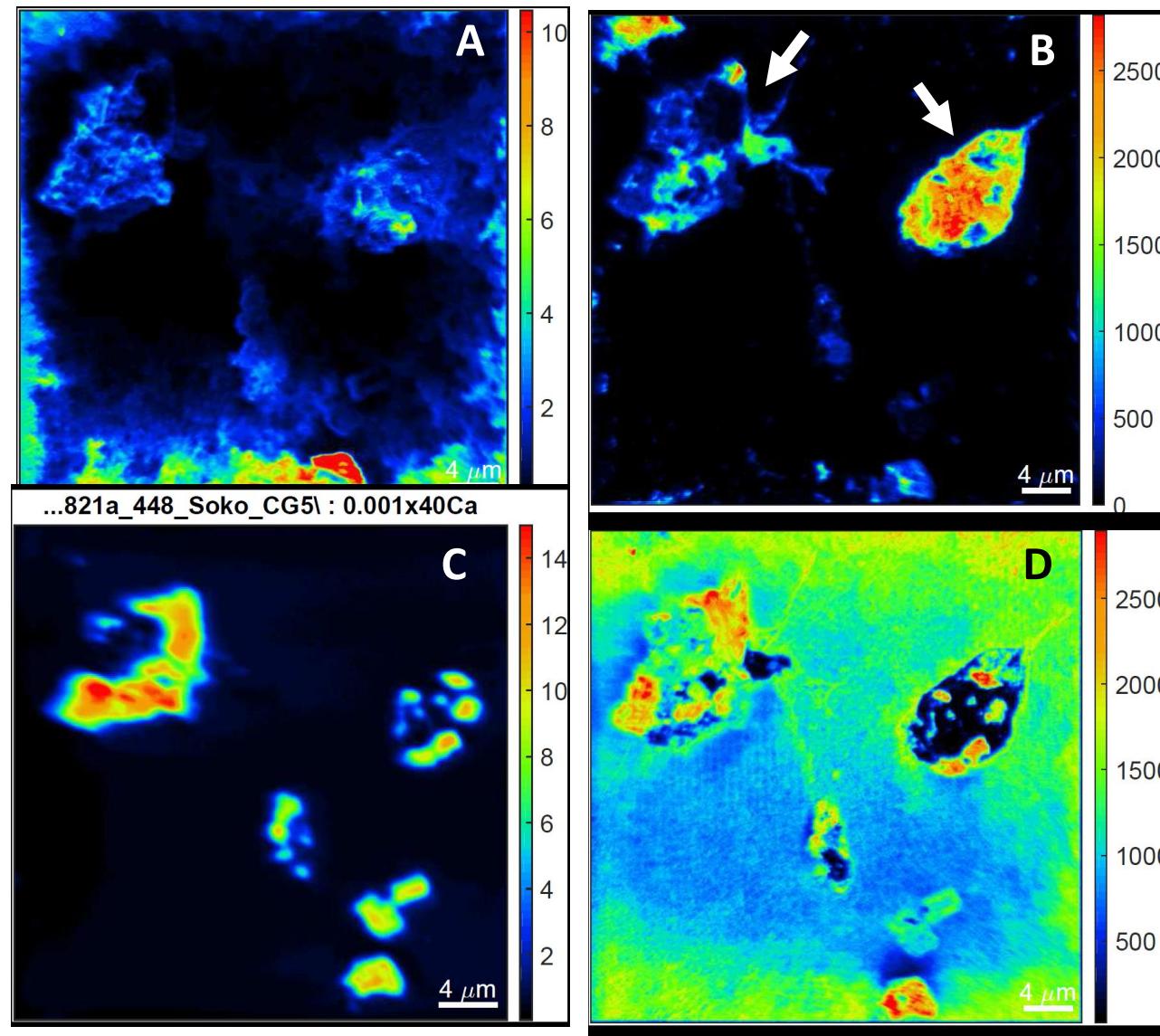
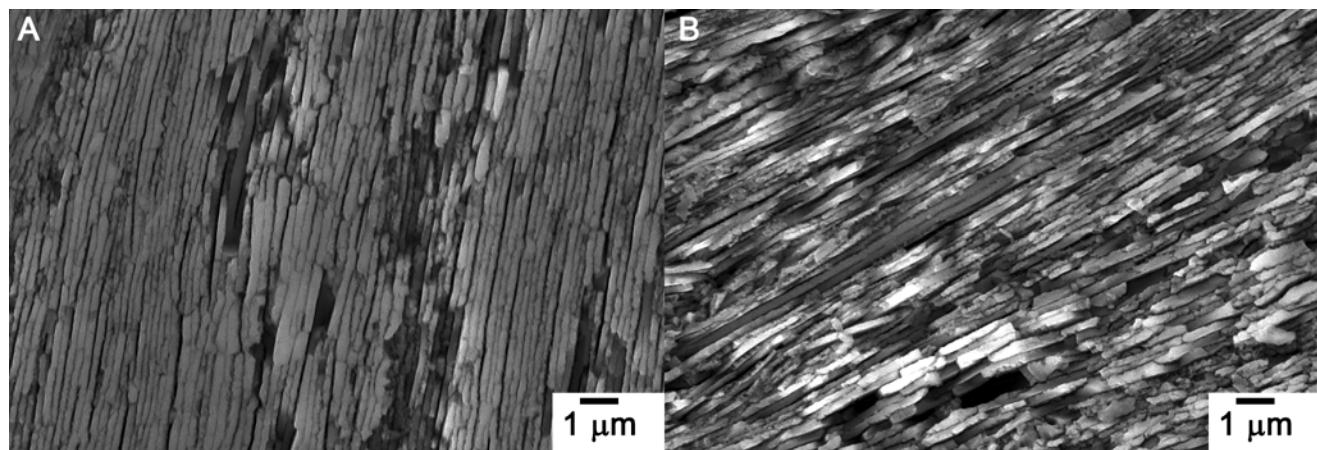


