcriptional regulator NarL	23.8	2.4	0.0062
Z5XPG9	Xaa-Pro dipeptidase	45.4	2.4	0.0011
Z5XKE4	Hydrolase	92.9	2.4	0.0004
Z5XM53	Glutamine synthetase	51.8	2.4	0.0001
Z5XMX9	Histidine ammonia-lyase	56.3	2.4	0.0040
Z5XVM0	Serine endoprotease DegQ	47.3	2.4	0.0010
Z5XKX1	Tryptophan 2,3-dioxygenase	44.3	2.3	0.0039
Z5XVA7	Bifunctional protein HldE	51.9	2.3	0.0049
Z5XSV8	RpiR family transcriptional regulator	30.1	2.3	0.0004
Z5XL89	30S ribosomal protein S10	11.7	2.3	0.0028
Z5XVW1	Malate dehydrogenase	32.0	2.3	0.0006
Z5XVM6	Ribosome maturation factor RimM	19.9	2.3	0.0003
Z5XKL5	Succinate-semialdehyde dehydrogenase	51.7	2.3	0.0001
Z5XLM9	Uncharacterized protein	24.6	2.3	0.0097
Z5XMV3	Acetylornithine aminotransferase	43.1	2.2	0.0000
Z5XTU9	2, 3, 4, 5-tetrahydropyridine-2,6-dicarboxylate *N*-succinyltransferase	29.8	2.2	0.0003
Z5XL51	Cysteine desulfurase	45.4	2.2	0.0039
Z5XS08	Ribosome-recycling factor	20.4	2.2	0.0012
Z5XKT2	30S ribosomal protein S5	17.6	2.2	0.0071
Z5XMW7	Deoxyribose-phosphate aldolase	26.0	2.2	0.0010
Z5XMI3	Histidine ammonia-lyase	53.9	2.2	0.0006
Z5XUP4	Oxidoreductase	22.9	2.1	0.0023
Z5XNW2	*L*-arabinose isomerase	55.2	2.1	0.0058
Z5XMY8	Dihydrodipicolinate synthase	33.3	2.1	0.0021
Z5XQP1	Diguanylate phosphodiesterase	46.3	2.1	0.0003
Z5XLJ2	Iron-binding protein IscA	11.4	2.1	0.0085
Z5XTQ3	Zn-dependent hydrolase	63.4	2.1	0.0011
Z5XNW7	ADP-ribose diphosphatase	21.2	2.1	0.0071
Z5XV90	Succinylglutamate desuccinylase	39.1	2.1	0.0036
Z5XLD8	Anhydrase	19.2	2.1	0.0016
Z5XQ09	ATP-dependent Clp protease proteolytic subunit	22.6	2.1	0.0005
Z5XVK6	Histidine triad (HIT) protein	15.2	2.1	0.0031
Z5XUG6	Tryptophan synthase alpha chain	28.9	2.0	0.0016
Z5XWC0	GTP cyclohydrolase 1 type 2 homolog	27.1	2.0	0.0077
Z5XVN2	Fatty acid metabolism regulator protein	27.1	2.0	0.0091
Z5XT51	3-hydroxydecanoyl-[acyl-carrier-protein] dehydratase	18.8	-2.0	0.0083
Z5XTA6	3-phosphoshikimate 1-carboxyvinyltransferase	46.0	-2.0	0.0092
Z5XMW5	Methionyl-tRNA formyltransferase	34.5	-2.0	0.0010
Z5XQ59	Dihydroxy-acid dehydratase	66.0	-2.1	0.0002
Z5XV60	Uncharacterized protein	17.2	-2.1	0.0044
Z5XWP1	5-methyltetrahydrofolate-homocysteine methyltransferase	38.9	-2.1	0.0054
Z5XKD1	Spermidine synthase	32.1	-2.2	0.0036
Z5XNI3	Chemotaxis protein CheW	34.3	-2.1	0.0047
A0A0N8HJK0	Chemotaxis protein	85.0	-2.1	0.0077
Z5XUM4	Phosphatase	49.9	-2.1	0.0054
Z5XWH0	AAA family ATPase	87.8	-2.1	0.0042
Z5XNF0	Polysaccharide deacetylase	38.7	-2.2	0.0063
Z5XQ68	Anti-sigma factor antagonist	11.4	-2.2	0.0025
Z5XQ99	Glucose-6-phosphate isomerase	60.4	-2.2	0.0003
Z5XSK7	ABC transporter ATP-binding protein	58.7	-2.2	0.0058
Z5XL14	Transcription termination factor Rho	47.1	-2.2	0.0041
Z5XVD0	Methyltransferase	29.9	-2.2	0.0009
Z5XR02	NUDIX hydrolase	15.1	-2.3	0.0050
Z5XPC4	Phosphoribosylformylglycinamidine synthase	140.4	-2.3	0.0014
Z5XVV6	Iron ABC transporter substrate-binding protein	37.3	-2.3	0.0004
Z5XM56	Thiopurine *S*-methyltransferase	23.8	-2.3	0.0016
Z5XKY1	Cytochrome C	16.3	-2.3	0.0015
Z5XRW3	6-phosphogluconolactonase	25.4	-2.3	0.0000
Z5XKV6	33 kDa chaperonin	31.6	-2.3	0.0001
Z5XX56	Uncharacterized protein	11.1	-2.3	0.0083
A0A0P7DQT4	Fatty acid oxidation complex subunit alpha	80.2	-2.4	0.0046
A0A0P7EE38	Flagellin	33.5	-2.4	0.0009
Z5XW09	Valine-tRNA ligase	108.4	-2.4	0.0036
Z5XTX7	tRNA hydroxylase	29.2	-2.4	0.0038
Z5XRE0	Chemotaxis protein CheY	25.9	-2.4	0.0095
Z5XP14	Cyanophycinase	61.6	-2.4	0.0055
Z5XTI3	Bifunctional purine biosynthesis protein PurH	56.6	-2.4	0.0021

