Supplementary Table 1 Formulation and approximate composition of experiment diets

Ingredient	Diets				
	D1	D2	D3	D4	D5
kelp powder	20	20	20	20	20
Spirulina platensis powder	5	5	5	5	5
Starch	25	20	15	10	5
Fish meal	10	15	20	25	30
Fish oil	7	7	7	7	7
Soybean meal	5	5	5	5	5
Yeast power	10	10	10	10	10
Marine mud	14	14	14	14	14
Multivitamins	1.5	1.5	1.5	1.5	1.5
$Ca(H_2PO_4)_2$	1	1	1	1	1
Multiminerals	1.5	1.5	1.5	1.5	1.5
Proximate composition (% of dry matter basis)					
Crude protein	20.67	24.02	27.37	30.72	34.07
Crude lipid	7.87	8.29	8.71	9.13	9.55
Ash	32.01	32.73	33.45	34.17	34.89
Carbohydrate [1]	39.46	34.97	30.48	25.99	21.50
Gross energy [2]	14.77	14.96	15.14	15.32	15.51

[1] Carbohydrate = 100 − crude protein − crude lipid − ash.

[2] Calculated values based on 23.6, 39.5 and 17.2 kJ/g for protein, lipid and carbohydrate, respectively.

Supplementary Table 2 Amino acid profiles of the experimental diets (dry matter % in the diet)

Amino acids	Diets				
	D1	D2	D3	D4	D5
Aspartic	0.83	1.03	1.11	1.26	1.49
Threonine	0.33	0.43	0.47	0.54	0.65
Serine	0.33	0.43	0.47	0.54	0.65
Glutamic	1.09	1.44	1.55	1.77	2.13
Proline	0.39	0.44	0.46	0.52	0.65
Glycine	0.40	0.52	0.57	0.69	0.82
Alanine	0.47	0.58	0.65	0.75	0.89
Valine	0.33	0.42	0.47	0.54	0.64
Isoleucine	0.28	0.37	0.40	0.46	0.52
Leucine	0.61	0.80	0.88	1.02	1.14
Tyrosine	0.26	0.31	0.37	0.41	0.47
Phenylalanine	0.33	0.41	0.45	0.51	0.61
Histidine	0.14	0.18	0.20	0.23	0.27
Lysine	0.43	0.57	0.62	0.76	0.92
Arginine	0.41	0.46	0.63	0.67	0.80
Methionine	0.15	0.18	0.19	0.24	0.28
Total[a] amino acids	6.78	8.57	9.50	10.96	12.96

[a] Except Cystine and Tryptophan.

Supplementary Table 3 Identification of SDMs in the coelomic fluid between EG2 and EG5 groups

MS2 name	MS2 score	rt	mz	mean EG2	mean EG5	VIP	P-value	Log_FC
Positive-ion mode								
Adenine	1.000	169.658	136.062	1.977	0.471	2.133	0.001	2.069
Thymine	0.998	89.436	127.050	0.286	0.141	1.787	0.010	1.017
Glycyl-Valine	0.998	396.520	175.108	1.457	3.316	2.218	0.004	-1.187
N6-Methyladenosine	0.998	316.982	282.119	0.340	0.463	1.133	0.086	-0.445
Trigonelline	0.996	310.937	138.055	8.096	4.641	1.746	0.033	0.803
N1-(alpha-D-ribosyl)-5,6-dimethyl-benzimidazole	0.991	75.653	279.134	0.340	0.542	1.619	0.037	-0.673
Betonicine	0.991	369.793	160.097	0.174	0.089	1.445	0.078	0.964
O-Acetylserine	0.986	405.496	148.060	0.155	0.073	1.272	0.095	1.095
Glycylproline	0.984	357.685	173.092	0.201	0.272	1.593	0.038	-0.435
Alanyl-Leucine	0.975	369.727	203.139	0.962	0.694	1.511	0.053	0.473
Deoxycytidine	0.975	226.285	228.098	0.264	0.059	1.733	0.064	2.163
(2S,4R,5S)-Muscarine	0.975	250.508	174.149	0.221	0.085	1.782	0.006	1.371