**Fig. S1.** Typical spectra of the enriched mineral fractions obtained from the hemocytes of pacific oysters. **A.** The predominant calcium carbonate phase is dolomite based on the presence of absorbance bands at 1464 cm<sup>-1</sup>, 878 cm<sup>-1</sup> and 724 cm<sup>-1</sup>. **B.** The predominant calcium carbonate phase in this spectrum is calcite based on the presence of absorbance peaks at 1422 cm<sup>-1</sup>, 879 cm<sup>-1</sup> and 712 cm<sup>-1</sup>. Note that the other unassigned peaks are due to the impurities. Variations in the calcium carbonate mineral phases in different preparations support the notion that the initial mineral phase is metastable and it transforms into different mineral phases during the preparation.

**Fig. S2.** NanoSIMS images of gold-coated samples of hemocytes of *C. gigas*.

A – secondary ion image showing 3D structure of the sample; B -  $^{12}\text{C}^{14}\text{N}$  signal distribution showing two hemocytes (indicated by arrows); C –  $^{40}\text{Ca}$  signal; D –  $^{16}\text{O}$  signal. Note co-localization of the hotspots for Ca and O signals within the hemocytes (panes C and D) indicating presence of calcium carbonate.





**Fig. S3.** SEM micrographs of shell's foliated layer of (A) *C. virginica* and (B) *C. gigas*

**Table S1.** Primers used to amplify the target biomineralization- and immune-related genes of *C. gigas* and *C. virginica*.

NCBI accession numbers of the sequences used for primer design and annealing temperatures <sup>°</sup> $\text{C}$  are given for each primer pair.