Z5XR11	UTP-glucose-1-phosphate uridylyltransferase	32.1	-2.4	0.0028
Z5XQT3	Inosine-5-monophosphate dehydrogenase	51.9	-2.4	0.0004
Z5XTN0	NAD-dependent malic enzyme	62.5	-2.4	0.0025
Z5XRJ7	Uncharacterized protein	51.7	-2.4	0.0023
Z5XSN2	tRNA-modifying protein YgfZ	33.6	-2.5	0.0007
Z5XSP8	Probable transcriptional regulatory protein AOG27_12610	26.7	-2.5	0.0068
Z5XUY3	Chemotaxis protein CheY	14.0	-2.5	0.0003
Z5XQP8	*N*-acetylmuramic acid 6-phosphate etherase	32.8	-2.5	0.0004
Z5XNR4	Acyl-peptide hydrolase	75.0	-2.5	0.0025
Z5XTC0	Adenylate cyclase	57.8	-2.6	0.0015
Z5XXE7	GntR family transcriptional regulator	30.7	-2.6	0.0006
Z5XU85	Alpha-amlyase	69.9	-2.6	0.0060
A0A0P7E1X8	Elongation factor G	76.1	-2.6	0.0075
Z5XNM3	UPF0061 protein AT00_20705	52.0	-2.6	0.0071
Z5XM90	Uncharacterized protein	26.7	-2.7	0.0074
Z5XRI5	Aspartate aminotransferase	39.8	-2.7	0.0005
Z5XTF9	Threonine-tRNA ligase	73.3	-2.7	0.0029
Z5XK99	Stress response kinase A	37.2	-2.7	0.0051
Z5XKU5	Arginine decarboxylase	69.6	-2.7	0.0072
A0A0P7EC28	Amino acid decarboxylase	71.4	-2.7	0.0013
Z5XUX6	Agmatine deiminase	39.3	-2.7	0.0042
A0A0N8HKN3	Aspartate aminotransferase	40.0	-2.7	0.0054
Z5XND2	Sucrose phosphorylase	54.2	-2.7	0.0003
Z5XUB9	Uncharacterized protein	45.8	-2.7	0.0029
Z5XLS6	DNA gyrase subunit B	90.4	-2.7	0.0004
Z5XP83	Peptide methionine sulfoxide reductase MsrA	20.1	-2.7	0.0020
Z5XW22	DNA mismatch repair protein MutT	19.5	-2.8	0.0042
Z5XKM4	Oxidoreductase	25.5	-2.8	0.0003
Z5XVH7	3-methylcrotonyl-CoA carboxylase	71.1	-2.8	0.0078
Z5XKN3	Cation tolerance protein CutA	12.2	-2.8	0.0013
Z5XTR2	Riboflavin biosynthesis protein RibD	40.8	-2.8	0.0047
Z5XT71	Succinyl-CoA-3-ketoacid-CoA transferase	22.9	-2.8	0.0011
A0A0P7ELC1	4-hydroxy-4-methyl-2-oxoglutarate aldolase	17.9	-2.8	0.0049
Z5XVM9	Arabinose 5-phosphate isomerase	34.2	-2.8	0.0016
Z5XTM2	Endonuclease	43.5	-2.9	0.0003
Z5XLR9	GTP cyclohydrolase 1	20.8	-2.9	0.0001
Z5XN15	Protein translocase subunit SecA	102.8	-2.9	0.0025
Z5XV41	CDP-diacylglycerol--serine O-phosphatidyltransferase	50.3	-2.9	0.0002
Z5XKK7	7,8-dihydro-8-oxoguanine-triphosphatase	14.9	-2.9	0.0001
Z5XKS7	Elongation factor G	76.1	-3.0	0.0009
Z5XNC3	RNA helicase	47.8	-3.0	0.0005
Z5XUR0	Carbamoyl-phosphate synthase small chain	41.0	-3.0	0.0000
Z5XKD6	GTP-binding protein TypA	66.9	-3.0	0.0006
Z5XV13	*L*-aspartate oxidase	60.0	-3.0	0.0027
Z5XR78	Glutamate decarboxylase	60.1	-3.0	0.0002
A0A0P7EGS3	Alpha,alpha-trehalase	57.4	-3.0	0.0055
Z5XR93	Phosphodiesterase	57.5	-3.0	0.0011
Z5XTN4	Glutathione S-transferase	22.4	-3.0	0.0064
Z5XZM4	Tryptophan halogenase	57.8	-3.0	0.0099
Z5XP77	Phosphodiesterase	44.6	-3.0	0.0041
Z5XSZ5	Peptide chain release factor 3	59.2	-3.0	0.0016
Z5XYZ6	1,4-*D*-glucanase	41.2	-3.0	0.0001
Z5XTE9	Nicotinate-nucleotide pyrophosphorylase	30.3	-3.1	0.0006
Z5XKD2	Aconitate hydratase B	93.8	-3.1	0.0024
Z5XYF0	Cob(I)yrinic acid a,c-diamide adenosyltransferase	22.1	-3.1	0.0006
Z5XSK4	Phosphate ABC transporter substrate-binding protein	14.3	-3.1	0.0003
Z5XQR0	Peptide chain release factor 2	33.4	-3.2	0.0004
Z5XMI1	Ribulokinase	59.1	-3.2	0.0015
Z5XLX1	Guanosine-3,5-*bis*(Diphosphate) 3-pyrophosphohydrolase	55.1	-3.2	0.0083
A0A0P7E568	Peptide chain release factor 1	40.4	-3.3	0.0002
Z5XMA9	Uncharacterized protein	13.8	-3.3	0.0071
Z5XU47	*S*-(hydroxymethyl)glutathione dehydrogenase	39.9	-3.4	0.0003
Z5XRS5	Ribosomal RNA small subunit methyltransferase D	23.1	-3.4	0.0011
Z5XUF5	Metal-dependent phosphohydrolase	58.0	-3.4	0.0008
Z5XPG4	Fructokinase	34.7	-3.4	0.0009
Z5XZG1	Glycerate dehydrogenase	33.9	-3.4	0.0000
Z5XV16	tRNA (guanine-*N*(1)-)-methyltransferase	28.1	-3.5	0.0031
Z5XQE6	Elongation factor Ts	30.4	-3.6	0.0045
Z5XKQ9	NH(3)-dependent NAD(+) synthetase	30.4	-3.5	0.0013
Z5XRT9	Gamma-glutamyl cyclotransferase	19.0	-3.5	0.0051
Z5XUY5	LysR family transcriptional regulator	35.3	-3.5	0.0011

Z5XQH6	Acetyl-coenzyme A carboxylase carboxyl transferase subunit beta	32.1	-3.6	0.0015
Z5XNS8	Arylsulfatase	56.1	-3.6	0.0074
Z5XN01	7-carboxy-7-deazaguanine synthase	24.9	-3.6	0.0049
Z5XQ80	Long-chain fatty acid-CoA ligase	56.1	-3.6	0.0061
Z5XTM9	Chemotaxis protein CheY	42.8	-3.6	0.0009
Z5XQ89	Chitinase	127.7	-3.6	0.0013
Z5XPP9	Uncharacterized protein	15.7	-3.7	0.0043
Z5XZH6	Twitching motility protein PilT	38.2	-3.7	0.0053
Z5XQ98	Chemotaxis response regulator protein-glutamate methylesterase	37.3	-3.7	0.0000
Z5XMV6	Shikimate dehydrogenase (NADP(+))	29.3	-3.7	0.0022
Z5XU20	Uncharacterized protein	16.5	-3.7	0.0063
Z5XLK4	LysR family transcriptional regulator	34.5	-3.7	0.0002
Z5XQ04	Oligoribonuclease	20.6	-3.8	0.0006
Z5XNK8	UDP-*N*-acetylenolpyruvoylglucosamine reductase	37.7	-3.9	0.0000
Z5XMY1	Chromosomal replication initiator protein DnaA	52.3	-3.9	0.0073
Z5XTB6	Glutamine--tRNA ligase	63.7	-4.0	0.0001
Z5XR64	N5-carboxyaminoimidazole ribonucleotide synthase	41.4	-4.0	0.0025
A0A0P7DTA7	XRE family transcriptional regulator	15.9	-4.0	0.0000
Z5XVJ3	Isoleucine-tRNA ligase	105.2	-4.0	0.0016
Z5XS67	Ribosomal RNA large subunit methyltransferase M	41.1	-4.1	0.0022
Z5XSF1	Adenosylcobinamide kinase	19.6	-4.1	0.0023
Z5XKR7	Uncharacterized protein	6.5	-4.1	0.0083
Z5XNJ8	DNA-binding protein	7.6	-4.1	0.0003
Z5XTL6	Diguanylate phosphodiesterase	82.1	-4.2	0.0010
Z5XRS7	Thioester dehydrase	13.0	-4.2	0.0090
Z5XN44	Histidine biosynthesis bifunctional protein HisB	38.7	-4.2	0.0019
Z5XSR9	Malonyl CoA-acyl carrier protein transacylase	32.1	-4.2	0.0000
Z5XR56	Alanine--tRNA ligase	93.9	-4.2	0.0076
Z5XSG1	*D*-3-phosphoglycerate dehydrogenase	44.4	-4.3	0.0001
Z5XU30	3-ketoacyl-CoA thiolase	46.2	-4.3	0.0000
Z5XW41	Methionine--tRNA ligase	75.9	-4.3	0.0023
Z5XW03	tRNA U34 carboxymethyltransferase	37.0	-4.3	0.0031
Z5XRG3	Glutathione peroxidase	21.5	-4.4	0.0044
Z5XSZ1	Redoxin	21.1	-4.4	0.0007
Z5XM83	Acyl-CoA thioesterase	29.5	-4.4	0.0062
Z5XS09	Anthranilate synthase component 1	57.3	-4.5	0.0007
Z5XUY1	Cyclic diguanosine monophosphate-binding protein	13.8	-4.5	0.0058
Z5XTH9	DNA primase	66.2	-4.5	0.0022
Z5XZC1	Uncharacterized protein	27.9	-4.6	0.0092
Z5XQ52	tRNA dimethylallyltransferase	34.8	-4.7	0.0000
Z5XXQ4	Sorbosone dehydrogenase	40.4	-4.7	0.0024
Z5XPN5	Acetolactate synthase 3 regulatory subunit	18.4	-4.7	0.0088
Z5XTG5	Uncharacterized protein	21.5	-4.7	0.0031
Z5XSE4	Glyoxalase	14.2	-4.7	0.0009
Z5XRX6	7-cyano-7-deazaguanine synthase	24.2	-4.8	0.0010
Z5XQL0	Peptidoglycan-binding protein	61.6	-4.8	0.0095
Z5XLA3	1-(5-phosphoribosyl)-5-[(5-phosphoribosylamino) methylideneamino] imidazole-4-carboxamide isomerase	26.6	-4.8	0.0012
Z5XPN1	Isoprenoid biosynthesis protein	22.9	-4.9	0.0029
Z5XKS1	FMN reductase	26.3	-4.9	0.0010
Z5XYF8	5-formyltetrahydrofolate cyclo-ligase	23.0	-5.0	0.0015
Z5XR77	Argininosuccinate synthase	43.7	-5.0	0.0003
Z5XT14	Asparagine--tRNA ligase	52.5	-5.0	0.0000
Z5XKB2	UPF0502 protein AT00_21440	23.7	-5.0	0.0000
Z5XR87	3-oxoacyl-[acyl-carrier-protein] synthase 3	37.7	-5.1	0.0039
Z5XUF9	Uncharacterized protein	84.1	-5.1	0.0033
Z5XTK5	Probable transcriptional regulatory protein AOG27_02490	26.3	-5.1	0.0033
Z5XMR3	Tail fiber protein	109.1	-5.2	0.0085
Z5XR97	Flagellar basal body-associated protein FliL-like protein	15.4	-5.2	0.0064
Z5XQB5	Chloramphenicol acetyltransferase	24.9	-5.2	0.0059
Z5XNP9	Uncharacterized protein	23.0	-5.2	0.0013
Z5XTQ8	Aspartate kinase	86.9	-5.3	0.0029
Z5XN26	Glycosyl hydrolase	25.7	-5.3	0.0001
Z5XN52	2Fe-2S ferredoxin	12.4	-5.4	0.0049
Z5XRH3	Ribonuclease D	43.8	-5.4	0.0001
Z5XKS2	Methylthioribose kinase	45.4	-5.4	0.0009
Z5XTI8	Pyrroline-5-carboxylate reductase	29.3	-5.4	0.0041
Z5XPA1	UDP-*N*-acetylmuramate-*L*-alanyl-gamma-*D*-glutamyl-meso-2,6-diaminoheptandioate ligase	49.1	-5.5	0.0056
Z5XRI2	Uncharacterized protein	21.4	-5.6	0.0064
Z5XN74	tRNA pseudouridine synthase B	34.4	-5.6	0.0035