Arecaidine	0.975	324.892	142.086	4.649	0.130	2.699	0.010	5.157
Racemethionine	0.973	310.005	150.058	0.400	0.140	1.485	0.097	1.516
Lysyl-Histidine	0.973	395.467	284.172	0.030	0.138	2.316	0.002	-2.205
Dethiobiotin	0.972	66.615	215.139	0.318	0.619	1.459	0.028	-0.959
L-Arginine	0.963	555.969	175.119	2.663	1.677	1.561	0.043	0.667
Hydroxyprolyl-Leucine	0.961	325.892	245.149	0.263	0.417	1.927	0.005	-0.668
Prolylglycine	0.948	389.638	173.092	0.359	0.093	2.474	0.000	1.950
Homocysteine thiolactone	0.919	171.480	118.032	0.350	0.233	2.116	0.001	0.585
1H-Indole-2,3-dione	0.913	42.276	148.039	0.378	0.220	1.490	0.058	0.778
4-Guanidinobutanoic acid	0.907	385.683	146.092	1.131	0.753	1.826	0.006	0.588
Methylimidazole acetaldehyde	0.900	151.967	125.071	0.621	0.321	2.267	0.002	0.953
Methoxypyrazine	0.879	223.535	111.061	2.197	0.576	2.224	0.016	1.932
2-(1-Pyrrolidinyl)-3-pentanone	0.873	63.126	156.138	0.369	0.873	1.406	0.027	-1.243
Imidazole-4-acetaldehyde	0.870	73.641	111.056	15.282	6.932	1.762	0.054	1.140
Violet-leaf aldehyde	0.833	63.611	139.112	5.947	14.856	1.514	0.022	-1.321
Valyl-Valine	0.789	402.806	217.154	9.209	5.469	1.480	0.060	0.752

2-Methyl-1,3-cyclohexadiene	0.773	63.126	95.086	1.016	2.389	1.471	0.023	-1.234
PC(P-18:1(9Z)/15:0)	0.757	169.632	730.574	0.053	0.085	1.296	0.066	-0.666
PC(P-18:1(11Z)/22:4(7Z,10Z,13Z,16Z))	0.755	163.462	820.622	0.023	0.053	1.299	0.062	-1.203
N6-Acetyl-L-lysine	0.753	345.459	189.123	0.893	22.898	1.477	0.088	-4.680
PE(P-18:1(11Z)/22:2(13Z,16Z))	0.739	165.109	782.606	0.050	0.086	1.614	0.030	-0.790
PE(P-18:1(9Z)/20:1(11Z))	0.732	166.804	756.589	0.069	0.108	1.357	0.052	-0.631
Ceramide (d18:1/20:0)	0.730	32.983	594.583	0.024	0.045	1.307	0.064	-0.882
LysoPC(14:0/0:0)	0.729	221.846	468.308	0.163	0.432	1.431	0.051	-1.407
(R)-Salsolinol	0.727	391.144	180.102	0.175	0.124	1.390	0.062	0.497
Tromethamine	0.719	38.199	122.081	0.166	0.127	1.920	0.006	0.389
2,2,4,4,6,6-Hexamethyl-1,3,5-trithiane	0.717	30.940	223.063	0.071	0.060	1.507	0.034	0.251
2'-O-Methyladenosine	0.714	70.744	282.119	2.042	1.257	1.648	0.028	0.700
N-Methylnicotinium	0.712	265.940	177.139	0.040	0.635	2.129	0.019	-4.006
LysoPC(18:2(9Z,12Z))	0.703	216.705	520.339	0.081	0.172	1.231	0.074	-1.088
3-(5-Methyl-2-furanyl)butanal	0.699	33.868	153.091	0.068	0.091	1.685	0.021	-0.431
(2R)-1-O-beta-D-Galactopyranosylglycerol	0.697	63.139	255.111	0.410	0.700	1.222	0.031	-0.773

