

From natural xanthenes to synthetic C-1 aminated 3,4-dioxygenated xanthenes as optimized antifouling agents

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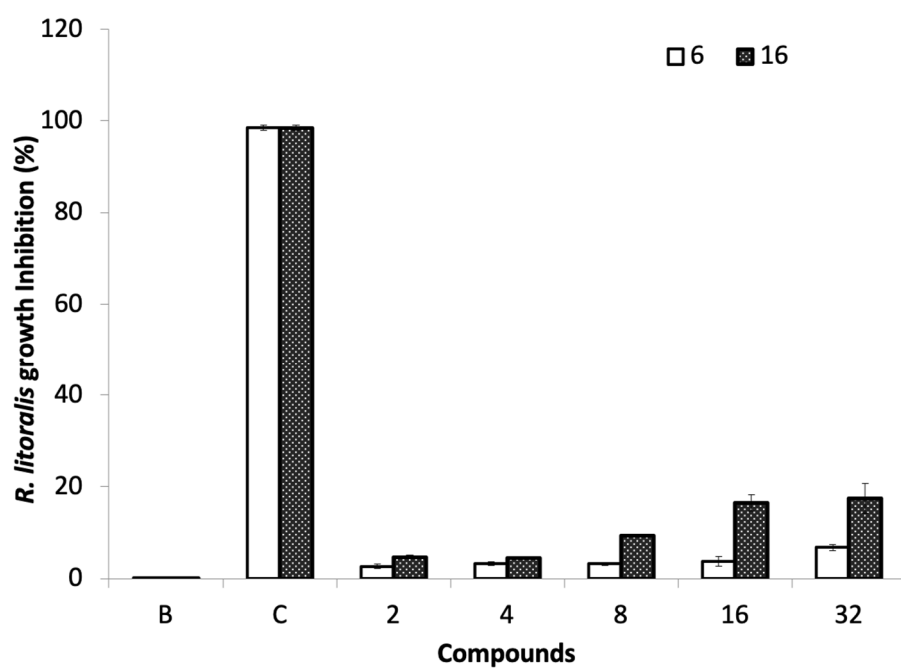


Figure S1. Concentration-response of antibacterial activity of the promising AF compounds 6 and 16 towards *Roseobacter litoralis*. (B: DMSO control; (C) penicillin-streptomycin-neomycin stabilized solution was used as positive control.

Table S1: Relative abundance values of proteins differentially expressed between control and group exposed to compound 21, and statistical results (mixed model ANOVA, P-value <0.05)

Protein ID	Mean of log ₂ (x+1)-transformed values		P-value	Description	Accession
	Control	compound 21			
2	4,6084	4,4047	0,024	beta-actin [Meretrix meretrix]	AEK81538.1
9	4,2412	4,0767	0,036	retrograde protein of 51 kDa-like isoform X4 [Crassostrea virginica]	XP_022320110.1
7	4,3863	4,0840	0,000	PREDICTED: tubulin beta chain [Priapulus caudatus]	XP_014664190.1
11	4,3091	4,1307	0,013	RecName: Full=Tropomyosin	Q25457.1
20	3,5028	3,2405	0,001	sodium/potassium-transporting ATPase subunit alpha-like [Crassostrea virginica]	XP_022323941.1
15	4,2940	4,0813	0,014	calponin-like protein [Mytilus galloprovincialis]	BAB60813.1
30	4,1447	3,9373	0,003	elongation factor 1 alpha [Mytilus galloprovincialis]	BAD35019.1
61	4,7393	4,5857	0,022	histone H2B [Mytilus edulis]	CAD37816.1
52	4,9618	4,7927	0,021	PREDICTED: histone H4 [Equus caballus]	XP_014590042.1
42	3,8546	3,6500	0,001	PREDICTED: 14-3-3 protein zeta isoform X1 [Hyaella azteca]	XP_018019106.1
122	3,8424	3,4942	0,000	cyclophilin A isoform 2 [Ruditapes philippinarum]	ACU83230.1
5	3,8240	3,5656	0,003	pedal retractor muscle myosin heavy chain partial [Mytilus galloprovincialis]	CAB64663.1
18	3,7831	3,5213	0,001	mitochondrial H+ ATPase a subunit [Pinctada fucata]	ABJ51956.1
49	3,7566	3,5304	0,005	myosin heavy chain isoform N [Anopheles sinensis]	KFB49247.1
51	4,0110	3,7157	0,000	arginine kinase-like protein-1 [Mytilus coruscus]	AKS48144.1
109	3,2714	2,9889	0,007	RNA-binding protein [Pinctada fucata]	ABP04054.1
35	3,8137	3,3956	0,000	glyceraldehyde-3-phosphate dehydrogenase partial [Mytilus galloprovincialis]	AKZ2450.1
34	3,7198	3,3952	0,001	pedal retractor muscle myosin heavy chain partial [Mytilus galloprovincialis]	CAB64663.1
95	4,2033	3,9771	0,000	histone H1 [Venerupis corrugata]	ABV25915.1
116	3,6801	3,3590	0,001	meprin A subunit alpha-like [Mizuhopecten yessoensis]	XP_021356192.1
115	3,4571	3,2421	0,025	PREDICTED: peroxiredoxin-6-like [Amphimedon queenslandica]	XP_003388603.1
17	3,8551	3,6858	0,028	pedal retractor muscle myosin heavy chain partial [Mytilus galloprovincialis]	CAB64663.1
82	3,5652	3,2784	0,000	elongation factor 2-like [Crassostrea virginica]	XP_022335104.1
40	3,4352	3,2845	0,032	PREDICTED: alpha-actinin sarcomeric isoform X2 [Crassostrea gigas]	XP_011425356.1
23	3,5226	3,1429	0,000	byssal HSP-like protein 1 [Mytilus coruscus]	ANN45953.1
14	3,8376	3,5327	0,000	procollagen-proline dioxygenase beta subunit [Mytilus galloprovincialis]	AFM30917.1
74	3,7002	3,3308	0,000	meprin A subunit alpha-like [Mizuhopecten yessoensis]	XP_021356192.1
65	3,3452	2,9697	0,000	PREDICTED: adenosylhomocysteinase A [Crassostrea gigas]	XP_011412005.1
66	3,4001	3,2653	0,022	uncharacterized protein LOC111134038 isoform X1 [Crassostrea virginica]	XP_022338516.1
91	3,4908	3,1630	0,000	40S ribosomal protein S14 [Mizuhopecten yessoensis]	XP_021365459.1
24	3,6329	3,3272	0,002	heat shock cognate 71 [Mytilus galloprovincialis]	CAH04109.1
55	3,4341	3,1075	0,001	ribosomal protein S8e partial [Mytilus trossulus]	ALX27203.1
93	3,5417	3,0424	0,000	PREDICTED: calcitriol-like [Lingula anatina]	XP_013397065.1
118	3,4992	3,2132	0,001	cytosolic malate dehydrogenase [Mytilus galloprovincialis]	AAZ79367.1
77	3,3442	3,0985	0,004	PREDICTED: plastin-3 [Crassostrea gigas]	XP_011415779.2
10	3,4426	3,1885	0,007	filamin-like protein-1 [Mytilus coruscus]	AKS48135.1
50	3,4594	3,1153	0,001	PREDICTED: 14-3-3 protein epsilon isoform X1 [Ictalurus punctatus]	XP_017346722.1
21	3,5785	3,2910	0,001	heat shock protein 90 [Mytilus galloprovincialis]	CAJ85741.1
80	3,2985	3,0979	0,012	PREDICTED: mitochondria-eating protein isoform X2 [Crassostrea gigas]	XP_011417414.1