Z5XVG4	Esterase	21.3	-5.6	0.0064
Z5XPR1	Uncharacterized protein	19.3	-5.6	0.0007
Z5XUP0	Uncharacterized protein	27.7	-5.6	0.0069
Z5XPL6	Imidazole glycerol phosphate synthase subunit HisF	28.4	-5.8	0.0003
Z5XL73	*N*-acylglucosamine 2-epimerase	47.3	-5.9	0.0051
Z5XTS7	Uncharacterized protein	12.2	-5.9	0.0005
Z5XR26	Uncharacterized protein	11.1	-6.0	0.0005
Z5XU71	Octanoyltransferase	24.6	-6.0	0.0050
Z5XTQ2	Glucose-6-phosphate 1-dehydrogenase	55.7	-6.1	0.0001
Z5XRR5	3-hydroxylacyl-ACP dehydratase	16.8	-6.1	0.0000
Z5XUS5	Alanine acetyltransferase	16.7	-6.2	0.0002
Z5XM08	Phosphatase	56.3	-6.2	0.0004
Z5XRM6	Polynucleotide adenylyltransferase	41.4	-6.3	0.0043
Z5XLL8	Uncharacterized protein	29.8	-6.4	0.0047
Z5XQI8	5-methyltetrahydropteroyltriglutamate--homocysteine methyltransferase	38.7	-6.4	0.0008
Z5XVK4	RNA helicase	49.2	-6.4	0.0001
Z5XLT7	Uncharacterized protein	14.1	-6.4	0.0013
Z5XSE9	Uncharacterized protein	23.5	-6.5	0.0050
Z5XLE8	Serine/threonine protein phosphatase	19.0	-6.6	0.0005
Z5XRJ1	Histidine biosynthesis bifunctional protein HisIE	22.5	-6.6	0.0000
Z5XQV0	Peptidase S8	191.0	-6.6	0.0023
Z5XPY7	Uncharacterized protein	30.3	-6.7	0.0066
Z5XRA1	D, D-heptose 1,7-bisphosphate phosphatase	21.2	-6.8	0.0009
Z5XQD6	Chemotaxis protein CheR	31.3	-6.8	0.0003
Z5XLV3	Soluble pyridine nucleotide transhydrogenase	52.6	-6.9	0.0045
Z5XKV2	Alpha-*N*-arabinofuranosidase	38.7	-7.0	0.0010
Z5XSF2	Recombination protein RecR	21.9	-7.1	0.0013
Z5XQM0	Exodeoxyribonuclease I	55.1	-7.1	0.0016
Z5XLU9	3-isopropylmalate dehydratase large subunit	50.0	-7.3	0.0008
Z5XN55	Diguanylate cyclase	57.7	-7.3	0.0034
Z5XMP9	Imidazole glycerol phosphate synthase subunit HisH	21.5	-7.5	0.0059
Z5XNI6	2-isopropylmalate synthase	56.6	-7.6	0.0069
Z5XWC5	Ribosomal RNA large subunit methyltransferase E	23.3	-7.8	0.0003
A0A0P7DV73	Transketolase	72.3	-7.9	0.0008
Z5XU72	Uncharacterized protein	19.0	-7.9	0.0011
Z5XWK0	Carbamoyl-phosphate synthase (glutamine-hydrolyzing)	117.3	-7.9	0.0019
Z5XR34	Uncharacterized protein	55.9	-8.0	0.0034
Z5XY81	Dihydropteroate synthase	30.8	-8.1	0.0010
Z5XTK9	3-mercaptopyruvate sulfurtransferase	30.5	-8.3	0.0025
Z5XU45	Chorismate mutase	42.3	-8.4	0.0000
Z5XYN4	CTP synthase	60.2	-8.5	0.0000
Z5XP09	Molybdopterin adenylyltransferase	19.4	-8.5	0.0040
Z5XUA3	Uracil-DNA glycosylase	25.1	-8.6	0.0084
Z5XK98	tRNA/tmRNA (uracil-C(5))-methyltransferase	42.2	-8.7	0.0011
Z5XTR8	Geranyl transferase	32.1	-8.7	0.0003
Z5XTS6	Uncharacterized protein	47.3	-8.7	0.0021
Z5XR51	Uncharacterized protein	106.5	-8.9	0.0003
Z5XPQ6	Ribosomal RNA small subunit methyltransferase B	48.0	-9.0	0.0029
Z5XUU3	Uncharacterized protein	35.8	-9.2	0.0039
Z5XVZ6	Acetate kinase	43.4	-9.2	0.0051
Z5XTP2	ABC transporter substrate-binding protein	34.5	-9.5	0.0014
Z5XV11	Amino acid ABC transporter substrate-binding protein	34.73	-10.1	0.0070
Z5XWB7	Sporulation control protein Spo0M	27.76	-10.3	0.0001
Z5XKN9	Thioesterase	14.99	-10.6	0.0093
Z5XWL0	Aspartate carbamoyltransferase	37.68	-11.5	0.0019
Z5XVP0	Uncharacterized protein	97.69	-11.7	0.0035
Z5XN07	NADP-binding protein	28.56	-11.9	0.0011
Z5XRN8	Glycogen operon protein GlgX homolog	77.06	-12.2	0.0081
Z5XTE3	SAM-dependent methlyltransferase	25.28	-12.5	0.0046
Z5XRV9	NADPH-dependent 7-cyano-7-deazaguanine reductase	31.95	-12.5	0.0001
Z5XM85	3-isopropylmalate dehydratase small subunit	22.82	-12.5	0.0002
A0A0P7DZD4	5-methylthioadenosine/*S*-adenosylhomocysteine nucleosidase	24.91	-13.0	0.0031
Z5XP65	Uncharacterized protein	18.51	-13.2	0.0018
Z5XQQ8	Cbb3-type cytochrome c oxidase subunit	35.31	-13.8	0.0072
Z5XLY3	Gluconolactonase	31.15	-14.1	0.0016
Z5XMB2	Carbon-nitrogen hydrolase	29.04	-14.3	0.0004
Z5XZ25	Riboflavin biosynthesis protein	34.13	-14.5	0.0088
Z5XKS0	Methylthioribulose-1-phosphate dehydratase	22.57	-14.5	0.0085
Z5XMQ9	LOG family protein	50.01	-14.8	0.0002
Z5XMZ0	Metallo-β–lactamase	82.44	-16.5	0.0012

Z5XRL9	Diguanylate phosphodiesterase	82.34	-17.6	0.0036
Z5XT52	Uncharacterized protein	17.01	-19.3	0.0036
Z5XSF7	Chemotaxis protein CheC	37.1	-19.7	0.0051
Z5XWG2	*D*-alanyl-*D*-alanine carboxypeptidase	42.5	-21.4	0.0039
Z5XTI5	*S*-formylglutathione hydrolase	31.1	-21.9	0.0090
Z5XPB5	Arginase	38.6	-25.1	0.0010
Z5XR10	6-phosphogluconate dehydrogenase, decarboxylating	49.4	-38.2	0.0061
A0A0P7D8Y1	TonB-dependent receptor	78.9	-43.6	0.0016
Z5XMU1	Glycogen synthase	57.0	-108.5	0.0091
Z5XSX1	TonB-dependent receptor	79.2	-131.1	0.0022

[a] Proteins listed in this table were found to be statistically differentially expressed with an absolute fold change greater than 2 and lower than 10; [b] According to Uniprot ID.