2-(3-Phenylpropyl)pyridine	0.679	37.594	198.128	0.009	1.283	1.820	0.010	-7.153
PC(P-18:1(11Z)/22:1(13Z))	0.676	165.117	826.668	0.005	0.020	1.208	0.041	-2.010
Isopropylbenzene	0.667	63.261	121.101	4.247	10.307	1.497	0.023	-1.279
L-Histidinol	0.666	130.150	142.097	0.122	0.271	2.305	0.000	-1.146
L-Theanine	0.637	357.759	175.108	0.070	0.906	1.385	0.099	-3.700
LysoPC(20:2(11Z,14Z))	0.627	212.914	548.371	0.009	0.029	1.220	0.060	-1.741
(E)-2,6-Dimethyl-2,5-heptadienoic acid	0.619	33.914	155.106	0.043	0.064	1.582	0.043	-0.578
PC(P-16:0/20:1(11Z))	0.609	167.882	772.622	0.046	0.118	1.626	0.031	-1.344
PC(P-18:0/14:0)	0.602	172.639	718.574	0.017	0.046	1.622	0.056	-1.381
6'-Hydroxyenterolactone	0.571	62.747	315.122	1.676	2.459	1.269	0.031	-0.553
LysoPC(16:1(9Z)/0:0)	0.551	218.327	494.324	0.022	0.055	1.159	0.094	-1.311
Thiomorpholine 3-carboxylate	0.532	355.381	148.042	1.145	0.679	1.643	0.033	0.755
(5alpha,8beta,9beta)-5,9-Epoxy-3,6-megastigmadien-8-ol	0.490	33.712	209.154	0.297	0.334	1.410	0.058	-0.170
Methyl n-formylanthranilate	0.479	51.700	180.065	0.158	0.071	1.536	0.064	1.152
PC(20:0/P-18:1(11Z))	0.454	165.765	800.653	0.017	0.046	1.426	0.060	-1.443
Negative-ion mode								

Ethyl tetradecanoate	1.000	38.487	255.233	41.177	84.233	1.750	0.054	-1.033
L-Phenylalanine	0.998	283.857	164.071	6.388	2.570	1.809	0.028	1.314
Thymidine	0.995	89.719	241.083	37.746	23.363	1.416	0.063	0.692
Glutaric acid	0.994	390.765	131.035	0.395	0.518	1.606	0.018	-0.392
alpha-Ketoisovaleric acid	0.969	143.931	115.040	5.104	9.505	1.544	0.032	-0.897
Erythrono-1,4-lactone	0.966	394.247	117.019	5.030	12.164	1.332	0.096	-1.274
Cholesterol sulfate	0.959	24.397	465.305	0.053	0.199	2.031	0.086	-1.922
L-Asparagine	0.928	405.896	131.046	0.966	0.427	1.758	0.054	1.177
Deoxyinosine	0.888	194.960	251.078	4.436	2.749	1.378	0.099	0.690
Deoxyuridine	0.839	106.075	227.067	3.282	1.237	1.905	0.028	1.408
Adenine	0.817	170.156	134.047	3.666	0.836	2.032	0.002	2.134
N4-Acetylcytidine	0.792	89.727	284.089	0.379	0.223	1.331	0.074	0.765
L-Glutamic acid	0.727	405.575	146.045	0.563	0.289	1.468	0.054	0.965
1H-Indole-2,3-dione	0.700	42.615	146.024	2.504	1.629	1.602	0.036	0.620
Prostaglandin D2	0.692	41.161	351.221	1.125	1.952	1.860	0.053	-0.794
2-Oxovaleric acid	0.665	73.635	115.039	19.994	33.824	2.237	0.002	-0.758