70	3,2833	3,0558	0,007	aldehyde dehydrogenase mitochondrial-like [Mizuhopecten yessoensis]	XP_021346041.1
78	3,5655	3,1869	0,000	predicted protein [methanotrophic endosymbiont of Bathymodiolus azoricus (Menez Gwen)]	SCN46548.1
39	3,5150	3,1624	0,000	uncharacterized protein LOC111107057 isoform X2 [Crassostrea virginica]	XP_022297716.1
103	3,7262	3,3918	0,004	mammalian ependymin-related protein 1-like [Mizuhopecten yessoensis]	XP_021339375.1
92	3,6673	3,3258	0,000	voltage-dependent anion channel 2-like protein [Haliotis diversicolor]	ADI56517.1
48	3,5458	3,0795	0,001	ribosomal protein [Mytilus galloprovincialis]	CAQ63458.1
99	3,1268	2,9581	0,011	twitchin-like protein-1 [Mytilus coruscus]	AKS48140.1
106	3,4244	3,1177	0,000	hypothetical protein LOTGIDRAFT_235900 [Lottia gigantea]	XP_009066140.1
74	3,4207	3,2090	0,008	fructose-bisphosphate aldolase-like [Crassostrea virginica]	XP_022340550.1
101	3,2671	3,0932	0,012	lamin Dm0-like [Mizuhopecten yessoensis]	XP_021357386.1
87	3,0554	2,6943	0,001	adenyl cyclase-associated protein 1-like isoform X3 [Crassostrea virginica]	XP_022334187.1
56	3,2693	2,9994	0,003	myosin heavy chain non-muscle-like isoform X4 [Mizuhopecten yessoensis]	XP_021350592.1
19	3,7421	3,4603	0,000	ATP synthase subunit beta mitochondrial [Mizuhopecten yessoensis]	XP_021356377.1
67	3,9791	3,8292	0,030	histone H2A.Z.2 [Mytilus galloprovincialis]	APR72375.1
119	3,2063	2,9276	0,007	Phosphoenolpyruvate carboxykinase [GTP] [Crassostrea gigas]	EKC27095.1
100	3,2320	2,9014	0,001	elongation factor 1-gamma-like [Crassostrea virginica]	XP_022332183.1
90	3,2416	2,8597	0,004	citrate synthase mitochondrial-like [Mizuhopecten yessoensis]	XP_021357329.1
105	3,0641	2,7813	0,034	flotillin-1-like isoform X1 [Mizuhopecten yessoensis]	XP_021361554.1
12	3,8573	3,5600	0,003	tubulin alpha-1A chain [Mizuhopecten yessoensis]	XP_021370666.1
123	3,6254	3,4409	0,002	ubiquitin-40S ribosomal protein S27a [Crassostrea gigas]	NP_001292281.1
53	3,1497	2,8956	0,006	tubulin beta chain-like [Crassostrea gigas]	NP_001292292.1
144	3,8766	3,5641	0,004	unknown	
86	2,7963	2,9463	0,047	PREDICTED: laminin subunit gamma-1 [Crassostrea gigas]	XP_011419247.1
249	3,1630	2,9970	0,012	uncharacterized protein ZK1073.1-like isoform X4 [Crassostrea virginica]	XP_022335676.1
152	3,3320	3,0606	0,001	PREDICTED: 40S ribosomal protein S3 [Crassostrea gigas]	XP_011438308.1
54	3,4558	3,1287	0,001	isocitrate dehydrogenase [Mytilus galloprovincialis]	AFI56365.1
114	3,4954	3,1848	0,001	uncharacterized protein LOC110457451 isoform X2 [Mizuhopecten yessoensis]	XP_021364413.1
200	3,0633	2,8996	0,006	uncharacterized protein LOC11111285 isoform X1 [Crassostrea virginica]	XP_022303867.1
113	3,2925	3,0384	0,004	PREDICTED: 60S ribosomal protein L11 [Biomphalaria glabrata]	XP_013068480.1
162	2,8043	2,4909	0,001	uncharacterized protein LOC110465734 isoform X2 [Mizuhopecten yessoensis]	XP_021377443.1
128	3,3487	3,0454	0,001	cathepsin D [Pteria penguin]	AEI58895.1
143	3,2502	2,7554	0,000	40S ribosomal protein S25-like [Mizuhopecten yessoensis]	XP_021370373.1
71	2,9901	2,7168	0,015	dolichyl-diphosphooligosaccharide-protein glycosyltransferase subunit 1-like [Mizuhopecten ye	XP_021341263.1
108	2,7362	2,4491	0,037	hemicentin-1-like partial [Mizuhopecten yessoensis]	XP_021352826.1
26	3,5214	3,1616	0,000	protein disulfide-isomerase A3-like [Crassostrea virginica]	XP_022329914.1
111	3,1931	3,0007	0,046	small heat shock protein 22 [Mytilus galloprovincialis]	AEP02967.1
137	3,4747	3,0260	0,000	PREDICTED: peptidyl-prolyl cis-trans isomerase [Crassostrea gigas]	XP_011444269.1
156	3,0107	2,6969	0,005	PREDICTED: major vault protein [Crassostrea gigas]	XP_011432755.1
132	3,4018	3,1217	0,001	malate dehydrogenase precursor [Nuccella lapillus]	AAF27650.1
102	2,9632	2,7625	0,017	twitchin [Mytilus galloprovincialis]	BAC00784.1
160	3,2879	2,9446	0,000	PREDICTED: protein SET [Crassostrea gigas]	XP_011443579.1
3678	2,6600	2,2732	0,000	PREDICTED: tektin-4 [Crassostrea gigas]	XP_011416098.1
7957	3,0717	2,6923	0,006	40S ribosomal protein S4-like [Crassostrea virginica]	XP_022290789.1
158	3,1664	2,8698	0,000	LOW QUALITY PROTEIN: cilia- and flagella-associated protein 161-like [Crassostrea virginica]	XP_022332848.1
169	3,0207	2,5181	0,035	dolichyl-diphosphooligosaccharide-protein glycosyltransferase 48 kDa subunit-like [Mizuhopec	XP_021367901.1