Table S4. Subset of proteins differentially expressed when *P. lipolytica* TC8 was cultured in planktonic conditions and treated with copper (Cu-treated) in comparison with controls (Ctrl).[a]

Protein ID[b]	Protein Name	Molecular weight (kDa)	Fold-Change Cu-treated/Ctrl	*p*-value
Z5XP59	RNA polymerase sigma factor RpoS	37.5	64.5	0.0012
Z5XPD5	Fis family transcriptional regulator	11.0	60.7	0.0036
Z5XN79	Hemolysin D	54.1	36.9	0.0003
Z5XQ22	Transporter	48.8	27.2	0.0027
Z5XLV1	Uncharacterized protein	17.8	24.5	0.0053
Z5XLJ3	Copper resistance protein CopA	67.6	16.1	0.0009
Z5XT64	tRNA 2-thiocytidine biosynthesis protein TtcA	34.2	13.7	0.0071
Z5XKE6	Alkyl hydroperoxide reductase	22.6	7.7	0.0004
Z5XM32	Isocitrate lyase	59.4	7.1	0.0076
Z5XXE1	Cyclic nucleotide-binding protein	71.6	7.0	0.0012
Z5XY08	Tryptophan synthase beta chain	42.5	6.9	0.0003
Z5XLJ6	Inositol monophosphatase	29.1	5.7	0.0022
Z5XSC8	Ribosomal RNA large subunit methyltransferase H	17.6	5.4	0.0020
Z5XUH2	RNA polymerase sigma factor RpoE	21.6	5.4	0.0003
Z5XKU0	Uncharacterized protein	93.4	5.3	0.0004
Z5XPZ1	RND transporter	38.4	5.2	0.0027
Z5XMH0	ATP-dependent protease subunit HslV	18.4	5.1	0.0008
Z5XR14	DNA-directed RNA polymerase subunit omega	9.8	4.9	0.0038
Z5XSC5	Transcriptional regulator	25.8	4.8	0.0006
Z5XVH9	Acyltransferase	64.7	4.6	0.0015
Z5XKL6	Iron-sulfur cluster assembly scaffold protein IscU	13.4	4.5	0.0002
Z5XQP7	Uridine kinase	24.0	4.5	0.0042
Z5XM60	Transcriptional regulator	35.2	4.5	0.0045
Z5XSB2	Transcriptional regulator	16.4	4.2	0.0028
Z5XNM7	Alpha-L-glutamate ligase	35.0	4.1	0.0033
A0A0P7E7H0	Uncharacterized protein	23.2	4.1	0.0043
Z5XMB1	TetR family transcriptional regulator	22.9	3.9	0.0009
Z5XQ35	ATP-dependent RNA helicase DeaD	68.5	3.9	0.0094
Z5XR70	Uncharacterized protein	33.6	3.5	0.0033
Z5XN55	Diguanylate cyclase	57.7	3.4	0.0027
Z5XSN1	Dipeptidyl carboxypeptidase II	80.9	3.4	0.0079
Z5XV10	RNA polymerase-binding transcription factor DksA	14.1	3.3	0.0056
Z5XLA0	ATP phosphoribosyltransferase	33.0	3.3	0.0002
Z5XVI3	Cell division protein FtsA	44.4	3.2	0.0058
Z5XPN5	Acetolactate synthase	18.4	3.0	0.0083
Z5XPA7	50S ribosomal protein L31	7.9	3.0	0.0020
Z5XSE8	Flagellar motor switch protein FliM	41.	3.0	0.0058
Z5XLA3	1-(5-phosphoribosyl)-5-[(5-phosphoribosylamino) methylideneamino] imidazole-4-carboxamide isomerase	26.6	3.0	0.0055
Z5XRM2	S-adenosylmethionine synthase	41.6	2.9	0.0004
Z5XPX8	UDP-3-O-acylglucosamine N-acyltransferase	36.5	2.9	0.0004
Z5XPM6	Der GTPase-activating protein YihI	23.0	2.9	0.0042
A0A0P7DSZ1	Uncharacterized protein	48.9	2.8	0.0033
Z5XM39	60 kDa chaperonin	57.3	2.8	0.0008
Z5XLR4	Potassium transporter peripheral membrane component	50.1	2.6	0.0064
Z5XTZ7	Translation initiation factor IF-2	96.6	2.6	0.0015
Z5XNE8	DNA-directed RNA polymerase subunit alpha	36.2	2.4	0.0025
Z5XKL5	Succinate-semialdehyde dehydrogenase	51.7	2.4	0.0031
Z5XMW0	DNA-directed RNA polymerase subunit beta	149.5	2.3	0.0031
Z5XPL0	Histidinol dehydrogenase	46.3	2.3	0.0002
Z5XKX7	Phosphoadenosine phosphosulfate reductase	28.2	2.3	0.0004
Z5XND8	Uncharacterized protein	21.3	2.3	0.0015
Z5XQI4	Polyribonucleotide nucleotidyltransferase	76.2	2.2	0.0000
Z5XVM0	Serine endoprotease DegQ	47.3	2.1	0.0030
Z5XPQ2	DNA-directed RNA polymerase subunit beta	154.4	2.1	0.0006
Z5XQ62	10 kDa chaperonin	10.3	2.0	0.0021
Z5XRZ3	Lipid-A-disaccharide synthase	42.6	-2.0	0.0006
Z5XRI4	Uncharacterized protein	23.9	-2.1	0.0082
Z5XZG1	Glycerate dehydrogenase	33.9	-2.2	0.0022
A0A0P7E568	Peptide chain release factor 1	40.4	-2.2	0.0021
Z5XST1	Aconitate hydratase	94.2	-2.2	0.0021
Z5XKE7	ABC transporter substrate-binding protein	42.0	-2.2	0.0011
Z5XNK8	UDP-*N*-acetylenolpyruvoylglucosamine reductase	37.7	-2.2	0.0032

Z5XVF1	Uncharacterized protein	33.3	-2.3	0.0091
Z5XSQ4	Monooxygenase	42.7	-2.4	0.0063
Z5XN26	Glycosyl hydrolase	25.7	-2.4	0.0043
Z5XPA1	UDP-*N*-acetylmuramate-*L*-alanyl-gamma-*D*-glutamyl-meso-2,6-diaminoheptandioate ligase	49.1	-2.4	0.0007
Z5XS79	Histidine phosphatase	17.7	-2.5	0.0068
Z5XM26	Gamma-glutamyl phosphate reductase	44.6	-2.6	0.0007
Z5XQP0	Diguanylate phosphodiesterase	28.9	-2.6	0.0008
Z5XTH9	DNA primase	66.2	-2.6	0.0069
Z5XN10	Alcohol dehydrogenase	35.8	-2.7	0.0040
Z5XSZ6	TonB-dependent receptor	84.3	-2.7	0.0020
Z5XLY3	Gluconolactonase	31.3	-2.8	0.0058
Z5XSZ4	UPF0229 protein AT00_03740	48.9	-3.0	0.0002
Z5XZM4	Tryptophan halogenase	57.8	-3.0	0.0029
Z5XRZ5	Iron-sulfur cluster carrier protein	38.3	-3.0	0.0031
Z5XL03	Uncharacterized protein	57.7	-3.1	0.0071
Z5XTQ8	Aspartate kinase	86.9	-3.2	0.0005
Z5XMF0	Chemotaxis protein CheY	44.9	-3.5	0.0049
Z5XTA5	Citrate synthase	41.5	-3.6	0.0044
Z5XSG2	Serine/threonine protein kinase	73.6	-3.6	0.0008
Z5XTL6	Diguanylate phosphodiesterase	82.1	-3.6	0.0057
Z5XM14	Diguanylate cyclase	50.4	-3.6	0.0008
A0A0P7DQX9	Flagellin	33.5	-3.6	0.0005
Z5XLE8	Serine/threonine protein phosphatase	19.0	-3.7	0.0008
Z5XMV9	Glycosyltransferase	39.8	-3.8	0.0072
Z5XWL0	Aspartate carbamoyltransferase	37.7	-3.8	0.0054
Z5XXP3	Glutamate-ammonia-ligase adenylyltransferase	106.2	-3.9	0.0007
Z5XKA5	Uncharacterized protein	16.3	-4.0	0.0041
Z5XUY3	Chemotaxis protein CheY	14.0	-4.0	0.0035
Z5XRN8	Glycogen operon protein GlgX homolog	77.1	-4.2	0.0041
Z5XQI2	Diguanylate cyclase	37.2	-4.4	0.0002
Z5XTC3	Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex	54.0	-4.5	0.0013
Z5XPS0	Sugar ABC transporter substrate-binding protein	41.4	-4.6	0.0030
Z5XQA9	Transcriptional regulator	20.0	-4.6	0.0049
Z5XPN1	Isoprenoid biosynthesis protein	22.9	-4.6	0.0008
Z5XQZ4	Diguanylate cyclase	34.2	-4.7	0.0010
Z5XP55	Porin	42.1	-4.8	0.0016
Z5XQ34	Peptidase	56.1	-4.8	0.0002
Z5XKM9	Uncharacterized protein	41.2	-4.9	0.0032
Z5XPG8	Uncharacterized protein	96.8	-5.8	0.0050
Z5XVG9	Histidine kinase	74.5	-5.9	0.0058
Z5XSH5	Amino acid ABC transporter substrate-binding protein	28.7	-6.1	0.0013
Z5XTE6	General secretion pathway protein GspE	62.2	-6.3	0.0099
Z5XM97	Histidine kinase	26.4	-6.5	0.0040
Z5XTK9	3-mercaptopyruvate sulfurtransferase	30.5	-6.9	0.0000
Z5XV81	*N*-acetyl-gamma-glutamyl-phosphate reductase	36.1	-7.0	0.0042
Z5XP93	Ornithine carbamoyltransferase	33.0	-7.1	0.0006
Z5XTP2	ABC transporter substrate-binding protein	34.5	-7.5	0.0015
Z5XVS8	GNAT family acetyltraansferase	17.6	-8.4	0.0003
Z5XUN7	Propionyl-CoA synthetase	69.5	-9.0	0.0002
Z5XQS7	Flagellar hook-length control protein Flg	79.2	-11.9	0.0060
Z5XTF3	Acetyltransferase component of pyruvate dehydrogenase complex	66.5	-12.7	0.0005
Z5XSX1	TonB-dependent receptor	79.2	-14.1	0.0071
Z5XTE1	Acetylglutamate kinase	27.0	-15.3	0.0000
Z5XR01	Ribonucleotide reductase subunit alpha	13.6	-18.5	0.0023
Z5XSH2	Peptidase S8	74.7	-56.9	0.0007