		<i>Crassostrea gigas</i>		<i>Crassostrea virginica</i>		
Target	Accession number	Primer sequence	Tm, (°C)	Accession number	Primer sequence	Tm, (°C)
CAI	XM_011439428.1	FW 5'-AGGGTTGATTCACTCCACATAC-3'	55	XM_011439428	FW 5'-AACCTTCACCCTCGATCAC-3'	62
		Rev 5'-GCTCCATGGGATAAGAGATTCC-3'			Rev 5'-ACCTCCCACCAAAACATTGGA-3'	
CAII	XM_011449596.1	FW 5'-CATCAACCAGCAGTCAGAAGTA-3'	55	XM_011449596	FW 5'-CTACATGGTCCAGGTCGGTG-3'	60
		Rev 5'-TGTTCCGATCCCTTGTCAATTAG-3'			Rev 5'-TTAGCTGTGTCGAAGGGCTC-3'	
CAXIV	XM_011437076.1	FW 5'-AGTGTCAAGGAGACCATCAAG-3'	55	XM_011437076	FW 5'-AGATGTTCGTTGCTGGTCGG-3'	60
		Rev 5'-CTGTGGTTGAGAGGCTGAATAG-3'			Rev 5'-CAGTGGTCCGGTCATGTTTC-3'	
V-type H <sup>+</sup> ATPase	XM_011420050.1	FW 5'-GCAGTGTCAGCATTGTAGGA-3'	55	XM_011420050	FW 5'-ATCGTACAACTCGTCGGCAA-3'	62
		Rev 5'-GTAGGAGATGAGCCAGTTGATG-3'			Rev 5'-GGCGTGTATCCATTCTGCT-3'	
Ca <sup>2+</sup> ATPase	XM_011430632.1	FW 5'-AGGCAAAGGCATCGTCATAG-3'	55	XM_011430632	FW 5'-CAGCAGAGGAAGCGTTCTA-3'	60
		Rev 5'-GATGAGCCCGATGATAACAGAAG-3'			Rev 5'-AGGCCAGCAGCAACAGTATC-3'	
PM Ca <sup>2+</sup> ATPase	XM_011442008.1	FW 5'-CAACAAAGTCGCCAACAAAG-3'	55	XM_011442008	FW 5'-GGACGAGAGTTCTTAACGGG-3'	60
		Rev 5'-GGTCAGTTGCCCTGTAGAA-3'			Rev 5'-TCACCAGCATCTTACCGCTG-3'	
NHX9	762071015_2093 292	FW 5'-TGGTGAAGCTGACTGGTATTG-3'	55	762071015_209 3292	FW 5'-CTGCTCTCTGCCTGGTCTT-3'	60
		Rev 5'-CAATGGTTGCCGTACAAAG-3'			Rev 5'-GTCCCCCAAAAGCCATAGTGA-3'	
NHE3	LOC105349034	FW 5'-GATGATCCAGAGGAGAGCAAAG-3'	55	LOC105349034	FW 5'-CCTGTGTCTGCTGTACAGGTT-3'	60
		Rev 5'-TTGTACGAGGGCTTCTGTTAG-3'			Rev 5'-CCGCCATAGGCCATGATGAA-3'	
Fibronectin Prot3	XM_011437620.1	FW 5'-CCAGGAGGAAATTGAGGAGAG-3'	55	XM_011437620	FW 5'-GGCGAGGTTATGAGACGTT-3'	60
		Rev 5'-GTACTCATAGGGCACTGGTTAG-3'			Rev 5'-TCCAGCCACATTACAGCAGG-3'	