107	3,2327	2,9822	0,043	PREDICTED: nucleolin-like partial [Biomphalaria glabrata]	XP_013075907.1
133	2,9688	2,2429	0,002	PREDICTED: 60S ribosomal protein L22-like [Crassostrea gigas]	XP_011451810.1
154	3,2849	2,7622	0,000	glutathione S-transferase sigma 2 [Mytilus galloprovincialis]	AFQ35984.1
110	2,9092	2,5755	0,001	PREDICTED: radixin isoform X3 [Crassostrea gigas]	XP_011453118.1
141	3,2149	2,1599	0,000	PREDICTED: uncharacterized protein LOC105329621 isoform X2 [Crassostrea gigas]	XP_011429241.1
258	1,9741	0,0000	0,010	uncharacterized protein LOC110464458 isoform X12 [Mizuhopecten yessoensis]	XP_021375365.1

76	2,9921	2,7453	0,025	histone variant H2A.X [Mytilus galloprovincialis]	AEH58057.1
147	3,2247	2,8937	0,026	glutathione S-transferase sigma 3 [Mytilus galloprovincialis]	AFQ35985.1
171	3,1081	2,8633	0,019	pedal retractor muscle myosin heavy chain partial [Mytilus galloprovincialis]	CAB64663.1
151	2,4658	0,6680	0,026	hypothetical protein HELRODRAFT_108067 partial [Helobdella robusta]	XP_009028970.1
124	3,2071	2,9931	0,005	RecName: Full=Calmodulin; Short=CaM	P27166.2
230	3,3076	3,0505	0,001	hypothetical protein AM593_04533 partial [Mytilus galloprovincialis]	OPL133555.1
220	2,3324	2,0789	0,002	T-complex protein 1 subunit eta-like [Crassostrea virginica]	XP_022288360.1
121	2,7496	2,5490	0,026	filamin-like protein-1 [Mytilus coruscus]	AKS48135.1
3693	1,4823	0,0000	0,031	clathrin heavy chain 1 isoform X1 [Mizuhopecten yessoensis]	XP_021354511.1
148	3,2640	2,9852	0,001	hypothetical protein AM593_00614 partial [Mytilus galloprovincialis]	OPL20910.1
256	3,0412	2,7527	0,003	60S ribosomal protein L7-like [Crassostrea virginica]	XP_022339290.1
44	3,4977	3,2103	0,001	hypothetical protein HELRODRAFT_186143 [Helobdella robusta]	XP_009029528.1
264	2,8252	2,5685	0,001	unknown	
197	2,8570	2,5373	0,000	PREDICTED: enolase-phosphatase E1 [Crassostrea gigas]	XP_011428851.1
7960	2,9838	2,6435	0,000	heterogeneous nuclear ribonucleoprotein D-like isoform X3 [Mizuhopecten yessoensis]	XP_021369725.1
1149	3,4198	3,1312	0,007	PREDICTED: centlein [Crassostrea gigas]	XP_019925172.1
7956	3,0254	2,8079	0,005	heterogeneous nuclear ribonucleoprotein K-like isoform X7 [Mizuhopecten yessoensis]	XP_021358952.1
202	3,0430	2,7488	0,000	60S ribosomal protein L23 [Mizuhopecten yessoensis]	XP_021373043.1
396	2,8174	2,4655	0,000	TCTP [Mytilus galloprovincialis]	AEV41412.1
209	2,9780	2,6400	0,000	60S ribosomal protein L9 [Mizuhopecten yessoensis]	OWF37275.1
89	3,0866	2,8297	0,012	putative calmodulin variant 1 [Taeniopygia guttata]	ACH46222.1
307	3,3333	3,5415	0,019	unknown	
342	2,8087	2,5753	0,001	tektin-2-like [Crassostrea virginica]	XP_022314135.1
255	2,9807	2,6094	0,000	60S ribosomal protein L12-like [Crassostrea virginica]	XP_022314628.1
201	3,0852	2,4743	0,001	unknown	
176	2,7170	2,5248	0,005	PREDICTED: 60S ribosomal protein L18-like [Lingula anatina]	XP_013398405.1
206	2,9052	2,7401	0,016	PREDICTED: guanine nucleotide-binding protein subunit beta [Crassostrea gigas]	XP_011419294.1
226	3,0508	2,8436	0,002	40S ribosomal protein S26-like [Mizuhopecten yessoensis]	XP_021375377.1
216	2,8254	2,5486	0,002	glutamate dehydrogenase mitochondrial-like [Crassostrea virginica]	XP_022314664.1
3688	2,8692	2,5381	0,001	hypothetical protein LOTGIDRAFT_214936 [Lottia gigantea]	XP_009053796.1
205	3,0505	2,6489	0,000	PREDICTED: 40S ribosomal protein S13 [Crassostrea gigas]	XP_011441368.1
164	3,0233	2,7728	0,001	PREDICTED: filamin-A isoform X3 [Crassostrea gigas]	XP_019922596.1
233	2,7204	2,4949	0,006	PREDICTED: nucleoredoxin [Strongylocentrotus purpuratus]	XP_011682183.1
368	2,7200	2,6087	0,027	T-complex protein 1 subunit beta-like [Crassostrea virginica]	XP_022286485.1
159	2,7381	2,4235	0,004	60S ribosomal protein L7a-like [Mizuhopecten yessoensis]	XP_021369622.1
211	2,7897	2,4614	0,006	calmodulin-like isoform X1 [Crassostrea virginica]	XP_022303657.1
217	2,5650	2,3167	0,004	insulin-like growth factor 2 mRNA-binding protein 2 isoform X1 [Crassostrea virginica]	XP_022305782.1
3692	2,9455	2,7034	0,001	60S ribosomal protein L10-like [Crassostrea virginica]	XP_022315909.1
235	2,5877	2,3636	0,010	PREDICTED: alcohol dehydrogenase class-3-like [Lingula anatina]	XP_013411149.1
186	3,0129	2,7163	0,002	PREDICTED: enolase-like [Crassostrea gigas]	XP_011436228.1