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[a] Proteins listed in this table were found to be statistically differentially expressed with an absolute fold change higher than 2 and lower than 10; [b] According to Uniprot ID.

Table S5. Subset of proteins differentially expressed when *P. lipolytica* TC8 was cultured in planktonic and biofilm conditions and treated with copper (Cu-treated) in comparison with controls (Ctrl).[a]

			Planktonic culture		**Biofilm culture**	
Protein ID[b]	**Protein name**	**Molecular weight (kDa)**	**Fold-Change Cu-treated/Ctrl**	***p*-value**	**Fold-change Cu-treated/Ctrl**	***p*-value**
Z5XQ22	Transporter	48.8	27.2	0.0027	104.1	0.0099
Z5XN79	Hemolysin	54.0	36.9	0.0003	37.2	0.0077
A0A0P7E7H0	Uncharacterized protein	23.2	4.1	0.0043	6.1	0.0000
Z5XQS7	Flagellar hook-length control protein	79.2	11.9	0.0060	150.6	0.0001
Z5XM32	Isocitrate lyase	59.4	7.1	0.0076	22.3	0.0010
Z5XLV1	Uncharacterized protein	17.8	24.5	0.0053	21.1	0.0000
Z5XLJ3	Copper resistance protein CopA	67.6	16.1	0.0009	16.9	0.0001
Z5XSC5	Transcriptional regulator	25.8	4.8	0.0006	11.2	0.0001
Z5XSE8	Flagellar motor switch protein FliM	41.2	2.8	0.0058	6.7	0.0002
Z5XUH2	RNA polymerase sigma factor RpoE	21.6	5.3	0.0003	6.5	0.0041
Z5XM39	60 kDa chaperonin	57.3	2.8	0.0008	6.1	0.0001
Z5XSN1	Dipeptidyl carboxypeptidase II	80.9	3.4	0.0079	5.6	0.0001
Z5XPZ1	RND transporter	38.4	5.2	0.0027	5.5	0.0003
Z5XQI4	Polyribonucleotide nucleotidyltransferase	76.2	2.2	0.0000	4.3	0.0000
Z5XY08	Tryptophan synthase beta chain	42.5	6.9	0.0003	3.6	0.0001
Z5XKE6	Alkyl hydroperoxide reductase	22.6	7.7	0.0004	3.3	0.0014
Z5XKU0	Uncharacterized protein	93.4	5.3	0.0004	3.2	0.0001
Z5XVI3	Cell division protein FtsA	44.4	3.2	0.0058	3.1	0.0013
Z5XKL6	Iron-sulfur cluster assembly scaffold protein IscU	13.4	4.5	0.0002	2.8	0.0004
Z5XVM0	Serine endoprotease DegQ	47.3	2.1	0.0030	2.4	0.0010
Z5XKL5	Succinate-semialdehyde dehydrogenase	51.7	2.4	0.0031	2.3	0.0001
Z5XUY3	Chemotaxis protein CheY	14.0	-4.0	0.0035	-2.5	0.0003
Z5XZM4	Tryptophan halogenase	57.8	-2.9	0.0029	-3.0	0.0099
A0A0P7E568	Peptide chain release factor 1	40.4	-2.2	0.0021	-3.3	0.0002
Z5XZG1	Glycerate dehydrogenase	33.9	-2.2	0.0022	-3.4	0.0000
Z5XNK8	UDP-N-acetylenolpyruvoylglucosamine reductase	37.7	-2.2	0.0032	-3.9	0.0000
Z5XTL6	Diguanylate phosphodiesterase	82.1	-3.6	0.0057	-4.2	0.0010
Z5XTH9	DNA primase	66.2	-2.6	0.0069	-4.5	0.0022
Z5XPN1	Isoprenoid biosynthesis protein	22.9	-4.5	0.0008	-4.9	0.0029
Z5XTQ8	Aspartate kinase	86.9	-3.2	0.0005	-5.3	0.0029
Z5XN26	Glycosyl hydrolase	25.7	-2.4	0.0043	-5.3	0.0001
Z5XPA1	UDP-*N*-acetylmuramate-*L*-alanyl-gamma-*D*-glutamyl-meso-2,6-diaminoheptandioate ligase	49.1	-2.4	0.0007	-5.4	0.0056
Z5XLE8	Serine/threonine protein phosphatase	19.0	-3.7	0.0008	-6.6	0.0005
Z5XTK9	3-mercaptopyruvate sulfurtransferase	30.5	-7.1	0.0000	-8.3	0.0025
Z5XTP2	ABC transporter substrate-binding protein	34.5	-7.7	0.0015	-9.5	0.0014
Z5XWL0	Aspartate carbamoyltransferase	37.7	-3.8	0.0054	-11.5	0.0019
Z5XRN8	Glycogen operon protein GlgX homolog	77.1	-4.2	0.0041	-12.2	0.0081
Z5XLY3	Gluconolactonase	31.2	-2.8	0.0058	-14.1	0.0016
Z5XSX1	TonB-dependent receptor	79.2	-14.3	0.0071	-131.1	0.0022

[a] Proteins listed in this table were found to be statistically differentially expressed with an absolute fold change higher than 2 and lower than 10; [b] According to Uniprot ID.

FIGURES

Figure S1. Growth inhibition curves of *P. lipolytica* TC8 cultured in VNSS (red squares) and MB (black dots) media supplemented with various copper concentrations (IC_{50} = 660 μM, Goodness of fit: R^2 = 0.944, *n* = 45 in VNSS; IC_{50} = 1313 μM, R^2 = 0.967, *n* = 78 in MB).

