

## Supporting Materials

**Table S1.** Primers used in this study.

**Table S2.** Analysis of similarity (ANOSIM) test the dissimilarities of sea cucumber gut microbiotas using Bray-Currit distance.

**Table S3.** Bacterial taxonomic profiling at the phylum level. Data are represented as the mean  $\pm$  SD (n=8).

**Table S4.** Bacterial taxonomic profiling at the family level. Data are represented as the mean  $\pm$  SD (n=8).

**Table S5.** The top 25 variables were extracted in positive and negative ion modes by OPLS-DA analysis, respectively.

**Figure S1.** OPLS loading S-plot for the total lipids of the 12 h, 48 h, 96 h and SUS groups and the negative control group detected in the (A) ESI<sup>+</sup> and (B) ESI<sup>-</sup> modes.

**Table S1.** Primers used in this study.

Biomarker	Primers sequences-upstream	Primers sequences-downstream
Aj $\beta$ -actin	CCATTCAACCCTAAAGCCAACA	ACACACCGTCTCCTGAGTCCAT
Aj IL17	GTTTGTGGTGCTGTTCTCTGTGA	GGACTTCGATCGGGTCTTTTG
Aj p105	TCTTCGCATTCCATTGAGCTG	ATGGTCCTTCACAGCCGTATCT
Aj TGF $\beta$	GGGATCTCGATTGGAAGTGG	GGTGAGGCGTTAGGGTTTGT
Aj VEGF	AGCCTAGGCCTGTGCTCCTA	CCACTTGCGCTGTATATACTTTCA
Aj MMIF	ATTCAGAGTTTGCGGAGGA	TATTCGGGCTCAGCTTGAGACC

**Table S2.** Analysis of similarity (ANOSIM) test the dissimilarities of sea cucumber gut microbiotas using Bray-Currit distance.

	Control		12 h		48 h		96 h		SUS	
	r	P	r	P	r	P	r	P	r	P
Control	—	—								
12 h	0.5502	<b>0.002</b>	—	—						
48 h	0.8415	<b>0.0002</b>	0.8119	<b>0.0002</b>	—	—				
96 h	0.8426	<b>0.0001</b>	0.9911	<b>0.0005</b>	0.856	<b>0.0004</b>	—	—		
SUS	0.8421	<b>0.0004</b>	0.793	<b>0.0004</b>	0.4883	<b>0.0006</b>	0.1345	0.0521	—	—

**Table S3.** Bacterial taxonomic profiling at the phylum level. Data are represented as the mean  $\pm$  SD (n=8).

Phylum	Control	12 h	48 h	96 h	SUS
Proteobacteria	61.55 $\pm$ 8.53	49.03 $\pm$ 6.39	45.90 $\pm$ 5.44	71.39 $\pm$ 4.56	74.80 $\pm$ 14.79
Firmicutes	14.57 $\pm$ 10.79	33.35 $\pm$ 8.75	38.21 $\pm$ 6.42	8.74 $\pm$ 1.31	12.52 $\pm$ 12.97
Bacteroidetes	8.46 $\pm$ 3.61	6.13 $\pm$ 2.24	9.41 $\pm$ 3.77	9.82 $\pm$ 5.01	7.49 $\pm$ 5.01

Actinobacteria	9.57±1.50	8.66±2.38	3.52±0.98	3.49±1.07	2.26±1.65
Verrucomicrobia	3.08±1.80	1.12±0.57	1.70±0.77	3.81±2.14	1.63±0.95
Fusobacteria	0.10±0.09	0.14±0.08	0.48±0.40	2.11±4.25	0.93±0.80
Chloroflexi	0.82±0.40	0.48±0.16	0.22±0.17	0.19±0.09	0.13±0.10
Acidobacteria	0.34±0.08	0.29±0.10	0.15±0.05	0.14±0.06	0.06±0.06
Others	1.50±0.16	0.80±0.22	0.41±0.15	0.30±0.12	0.19±0.19