168	2,7762	2,4933	0,025	eukaryotic initiation factor 4A-I-like [Crassostrea virginica]	XP_022288944.1
117	2,5597	2,3111	0,012	LOW QUALITY PROTEIN: annexin A4-like [Crassostrea virginica]	XP_022316814.1
260	2,5457	2,1316	0,001	cytochrome c oxidase subunit IV partial [Mytilus edulis]	ACA23124.1
104	2,6860	2,3371	0,001	Ras-related protein Rab-1A [Haliotis discus discus]	ABO26625.1
251	2,5156	2,1923	0,001	PREDICTED: protein disulfide-isomerase A6 [Crassostrea gigas]	XP_011446200.1
5888	2,4391	2,2288	0,006	testis-specific gene 10 protein-like isoform X2 [Mizuhopecten yessoensis]	XP_021348266.1
155	2,6237	2,1962	0,000	PREDICTED: nucleoside diphosphate kinase A [Crassostrea gigas]	XP_011449577.1
227	2,4564	1,4509	0,048	PREDICTED: cilia- and flagella-associated protein 52 [Crassostrea gigas]	XP_011416101.1
59	2,4320	2,1272	0,010	RecName: Full=Histone H2A	Q6WV66.3
297	2,4459	2,1472	0,001	PREDICTED: limbin-like isoform X2 [Crassostrea gigas]	XP_011443052.1
7955	3,0369	2,8432	0,038	LKD-rich protein-1 [Mytilus galloprovincialis]	AKS48185.1
3689	2,7744	2,5032	0,002	pyruvate kinase PKM-like isoform X6 [Crassostrea virginica]	XP_022311729.1
271	2,7173	2,3857	0,002	hypothetical protein AM593_10055 partial [Mytilus galloprovincialis]	OPL21226.1
7958	2,5175	2,2083	0,005	PREDICTED: aspartate aminotransferase cytoplasmic [Crassostrea gigas]	XP_011430094.1
244	2,4733	2,1115	0,002	ras [Mytilus edulis]	AAT81171.1
214	2,5957	2,3405	0,044	6-phosphogluconate dehydrogenase decarboxylating-like [Crassostrea virginica]	XP_022343934.1
231	2,5772	2,2819	0,000	PREDICTED: cytosolic non-specific dipeptidase isoform X1 [Crassostrea gigas]	XP_019928389.1
222	2,5655	2,1826	0,000	annexin B9-like [Crassostrea virginica]	XP_022317867.1
263	2,7963	2,5108	0,016	major vault protein-like [Crassostrea virginica]	XP_022342755.1
268	2,8869	2,6757	0,003	14-3-3 protein homolog 2-like [Crassostrea virginica]	XP_022343021.1
5863	2,4225	0,8739	0,032	PREDICTED: transketolase-like protein 2 isoform X1 [Crassostrea gigas]	XP_011427761.1
131	2,5675	1,8677	0,001	60S ribosomal protein L10a-2-like [Mizuhopecten yessoensis]	XP_021379854.1
312	2,8012	2,6169	0,020	PREDICTED: troponin T-like [Biomphalaria glabrata]	XP_013095195.1
5871	2,4403	1,7548	0,011	radial spoke head protein 4 homolog A-like [Mizuhopecten yessoensis]	XP_021370563.1
85	2,9117	2,6880	0,022	filamin-like protein-3 partial [Mytilus coruscus]	AKS48150.1
3694	2,3432	1,6698	0,008	radial spoke head protein 9 homolog [Mizuhopecten yessoensis]	XP_021363337.1

Table S2: Relative abundance values of proteins differentially expressed between control and group exposed to compound 23, and statistical results (mixed model ANOVA, P-value <0.05)

Protein ID	Mean of log ₁₀ (x+1)-transformed values		P-value (a)	protein description	Accession
	Control	compound 23			
48	3,545820403	3,12534832	0,000	ribosomal protein [Mytilus galloprovincialis]	CAQ63458.1
220	2,332414357	2,115023251	0,000	T-complex protein 1 subunit eta-like [Crassostrea virginica]	XP_022288360.1
75	3,345207927	3,056096356	0,000	PREDICTED: adenosylhomocysteinase A [Crassostrea gigas]	XP_011412005.1
151	2,465766659	0	0,000	hypothetical protein HELRODRAFT_108067 partial [Helobdella robusta]	XP_009028970.1
200	3,063263125	2,893022785	0,000	uncharacterized protein LOC111111285 isoform X1 [Crassostrea virginica]	XP_022303867.1
14	3,83764251	3,605742532	0,000	procollagen-proline dioxygenase beta subunit [Mytilus galloprovincialis]	AFM30917.1
128	3,34871817	3,075801472	0,001	cathepsin D [Pteris penguin]	AEI58895.1
147	3,224718342	2,737205761	0,001	glutathione S-transferase sigma 3 [Mytilus galloprovincialis]	AFQ35985.1
312	2,801211375	2,469386138	0,001	PREDICTED: troponin T-like [Biomphalaria glabrata]	XP_013095195.1
124	3,207143385	3,00324297	0,001	RecName: Full=Calmodulin; Short=CaM	P27166.2
93	3,541707496	3,228150096	0,001	PREDICTED: calreticulin-like [Lingula anatina]	XP_013397065.1
396	2,817361952	2,54494681	0,001	TCTP [Mytilus galloprovincialis]	AEV41412.1
204	3,233751495	2,998238284	0,001	PREDICTED: 40S ribosomal protein SA [Crassostrea gigas]	XP_011438171.1
123	3,625407615	3,445274517	0,002	ubiquitin-40S ribosomal protein S27a [Crassostrea gigas]	NP_001292281.1
209	2,977999002	2,756523602	0,002	60S ribosomal protein L9 [Mizuhopecten yessoensis]	OWF37275.1