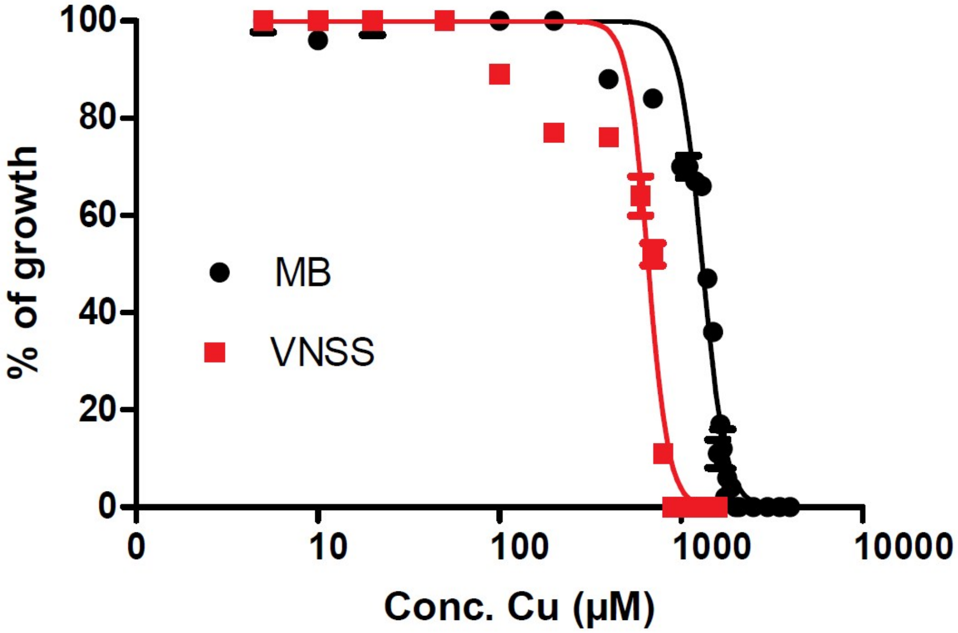

Figure S2. Copper pseudopolarograms obtained in (A) VNSS and (B) MB media 1000-fold diluted in UV-irradiated seawater at pH ~ 8.0, in comparison with UV-irradiated seawater at pH < 2, in presence of 500 nM of Cu.

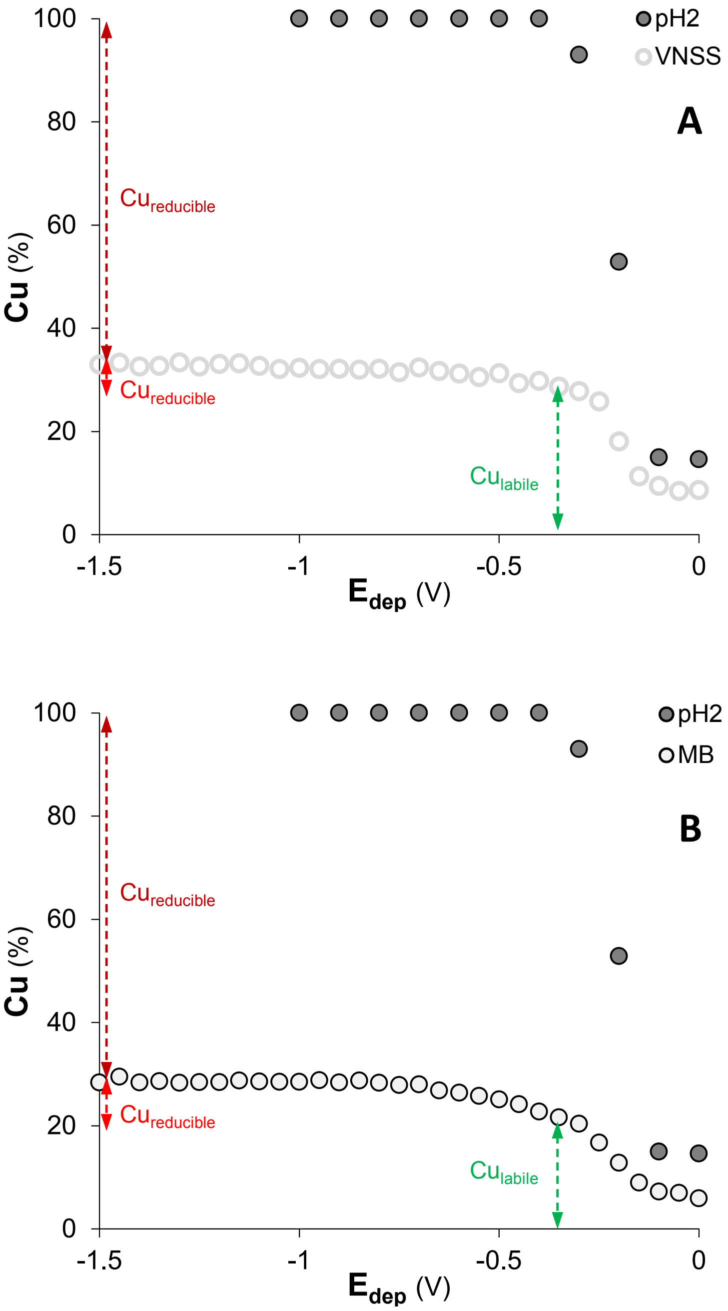

Figure S3. Variation of (A) labile and (B) non-labile (i.e. dissociable and inert organic complexes) Cu fractions in function of total Cu concentrations in VNSS and MB media 1000-fold diluted in UV-irradiated seawater at pH ~ 8.0. Variation of (C) labile and (D) non-labile Cu fractions, in VNSS and MB media 1000-fold diluted in UV-irradiated seawater at pH ~ 8.0, in function of total Cu concentrations multiplied by 1000 (i.e. converted in levels for undiluted medium).

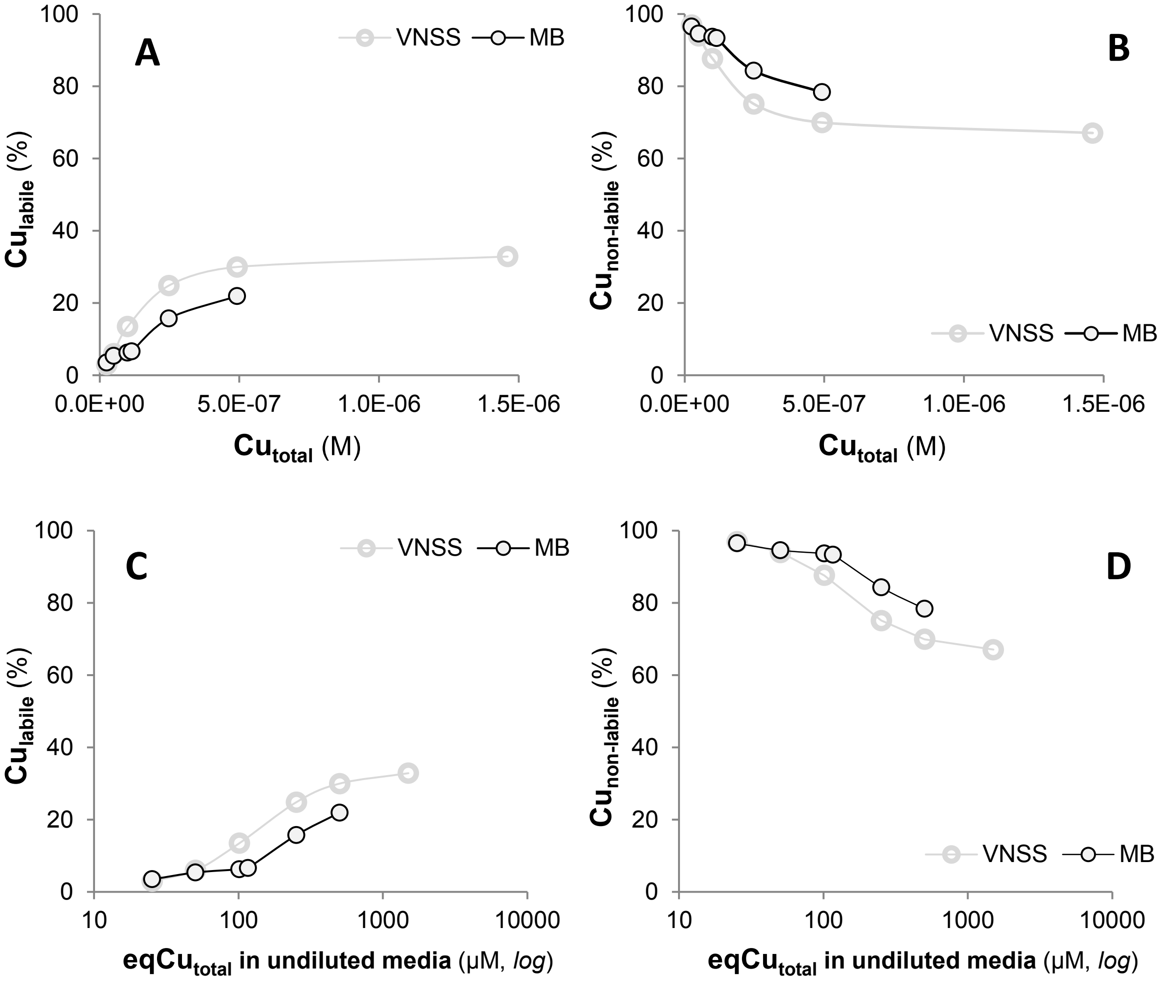

Figure S4. Copper effect on the viability of *P. lipolytica* TC8 in VNSS (red squares) and MB media supplemented with various copper concentrations (LC_{50} = 1611 μM, Goodness of fit: R^2 = 0.979, *n* = 48 in VNSS; LC_{50} = 2100 μM, R^2 = 0.950, *n* = 45 in MB).