Cytosine	0.605	245.048	110.035	0.307	2.019	2.016	0.026	-2.719
Imidazoleacetic acid	0.583	89.658	125.035	2.383	1.508	1.513	0.054	0.660
Ethyl hexadecanoate	0.554	38.781	283.265	40.792	63.778	1.564	0.022	-0.645
Phenylpyruvic acid	0.511	76.072	163.040	4.674	2.273	1.481	0.061	1.040
8,9-DiHETrE	0.510	44.276	337.237	2.236	3.331	1.723	0.056	-0.575
m-Coumaric acid	0.491	58.483	163.040	11.850	6.197	1.626	0.049	0.935
Cortisone	0.439	26.176	421.204	0.225	0.313	1.706	0.030	-0.473
Racemethionine	0.325	309.374	148.043	0.600	0.237	1.529	0.065	1.343

Supplementary Table 4 Metabolic pathways identified on the significantly differential metabolites from the the coelomic fluid between group EG2 and EG5

Pathway	Total	Hits	Raw p	-ln(p)	Impact	Hits Cpd
Positive-ion mode						
Histidine metabolism	8	2	0.010875	4.521	0	Imidazole-4-acetaldehyde cpd:C05130; Methylimidazole acetaldehyde cpd:C05827
Sulfur metabolism	7	1	0.1386	1.976	0.167	O-Acetylserine cpd:C00979
Riboflavin metabolism	10	1	0.19224	1.649	0	N1-(alpha-D-ribosyl)-5,6-dimethyl-benzimidazole cpd:C05775
Selenoamino acid metabolism	17	1	0.30537	1.186	0.031	O-Acetylserine cpd:C00979
Cysteine and methionine metabolism	26	1	0.42888	0.847	0	O-Acetylserine cpd:C00979
Arginine and proline metabolism	28	1	0.45334	0.791	0	L-Arginine cpd:C00062
Pyrimidine metabolism	40	1	0.58053	0.544	0	Deoxycytidine cpd:C00881
Purine metabolism	54	1	0.69348	0.366	0.008	Adenine cpd:C00147
Aminoacyl-tRNA biosynthesis	66	1	0.76672	0.266	0	L-Arginine cpd:C00062
Negative-ion mode						

Phenylalanine, tyrosine and tryptophan biosynthesis	4	2	0.001728	6.361	0.500	Phenylpyruvic acid cpd:C00166; L-Phenylalanine cpd:C00079
Phenylalanine metabolism	8	2	0.007735	4.862	1	L-Phenylalanine cpd:C00079; Phenylpyruvic acid cpd:C00166
Alanine, aspartate and glutamate metabolism	20	2	0.046361	3.071	0.308	L-Glutamic acid cpd:C00025; L-Asparagine cpd:C00152
D-Glutamine and D-glutamate metabolism	5	1	0.085601	2.458	1	L-Glutamic acid cpd:C00025
Aminoacyl-tRNA biosynthesis	66	3	0.10503	2.254	0	L-Asparagine cpd:C00152; L-Phenylalanine cpd:C00079; L-Glutamic acid cpd:C00025
Histidine metabolism	8	1	0.13361	2.013	0	Imidazoleacetic acid cpd:C02835
Nitrogen metabolism	9	1	0.14908	1.903	0	L-Glutamic acid cpd:C00025
Pyrimidine metabolism	40	2	0.15509	1.864	0.047	Deoxyuridine cpd:C00526; Cytosine cpd:C00475 Thymidine cpd:C00214
Porphyrin and chlorophyll metabolism	11	1	0.17925	1.719	0	L-Glutamic acid cpd:C00025

Purine metabolism	54	2	0.24698	1.399	0.008	Deoxyinosine cpd:C05512; Adenine cpd:C00147
Butanoate metabolism	19	1	0.29018	1.237	0	L-Glutamic acid cpd:C00025
Glutathione metabolism	25	1	0.36398	1.011	0.095	L-Glutamic acid cpd:C00025
Arginine and proline metabolism	28	1	0.39812	0.921	0.151	L-Glutamic acid cpd:C00025

[a]Hits is the number of significantly differential metabolites in one pathway.

[b]Raw *P* is *P* value calculated from the pathway enrichment analysis.

[c]Impact represents impact value in the pathway topology analysis.