39	3,515027408	3,273928967	0,002	uncharacterized protein LOC111107057 isoform X2 [Crassostrea virginica]	XP_022297716.1
164	3,023345072	2,790851915	0,002	PREDICTED: filamin-A isoform X3 [Crassostrea gigas]	XP_019922596.1
7957	3,071678554	2,708424086	0,002	40S ribosomal protein S4-like [Crassostrea virginica]	XP_022290789.1
19	3,742052665	3,5100083	0,002	ATP synthase subunit beta mitochondrial [Mizuhopecten yessoensis]	XP_021356377.1
211	2,789723988	2,370858204	0,002	calmodulin-like isoform X1 [Crassostrea virginica]	XP_022303657.1
71	2,990050751	2,725199804	0,002	dolichyl-diphosphooligosaccharide-protein glycosyltransferase subunit 1-like [Mizuhopecten yessoensis]	XP_021341263.1

118	3,499157843	3,248432026	0,003	cytosolic malate dehydrogenase [Mytilus galloprovincialis]	AAZ79367.1
11	4,309132629	4,113950451	0,003	RecName: Full=Tropomyosin	QZ5457.1
116	3,680084414	3,459045841	0,003	meprin A subunit alpha-like [Mizuhopecten yessoensis]	XP_021356192.1
64	3,700154371	3,452822857	0,003	meprin A subunit alpha-like [Mizuhopecten yessoensis]	XP_021356192.1
95	4,203265567	4,025946156	0,003	histone H1 [Venerupis corrugata]	ABV25915.1
152	3,332009681	3,112969466	0,003	PREDICTED: 40S ribosomal protein S3 [Crassostrea gigas]	XP_011438308.1
154	3,284865997	2,976084697	0,003	glutathione S-transferase sigma 2 [Mytilus galloprovincialis]	AFQ35984.1
143	2,983821018	2,850487771	0,003	40S ribosomal protein S25-like [Mizuhopecten yessoensis]	XP_021370373.1
216	2,825359561	2,536664209	0,003	glutamate dehydrogenase mitochondrial-like [Crassostrea virginica]	XP_022314664.1
107	3,232661416	3,009390822	0,003	PREDICTED: nucleolin-like partial [Biomphalaria glabrata]	XP_013075907.1
104	2,686042679	2,428289828	0,003	Ras-related protein Rab-1A [Haliotis discus discus]	ABO26625.1
121	2,749600201	2,525639385	0,003	filamin-like protein-1 [Mytilus coruscus]	AKS48135.1
101	3,267113764	3,060893175	0,003	lamin Dm0-like [Mizuhopecten yessoensis]	XP_021357386.1
18	3,783148688	3,583237842	0,003	mitochondrial H+ ATPase a subunit [Pinctada fucata]	ABJ51956.1
7	4,386337293	4,161511387	0,003	PREDICTED: tubulin beta chain [Priapulus caudatus]	XP_014664190.1
7960	2,983821018	2,703736298	0,003	heterogeneous nuclear ribonucleoprotein D-like isoform X3 [Mizuhopecten yessoensis]	XP_021369725.1
92	3,667347121	3,408954738	0,003	voltage-dependent anion channel 2-like protein [Haliotis diversicolor]	ADJ56517.1
160	3,287916402	3,061218026	0,003	PREDICTED: protein SET [Crassostrea gigas]	XP_011443579.1
156	3,010691413	2,820181491	0,003	PREDICTED: major vault protein [Crassostrea gigas]	XP_011432755.1
51	4,011009496	3,768665654	0,004	arginine kinase-like protein-1 [Mytilus coruscus]	AKS48144.1
34	3,719836167	3,465417116	0,004	pedal retractor muscle myosin heavy chain partial [Mytilus galloprovincialis]	CAB64663.1
91	3,490803585	3,195927616	0,004	40S ribosomal protein S14 [Mizuhopecten yessoensis]	XP_021365459.1
255	2,980681499	2,752204267	0,004	60S ribosomal protein L12-like [Crassostrea virginica]	XP_022314628.1
106	3,424376599	3,176929458	0,004	hypothetical protein LOTGIDRAFT_235900 [Lottia gigantea]	XP_009064140.1
2	4,608357188	4,331231822	0,004	beta-actin [Meretrix meretrix]	AEK81538.1
23	3,522644814	3,253016622	0,004	byssal HSP-like protein 1 [Mytilus coruscus]	ANN45953.1
66	3,400147735	3,24873257	0,004	uncharacterized protein LOC11134038 isoform X1 [Crassostrea virginica]	XP_022338516.1
277	3,618155895	3,353228755	0,004	PREDICTED: cilia- and flagella-associated protein 52 [Crassostrea gigas]	XP_011416101.1
82	3,56516495	3,338983112	0,004	elongation factor 2-like [Crassostrea virginica]	XP_022335104.1
109	3,271415559	3,068852017	0,004	RNA-binding protein [Pinctada fucata]	ABP04054.1
3678	2,660018778	2,383571891	0,004	PREDICTED: tektin-4 [Crassostrea gigas]	XP_011416098.1
21	3,578521812	3,322667625	0,004	heat shock protein 90 [Mytilus galloprovincialis]	CAJ85741.1
3	4,156373944	4,010703168	0,005	actin adductor muscle [Crassostrea virginica]	XP_022325998.1
176	2,717024295	2,476587647	0,005	PREDICTED: 60S ribosomal protein L18-like [Lingula anatina]	XP_013398405.1
100	3,23199652	2,965995553	0,005	elongation factor 1-gamma-like [Crassostrea virginica]	XP_022332183.1
158	3,166385086	2,973392825	0,005	LOW QUALITY PROTEIN: cilia- and flagella-associated protein 161-like [Crassostrea virginica]	XP_022332848.1