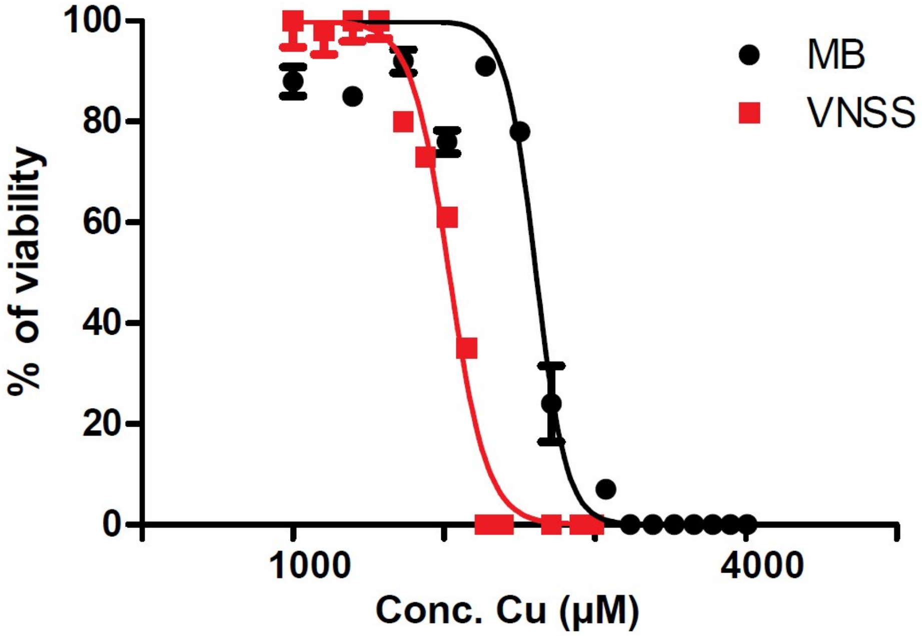

Figure S5. Copper effect on the adhesion of *P. lipolytica* TC8 in ASW medium supplemented with various copper concentrations (EC_{50} = 707 μM, R^2 = 0.975, *n* = 69).

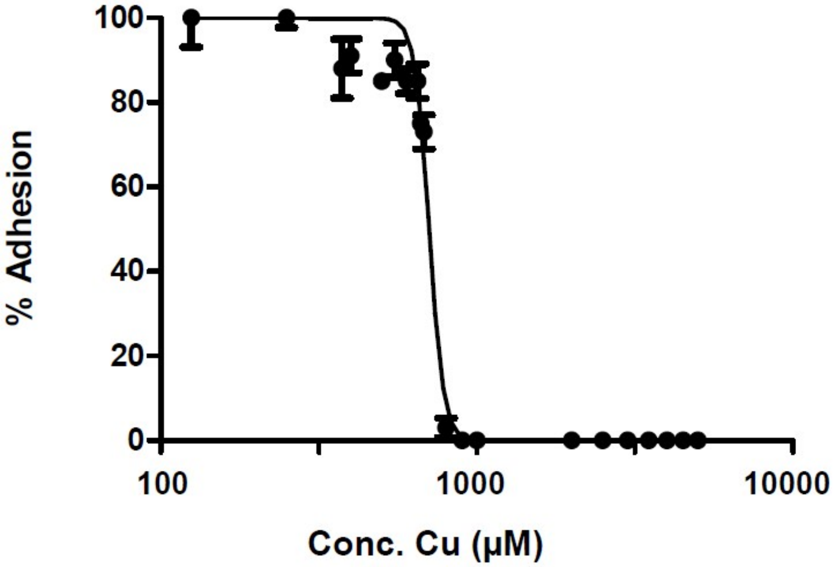

Figure S6. PCA score plot based on UPLC-HRMS metabolomics data of planktonic and biofilm samples of *P. lipolytica* TC8 cultured without (Ctrl: control) and with Cu supplement (1000 μM: Cu-1000, 1400 μM: Cu-1400).

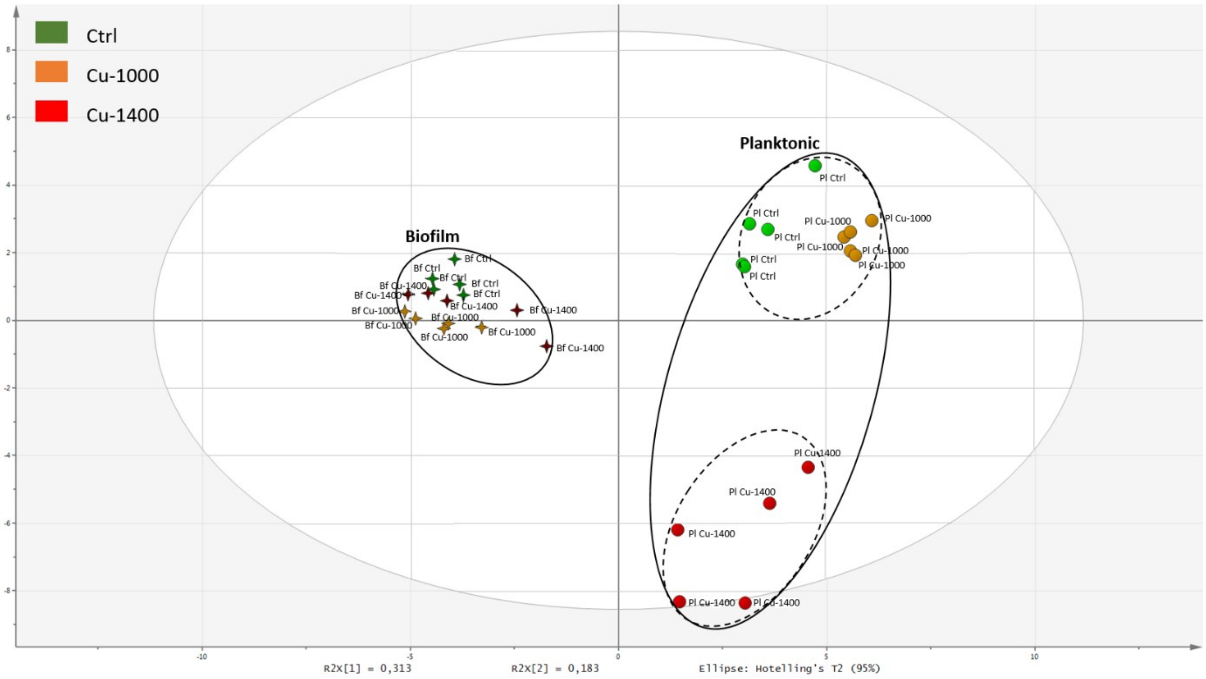

Figure S7. HCA based on PLS-DA of UPLC-HRMS metabolomics data of planktonic (Pl) and biofilm (Bf) samples of *P. lipolytica* TC8 cultured without (Ctrl: control) and with Cu supplement (1000 μM: Cu-1000, 1400 μM: Cu-1400).

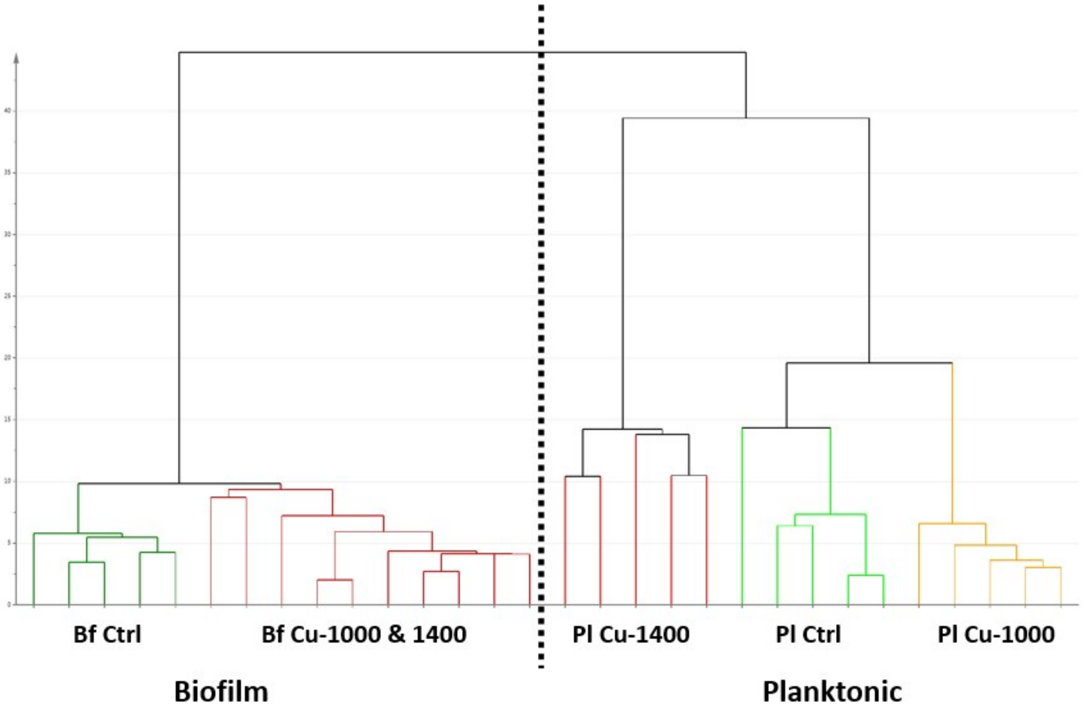

Figure S8. Venn diagram representing proteins identified in the three sample replicates of each culture condition of *P. lipolytica* TC8 (Pl: planktonic, Bf: biofilm, Ctrl: control). The total number of proteins in each condition is given in brackets.