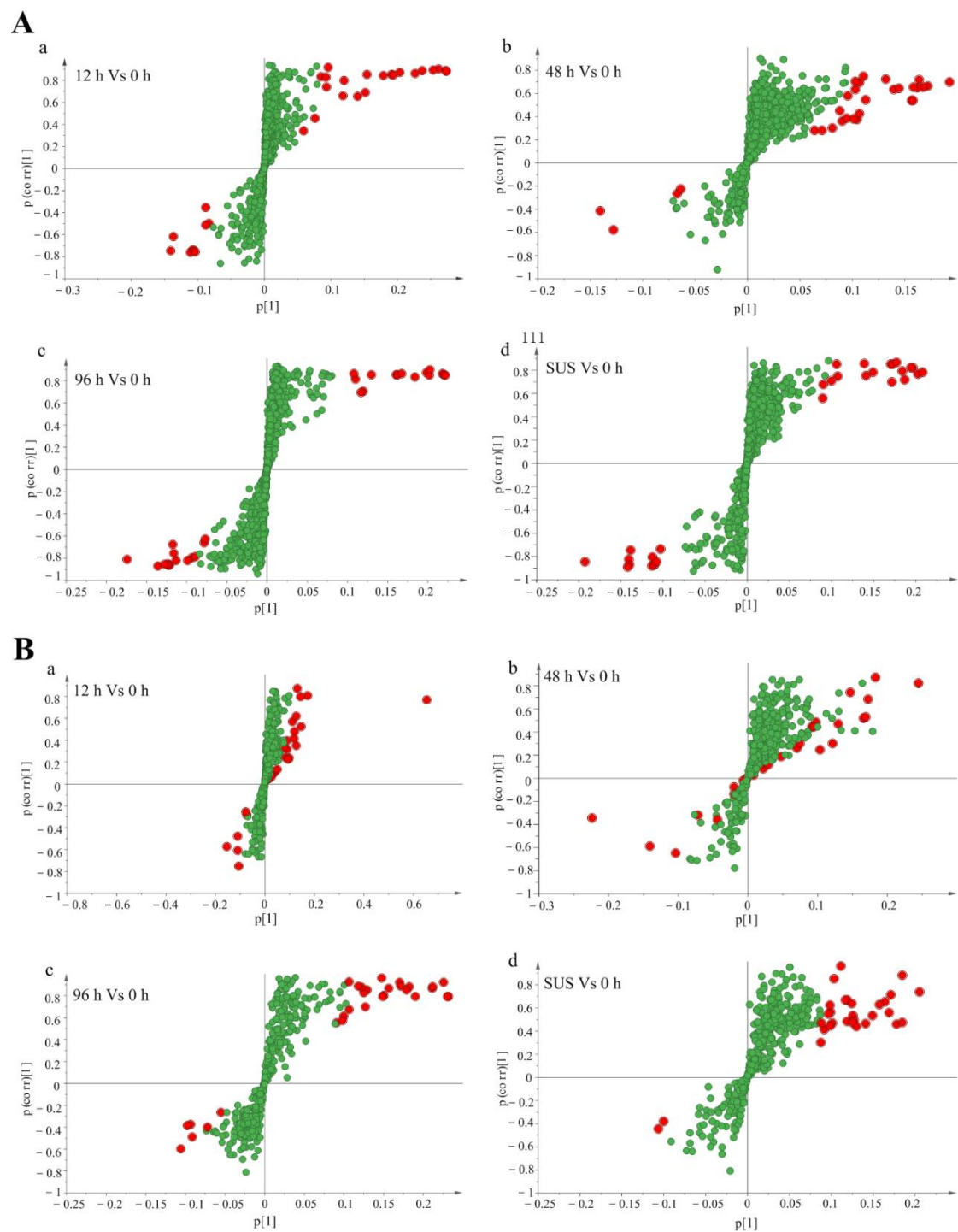
**Table S4.** Bacterial taxonomic profiling at the family level. Data are represented as the mean ± SD (n=8).

Family	Control	12 h	48 h	96 h	SUS
Rhodobacteraceae	19.76±6.52	11.51±3.47	20.89±4.81	47.13±11.65	47.81±21.88
Flavobacteriaceae	6.65±3.64	4.00±2.01	8.84±3.84	8.93±5.04	6.65±5.56
Desulfobulbaceae	5.17±3.65	2.31±2.33	1.45±0.44	0.55±0.16	0.53±0.52
Vibrionaceae	2.19±1.16	4.76±2.16	5.49±2.78	4.89±2.48	5.40±8.43
Bacillaceae	3.83±3.10	21.48±8.76	34.40±6.78	4.56±1.09	9.21±12.11
Pseudoalteromonadaceae	3.30±2.71	5.81±2.01	1.46±0.80	0.97±0.42	0.84±0.69
Verrucomicrobiaceae	3.05±1.81	1.08±0.59	1.68±0.77	3.80±2.14	1.63±0.95
Planococcaceae	2.69±1.94	4.62±1.20	1.44±0.85	1.66±0.64	0.95±0.73
OM60	7.22±4.94	1.58±0.63	1.36±0.34	0.88±0.24	0.82±0.79
Psychromonadaceae	0.71±0.49	0.88±0.47	5.34±2.72	5.18±6.24	7.11±4.20
Phyllobacteriaceae	0.53±0.13	1.40±1.30	1.54±1.52	4.32±3.87	5.91±8.11
Others	44.89±12.31	40.58±7.53	16.11±3.46	17.13±4.77	13.14±6.89