202	3,043023332	2,836147023	0,005	60S ribosomal protein L23 [Mizuhopecten yessoensis]	XP_021373043.1
3688	2,869157615	2,61767721	0,005	hypothetical protein LOTGIDRAFT_214936 [Lottia gigantea]	XP_009053796.1
55	3,434052278	3,15028305	0,005	ribosomal protein S8e partial [Mytilus trossulus]	ALX27203.1
10	3,442643459	3,231196414	0,005	filamin-like protein-1 [Mytilus coruscus]	AKS48135.1
122	3,842354494	3,616537791	0,005	cyclophilin A isoform 2 [Ruditapes philippinarum]	ACU83230.1
162	2,804256103	2,590340589	0,005	uncharacterized protein LOC110465734 isoform X2 [Mizuhopecten yessoensis]	XP_021377443.1
119	3,206300065	2,925458855	0,005	Phosphoenolpyruvate carboxykinase [GTP] [Crassostrea gigas]	EKC27095.1
3689	2,774369561	2,540129165	0,005	pyruvate kinase PKM-like isoform X6 [Crassostrea virginica]	XP_022311729.1
24	3,632923283	3,395332457	0,005	heat shock cognate 71 [Mytilus galloprovincialis]	CAH04109.1
250	2,827231292	2,596015272	0,005	triosephosphate isomerase-like [Crassostrea virginica]	XP_022336561.1
197	2,856985484	2,639983825	0,006	PREDICTED: enolase-phosphatase E1 [Crassostrea gigas]	XP_011428851.1
52	4,961802114	4,698221583	0,006	PREDICTED: histone H4 [Equus caballus]	XP_014590042.1
3681	3,17637219	2,982573632	0,006	unknown	
7956	3,025394087	2,823155779	0,006	heterogeneous nuclear ribonucleoprotein K-like isoform X7 [Mizuhopecten yessoensis]	XP_021358952.1
305	2,573678629	2,324506715	0,006	centrosome-associated protein 350-like isoform X1 [Mizuhopecten yessoensis]	XP_021341745.1
20	3,502750242	3,293095048	0,007	sodium/potassium-transporting ATPase subunit alpha-like [Crassostrea virginica]	XP_022323941.1
77	3,344192149	3,110542141	0,007	PREDICTED: plastin-3 [Crassostrea gigas]	XP_011415779.2
87	3,055405599	2,831648317	0,007	adenyllyl cyclase-associated protein 1-like isoform X3 [Crassostrea virginica]	XP_022334187.1
214	2,595710721	2,248472079	0,007	6-phosphogluconate dehydrogenase decarboxylating-like [Crassostrea virginica]	XP_022343934.1
3687	2,536499433	2,175207381	0,007	hypothetical protein LOTGIDRAFT_187321 [Lottia gigantea]	XP_009050935.1
5	3,823973507	3,623290062	0,007	pedal retractor muscle myosin heavy chain partial [Mytilus galloprovincialis]	CAB64663.1
56	2,629261884	2,947746249	0,007	myosin heavy chain non-muscle-like isoform X4 [Mizuhopecten yessoensis]	XP_021335092.1
231	2,577154658	2,369180242	0,007	PREDICTED: cytosolic non-specific dipeptidase isoform X1 [Crassostrea gigas]	XP_019928389.1
7958	2,517463899	2,266455214	0,007	PREDICTED: aspartate aminotransferase cytoplasmic [Crassostrea gigas]	XP_011430094.1
264	2,825249311	2,641177745	0,007	unknown	
186	3,012938137	2,794362418	0,008	PREDICTED: enolase-like [Crassostrea gigas]	XP_011436228.1
661	3,157541051	2,925461753	0,008	hypothetical protein KP79_PYT11668 [Mizuhopecten yessoensis]	OWF55888.1
138	3,268109035	3,051029842	0,008	hypothetical protein AM593_06933 partial [Mytilus galloprovincialis]	OPL33400.1
205	3,050502734	2,821032635	0,008	PREDICTED: 40S ribosomal protein S13 [Crassostrea gigas]	XP_011441368.1
70	3,283349288	3,051638549	0,008	aldehyde dehydrogenase mitochondrial-like [Mizuhopecten yessoensis]	XP_021346041.1
74	3,420666821	3,219288181	0,008	fructose-bisphosphate aldolase-like [Crassostrea virginica]	XP_022340550.1
30	4,144743792	3,943383122	0,008	elongation factor 1 alpha [Mytilus galloprovincialis]	BAD35019.1
103	3,726238911	3,491007989	0,009	mammalian ependymin-related protein 1-like [Mizuhopecten yessoensis]	XP_021339375.1
244	2,473319478	2,185610261	0,009	ras [Mytilus edulis]	AAT81171.1
35	3,813745702	3,559079375	0,009	glyceraldehyde-3-phosphate dehydrogenase partial [Mytilus galloprovincialis]	AIK22450.1
3692	2,945486676	2,718155921	0,009	60S ribosomal protein L10-like [Crassostrea virginica]	XP_022315909.1
40	3,435168894	3,232487305	0,009	PREDICTED: alpha-actinin sarcomeric isoform X2 [Crassostrea gigas]	XP_011425356.1
230	3,30764614	3,124902897	0,009	hypothetical protein AM593_04533 partial [Mytilus galloprovincialis]	OPL33555.1
61	4,739270666	4,496380037	0,009	histone H2B [Mytilus edulis]	CAD37816.1
131	2,576491164	2,155544421	0,009	60S ribosomal protein L10a-2-like [Mizuhopecten yessoensis]	XP_021379854.1
57	3,314710065	3,018562514	0,009	PREDICTED: tektin-3-like isoform X1 [Crassostrea gigas]	XP_011450983.1