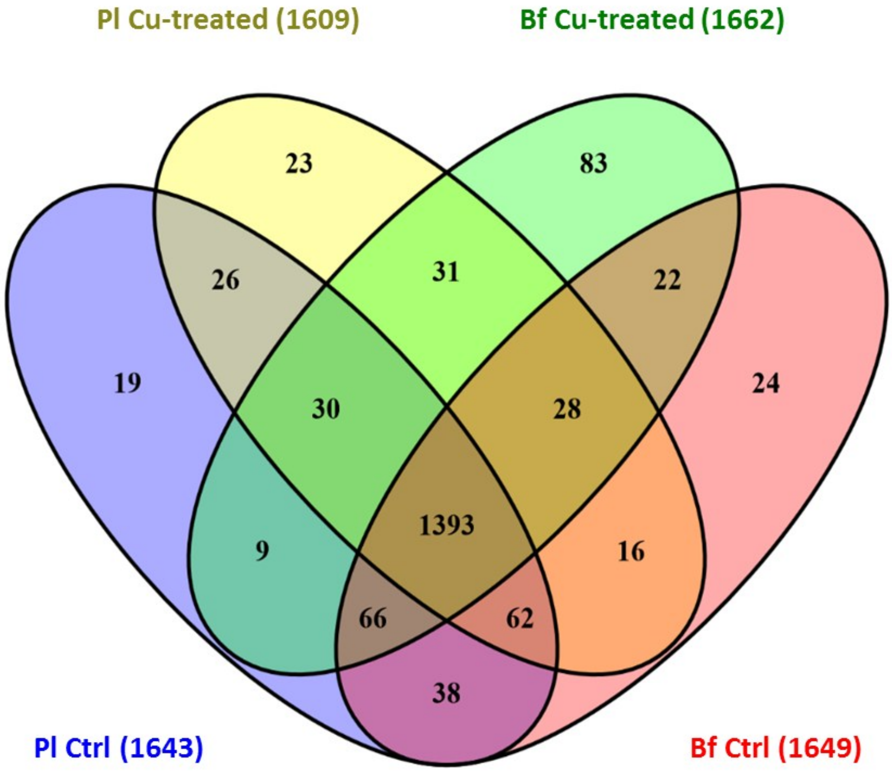

Figure S9. Venn diagrams representing the proteins (A) up- and (B) down-regulated under copper exposure in planktonic and biofilm cultures of *P. lipolytica* TC8. The total number of proteins in each condition is given in brackets.

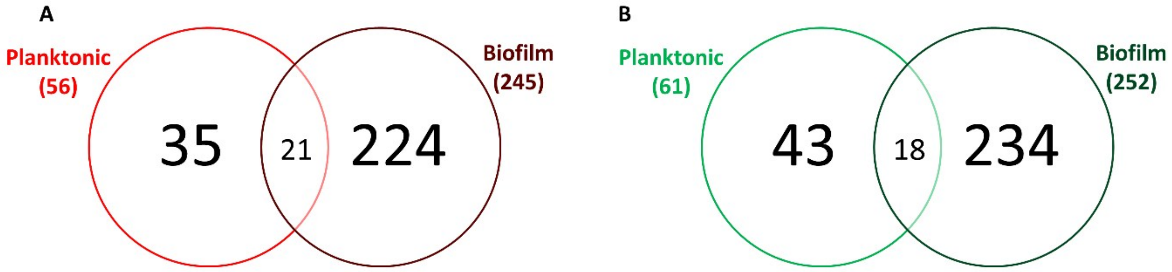

Figure S10. PCA score plot based on proteomes of controls (Ctrl) and Cu-treated planktonic (Pl) and biofilm (Bf) cultures of *P. lipolytica* TC8.

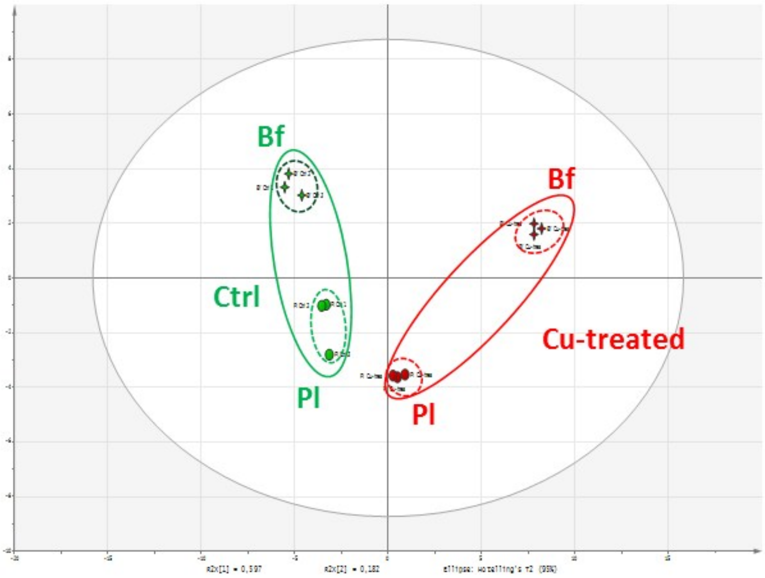

Figure S11. HCA based on PLS-DA built with proteomes of controls (Ctrl) and Cu-treated planktonic (Pl) and biofilm (Bf) cultures of *P. lipolytica* TC8.

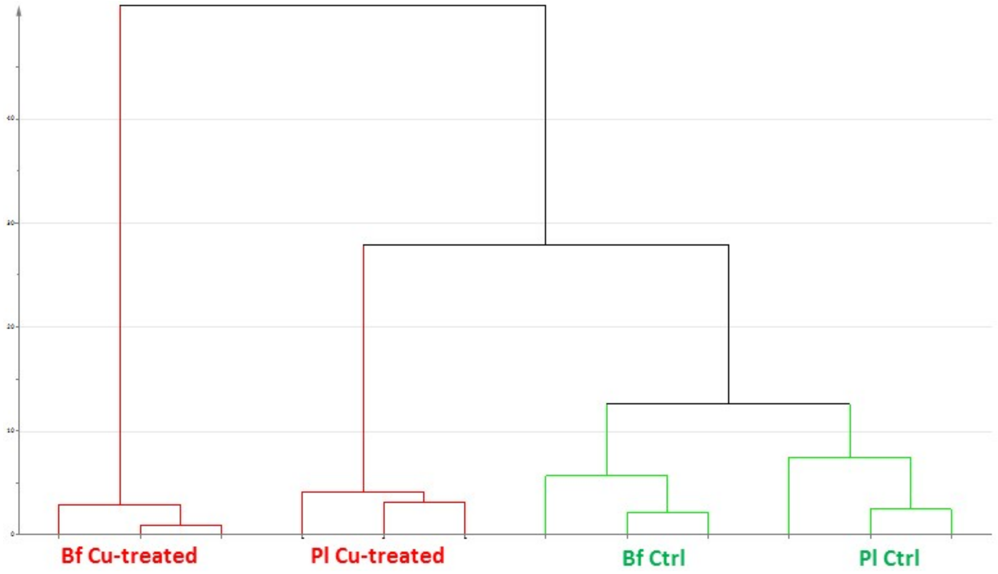

Figure S12. S-plot representing the distribution of the 200 VIPs with a VIP score value > 1 of the OPLS-DA built with the proteomes of controls (Ctrl) and Cu-treated planktonic (Pl) and biofilm (Bf) cultures of *P. lipolytica* TC8.