**Table S5.** The top 25 variables were extracted in positive and negative ion modes by OPLS-DA analysis, respectively.

m/z	BaseRt	Class	FA	Formula	MainIon	VIP
<b>ESI<sup>+</sup></b>						
903.7404	27.041	TG	18:1/18:2/18:2	C57 H100 O6	+Na	6.55
901.7253	25.072	TG	18:2/18:2/18:2	C57 H98 O6	+Na	6.52
850.7409	29.432	TG	16:0/16:0/18:1	C53 H100 O6	+NH4	5.98
877.7256	26.865	TG	16:0/18:2/18:2	C55 H98 O6	+Na	5.46
905.7569	29.336	TG	18:0/16:0/20:4	C57 H102 O6	+Na	4.76
905.7567	28.966	TG	18:1/18:1/18:2	C57 H102 O6	+Na	4.59
879.7409	28.883	TG	16:0/18:1/18:2	C55 H100 O6	+Na	4.17
878.8166	29.752	TG	18:0/16:0/18:1	C55 H104 O6	+NH4	3.98
639.4954	11.996	DG	18:2/18:2	C39 H68 O5	+Na	3.39
822.7564	28.633	TG	16:0/14:0/18:1	C51 H96 O6	+NH4	3.33
824.7701	29.399	TG	16:0/16:0/16:0	C51 H98 O6	+NH4	3.31
823.6786	24.281	TG	16:1/16:1/16:1	C51 H92 O6	+Na	3.18
825.6937	26.287	TG	16:0/16:1/16:1	C51 H94 O6	+Na	3.02
903.7435	27.598	TG	18:1/18:1/18:3	C57 H100 O6	+Na	2.89
566.551	13.865	Cer	d22:1/14:0	C36 H71 O3 N1	+H	2.64
801.6943	28.569	TG	16:0/14:0/16:0	C49 H94 O6	+Na	2.58
852.8012	29.745	TG	18:0/16:0/16:0	C53 H102 O6	+NH4	2.50

875.7101	24.913	TG	16:1/18:2/18:2	C55 H96 O6	+Na	2.36
799.678	26.165	TG	16:0/14:0/16:1	C49 H92 O6	+Na	2.25
899.7092	23.568	TG	18:3/18:2/18:2	C57 H96 O6	+Na	2.22
906.8484	29.944	TG	20:0-16:0-18:1	C57 H108 O6	+NH4	2.17
568.5662	15.544	Cer	d22:0/14:0	C36 H73 O3 N1	+H	2.09
877.7254	27.448	TG	16:0-16:1-20:3	C55 H98 O6	+Na	1.91
871.6784	22.64	TG	16:1/16:1/20:5	C55 H92 O6	+Na	1.83
864.8014	29.592	TG	16:0/17:0/18:1	C54 H102 O6	+NH4	1.81
<b>ESI<sup>-</sup></b>						
555.2849	1.67	SQMG	16:0	C25 H48 O11 S1	-H	7.51
688.4931	10.198	PE	16:0/16:1	C37 H72 O8 N1 P1	-H	3.46
719.488	11.396	PG	16:0/16:1	C38 H73 O10 N0 P1	-H	3.35
745.5036	11.876	PG	16:0/18:2	C40 H75 O10 N0 P1	-H	3.27
481.2576	1.49	LPG	16:1	C22 H43 O9 N0 P1	-H	3.08
450.2631	1.311	LPE	16:1	C21 H42 O7 N1 P1	-H	2.97
714.509	10.461	PE	16:1/18:1	C39 H74 O8 N1 P1	-H	2.67
483.2734	1.873	LPG	16:0	C22 H45 O9 N0 P1	-H	2.59
507.315	1.578	LPG	18:2	C24 H45 O9 N0 P1	-H	2.43
686.4776	7.996	PE	16:1/16:1	C37 H70 O8 N1 P1	-H	2.31
452.2788	1.622	LPE	16:0	C21 H44 O7 N1 P1	-H	2.24
717.4722	9.062	PG	16:1/16:1	C38 H71 O10 N0 P1	-H	2.18
563.3443	1.78	MGMG	18:1	C27 H50 O9	+HCOO	2.17
714.5087	11.075	PE	16:0/18:2	C39 H74 O8 N1 P1	-H	2.08
509.2889	1.957	LPG	18:1	C24 H47 O9 N0 P1	-H	1.98
476.2786	1.37	LPE	18:2	C23 H44 O7 N1 P1	-H	1.97
838.5974	12.007	PC	18:1/20:4	C46 H84 O7 N1 P1	+HCOO	1.86
478.2941	1.675	LPE	18:1	C23 H46 O7 N1 P1	-H	1.80
740.5244	10.875	PE	18:1/18:2	C41 H76 O8 N1 P1	-H	1.72
850.5611	8.554	PC	18:1/20:5	C46 H80 O8 N1 P1	+HCOO	1.66
581.3002	1.748	SQMG	18:1	C27 H50 O11 S1	-H	1.64
743.4877	9.515	PG	16:1/18:2	C40 H73 O10 N0 P1	-H	1.61
747.5191	14.253	PG	16:0/18:1	C40 H77 O10 N0 P1	-H	1.52
716.5247	12.879	PE	16:0/18:1	C39 H76 O8 N1 P1	-H	1.47
771.519	12.144	PG	18:1/18:2	C42 H77 O10 N0 P1	-H	1.46



**Figure S1.** OPLS loading S-plot for the total lipids of the 12 h, 48 h, 96 h and SUS groups and the negative control group detected in the (A) ESI<sup>+</sup> and (B) ESI<sup>-</sup> modes.