168	2,776191705	2,491219533	0,009	eukaryotic initiation factor 4A-1-like [Crassostrea virginica]	XP_022288944.1
251	2,515581532	2,250862418	0,010	PREDICTED: protein disulfide-isomerase A6 [Crassostrea gigas]	XP_011446200.1
42	3,854636586	3,682162944	0,010	PREDICTED: 14-3-3 protein zeta isoform X1 [Hyalella azteca]	XP_018019106.1
159	2,738066745	2,428038805	0,010	60S ribosomal protein L7a-like [Mizuhopecten yessoensis]	XP_021369622.1
89	3,086601511	2,893283642	0,010	putative calmodulin variant 1 [Taeniopygia guttata]	ACH46222.1
54	3,455775518	3,17412769	0,011	isocitrate dehydrogenase [Mytilus galloprovincialis]	AFI56365.1
226	3,050841993	2,853249747	0,011	40S ribosomal protein S26-like [Mizuhopecten yessoensis]	XP_021375377.1
141	3,214948241	2,638804997	0,011	PREDICTED: uncharacterized protein LOC105329621 isoform X2 [Crassostrea gigas]	XP_011429241.1
297	2,445944845	2,170092336	0,011	PREDICTED: limbin-like isoform X2 [Crassostrea gigas]	XP_011443052.1
67	3,979066934	3,763014465	0,012	histone H2A.Z.2 [Mytilus galloprovincialis]	APR72375.1

171	3,108084961	2,872964259	0,012	pedal retractor muscle myosin heavy chain partial [Mytilus galloprovincialis]	CAB64663.1
290	3,597978116	3,986360585	0,012	multidrug resistance-associated protein 5-like [Crassostrea virginica]	XP_022324434.1
7955	3,036888247	2,769293038	0,012	LKD-rich protein-1 [Mytilus galloprovincialis]	AKS48185.1
256	3,0412126	2,731814666	0,012	60S ribosomal protein L7-like [Crassostrea virginica]	XP_022339290.1
50	3,4593682	3,207952064	0,013	PREDICTED: 14-3-3 protein epsilon isoform X1 [Ictalurus punctatus]	AAF27650.1
132	3,401788602	3,182253001	0,013	malate dehydrogenase precursor [Nucella lapillus]	XP_011453118.1
110	2,909183169	2,667474306	0,013	PREDICTED: radixin isoform X3 [Crassostrea gigas]	OPL20910.1
148	3,264003471	3,054397116	0,013	hypothetical protein AM593_00614 partial [Mytilus galloprovincialis]	XP_021364413.1
114	3,49538502	3,264693653	0,014	uncharacterized protein LOC110457451 isoform X2 [Mizuhopecten yessoensis]	No_Hits
201	3,085176892	2,825275593	0,014	unknown	XP_022331028.1
3680	2,971967263	2,746192082	0,014	probable methylmalonate-semialdehyde dehydrogenase [acylating] mitochondrial [Crassostrea virginica]	KFB49247.1
49	3,756631422	3,544568849	0,014	myosin heavy chain isoform N [Anopheles sinensis]	XP_021370666.1
12	3,857270689	3,626956434	0,015	tubulin alpha-1A chain [Mizuhopecten yessoensis]	XP_022343021.1
268	2,886887969	2,682676468	0,015	14-3-3 protein homolog 2-like [Crassostrea virginica]	AEH58057.1
76	2,992121234	2,770492849	0,015	histone variant H2A.X [Mytilus galloprovincialis]	XP_011444269.1
137	3,474746041	3,147817508	0,015	PREDICTED: peptidyl-prolyl cis-trans isomerase [Crassostrea gigas]	XP_011682183.1
233	2,720369268	2,505415611	0,015	PREDICTED: nucleoredoxin [Strongylocentrotus purpuratus]	AKS48140.1
99	3,126761993	2,899738829	0,016	twitchin-like protein-1 [Mytilus coruscus]	XP_021361554.1
105	3,064106025	2,735584039	0,016	flotillin-1-like isoform X1 [Mizuhopecten yessoensis]	XP_013068480.1
113	3,292454202	3,080518443	0,016	PREDICTED: 60S ribosomal protein L11 [Biomphalaria glabrata]	XP_021367901.1
169	3,020716799	2,388227171	0,017	dolichyl-diphosphooligosaccharide-protein glycosyltransferase 48 kDa subunit-like [Mizuhopecten yessoensis]	OPL21226.1
271	2,717329052	2,430972595	0,018	hypothetical protein AM593_10055 partial [Mytilus galloprovincialis]	ACA23124.1
260	2,545741083	2,309469002	0,018	cytochrome c oxidase subunit IV partial [Mytilus edulis]	XP_022317867.1
222	2,565493834	2,327268004	0,019	annexin B9-like [Crassostrea virginica]	BAB17763.1
161	2,620104329	2,352810492	0,021	twitchin partial [Mytilus galloprovincialis]	AEP02967.1
111	3,193063225	3,003300028	0,022	small heat shock protein 22 [Mytilus galloprovincialis]	XP_022318647.1
7964	2,839162383	2,517217332	0,023	trichohyalin-like isoform X4 [Crassostrea virginica]	BAB60813.1
15	4,294007307	4,082692656	0,023	calponin-like protein [Mytilus galloprovincialis]	XP_022286485.1
368	2,720025856	2,589036733	0,023	T-complex protein 1 subunit beta-like [Crassostrea virginica]	XP_012945445.1
225	1,968699847	0	0,024	PREDICTED: heterogeneous nuclear ribonucleoprotein 87F-like isoform X3 [Aplysia californica]	XP_022314135.1
342	2,808698205	2,648177703	0,025	tektin-2-like [Crassostrea virginica]	XP_019925172.1
1149	3,419776302	3,146196286	0,026	PREDICTED: centlein [Crassostrea gigas]	XP_013411149.1
235	2,587665791	2,433906158	0,026	PREDICTED: alcohol dehydrogenase class-3-like [Lingula anatina]	XP_022329914.1
26	3,521384225	3,314636334	0,026	protein disulfide-isomerase A3-like [Crassostrea virginica]	XP_022316814.1
117	2,559659846	2,323211355	0,026	LOW QUALITY PROTEIN: annexin A4-like [Crassostrea virginica]	XP_022335676.1
249	3,162984532	3,002267821	0,028	uncharacterized protein ZK1073.1-like isoform X4 [Crassostrea virginica]	BAC00784.1
102	2,963224744	2,738570733	0,028	twitchin [Mytilus galloprovincialis]	XP_011416101.1
227	2,45641341	2,284274011	0,028	PREDICTED: cilia- and flagella-associated protein 52 [Crassostrea gigas]	XP_009029528.1
44	3,497746166	3,336378797	0,028	hypothetical protein HELRODRAFT_186143 [Helobdella robusta]	XP_022305782.1
217	2,565041916	2,379855841	0,029	insulin-like growth factor 2 mRNA-binding protein 2 isoform X1 [Crassostrea virginica]	No_Hits
307	3,333337048	3,545860356	0,035	No_Hits	XP_011417460.1
252	2,597587435	1,80007368	0,035	PREDICTED: villin-1 isoform X1 [Crassostrea gigas]	XP_021357329.1
90	3,241577044	2,928062732	0,035	citrate synthase mitochondrial-like [Mizuhopecten yessoensis]	AKS48133.1
27	3,511154726	3,378470728	0,036	filament-like protein-2 [Mytilus coruscus]	XP_021375365.1
258	1,974097387	0	0,037	uncharacterized protein LOC110464458 isoform X12 [Mizuhopecten yessoensis]	No_Hits
144	3,876583641	3,630314254	0,037	No_Hits	XP_021348266.1
5888	2,439054532	2,261881695	0,038	testis-specific gene 10 protein-like isoform X2 [Mizuhopecten yessoensis]	OWF45664.1
229	2,513041968	2,363350566	0,040	Lethal(2) giant larvae protein-like 1 [Mizuhopecten yessoensis]	XP_021354511.1
3693	1,482260274	0	0,043	clathrin heavy chain 1 isoform X1 [Mizuhopecten yessoensis]	XP_022320110.1
9	4,241189316	4,086966549	0,048	retrograde protein of 51 kDa-like isoform X4 [Crassostrea virginica]	XP_022332780.1
25	0	1,28591816	0,049	tropomyosin isoform X9 [Crassostrea virginica]	

Table S3: Functional analysis and enrichment of differentially expressed proteins identified in mussel plantigrade larvae. Only the GO category Biological Process is represented in the analysis. GO = gene ontology term; term_size = number of gene sequences related to the GO term in the database; effective_domain_size = total number of gene sequences in the database.

term_name	term_id	term_size	effective_domain_size	adjusted_p_value_XA21	query_size_XA21	intersection_size_XA21	adjusted_p_value_XA23	query_size_XA23	intersection_size_XA23
organonitrogen compound biosynthetic process	GO:1901566	629	8980	1.17856E-05	70	20	8.93813E-06	69	20
translation	GO:0006412	292	8980	0.000741043	70	12	8.80207E-05	69	13
peptide biosynthetic process	GO:0043043	300	8980	0.00098223	70	12	0.000120158	69	13
amide biosynthetic process	GO:0043604	312	8980	0.001474339	70	12	0.000388239	69	13
peptide metabolic process	GO:0006518	319	8980	0.001852446	70	12	0.000242306	69	13
cellular amide metabolic process	GO:0043603	358	8980	0.005961851	70	12	0.000884403	69	13
small molecule metabolic process	GO:0044281	526	8980	0.0006609304	70	16	0.002609155	69	15
cellular component biogenesis	GO:0044085	349	8980	0.024340054	70	11	0.003936325	69	12
cilium movement involved in cell motility	GO:0060294	10	8980	0.000231887	70	4	0.016823585	69	3
cilium-dependent cell motility	GO:0060285	11	8980	0.000362252	70	4	0.023005128	69	3
cilium or flagellum-dependent cell motility	GO:001339	13	8980	0.000775683	70	4	0.039438064	69	3
purine ribonucleoside triphosphate metabolic process	GO:0009205	17	8980	0.000521873	70	4	0.09172431	69	3
purine ribonucleoside triphosphate biosynthetic process	GO:0009206	17	8980	0.002521873	70	4	0.09172431	69	3
purine nucleoside triphosphate metabolic process	GO:0009144	17	8980	0.002521873	70	4	0.09172431	69	3
purine nucleoside triphosphate biosynthetic process	GO:0009145	17	8980	0.002521873	70	4	0.09172431	69	3
cilium movement	GO:0003341	18	8980	0.003223374	70	4	0.109464658	69	3
ribonucleoside triphosphate metabolic process	GO:0009199	19	8980	0.004058976	70	4	0.129275572	69	3
nucleoside triphosphate biosynthetic process	GO:0009142	19	8980	0.004058976	70	4	0.129275572	69	3
ribonucleoside triphosphate biosynthetic process	GO:0009201	19	8980	0.004058976	70	4	0.129275572	69	3