Fibronectin Prot2	XM_011415803.1	FW 5'- CTCCAGTACACCACAAGTCATC-3'	55	XM_011415803	FW 5'- CGGAATGCAGATGGGTGGAT-3'	62
		Rev 5'- AGACACAACTCCGGCAATATC-3'			Rev 5'- GGGCTGTTGCAACTGATTACC-3'	
Fibronectin - ankyrin	XM_011451952.1	FW 5'- CTAACAGTGTCCACCACTAAGG-3'	55	XM_011451952	FW 5'- TGGGCCAAAGTATGACGACT-3'	60
		Rev 5'- CCTGTGTCCAGTATCCTCTCTA-3'			Rev 5'- CGTCAGCACCGTCTTGATG-3'	
VEGF	XM_011451443.1	FW 5'- CCGGTGCATGTGTACCAATA-3'	55	XM_011451443	FW 5'- CCACCGCTGATCCTAACAT-3'	60
		Rev 5'- TGATTTCCCTCGTCAGTCATTCC-3'			Rev 5'- ACGGAAC TGAA GCAT GCACT-3'	
VEGF-R	XM_011457891.1	FW 5'- CCGTCTATGGCTCTGCATAAA-3'	55	XM_011457891	FW 5'- CATGTGGGGTCCTGAAAGC-3'	64
		Rev 5'- CAAATGCACCTTGACCCAATAC-3'			Rev 5'- ATGCTCCTCTTGGCCTTTGG-3'	
Casein kinase I	XM_011448074.1	FW 5'- GGAGGTGGCTGTTAAGTTAGAG-3'	55	XM_011448074	FW 5'- TGGCAAGGACTTAAAGCCAAC-3'	60
		Rev 5'- GCGAGCAGAAGTTGAAGAGA-3'			Rev 5'- ACATGGCAAATTCTGCAGGGA-3'	
Casein kinase II	XM_011419091.1	FW 5'- CGATGAAGCAGAGATCCCATTAA-3'	55	XM_011419091	FW 5'- AGTGGCAAACGGTGAACGTA-3'	60
		Rev 5'- CAAACAGCACATGACCAACTAC-3'			Rev 5'- GTGCCAATAGGCTGATGGGG-3'	
Chitin synthase II	XM_011425426.1	FW 5'-CGCAACAATGGGCAATAGAG-3'	55	XM_011425426	FW 5'- CCGCCATTTCACACCTTGCC-3'	60
		Rev 5'- CTGATATCGAGGCGGTGAATAG-3'			Rev 5'- CTCGTCGTCGACCCCTAGTA-3'	
Chitin synthase III	EKC25899	FW 5'-GTACAAATGGCTCTGGATAG-3'	55	EKC25899	FW 5'-TCAATGCAACAACCAGCAAA-3'	60
		Rev 5'-GTCGAACTCACACTGGAAGAA-3'			Rev 5'-ATGCGAGTCCCGCAAGATAG-3'	
Nacrein	NM_001305309.1	FW 5'-CGCCGAGAAGAACCTCTAAAT-3'	55	NM_001305309	FW 5'-TTGACGGCAGACATTACCCA-3'	60
		Rev 5'-CCAGAGCCAAACTACGTCTTAC-3'			Rev 5'-ACGCCTTGATTTCTTGACCAT-3'	
SLP	AB290411.1	FW 5'- GATCTTCCGTCTTACGTCTATC-3'	55	AB290411	FW 5'-CCAGTACTCGGAACTCGTCG-3'	60
		Rev 5'- AACCGGAGTAAGGTGTTGTATC-3'			Rev 5'-AGAACCGCCTGTTCAACGTA-3'	

Calmodulin	JF508172.1	FW 5'-CCAATGGTGCAGAAGCTACTA-3'	55	JF508172	FW 5'-TCGGTCGAAGCGAGATCCAT-3'	60
		Rev 5'-AGGCTGATTAGACGGTGATG-3'			Rev 5'-TTGATCATGTGTGGCTGCTCT-3'	
Integrin	XM_011444113.2	FW 5'-GTTTCATGATGCACTGAAGG-3'	58	MGID95214	FW 5'-CTGCTCCGATCTGATCAACA-3'	55
		Rev 5'-CAATCCTTTAACGAAACCCG-3'			Rev 5'-CATACGTGTCCCCCTGTCTT-3'	
Killer cell lectin like Rec	XM_011421247.2	FW 5'-AGACGTCTCAAAGGTTCAAA-3'	56	BG624932.1	FW 5'-AAAGCCGGTCCTTACTTATGAA-3'	60
		Rev 5'-TTGATTCTGCCAACACGTAAAC-3'			Rev 5'-GCCGGATATGCACCTGTAATA-3'	
TLR2	EKC29626.1	FW 5'-TCAGGGAACATTGTCACATC-3'	58	JH819194.1	FW 5'-GCGCTTTATTGACGTTAGAC-3'	58
		Rev 5'-GTGATAGCCATTGCAATTG-3'			Rev 5'-CGTAAACACATGAAACTGGT-3'	
TLR3	JH816729.1	FW 5'-GTGGGAAGACAGTTCTAAG-3'	58	MGID92145	FW 5'-TTTGGTTCAAGAACTGGGTT-3'	58
		Rev 5'-GCATGTTGCTATAAAATGCAG-3'			Rev 5'-GATTAAGGCTCAACAATGGC-3'	
TLR4	JH817360.1	FW 5'-CAGACGCCGTATATTGGTA-3'	58	MGID89881	FW 5'-GCCTCCGACTGATTGATTAA-3'	58
		Rev 5'-TATTTAACGCTCGGGATGTCG-3'			Rev 5'-ATACCTCTGAGGATAGGACG-3'	
Mannose Rec2	XM_011414451.2	Fw GTTCACTTTACGTTCACCC-3'	58	XM_011414451. 2	Fw GTTCACTTTACGTTCACCC-3'	58
		Rev 5'-TTTGTGACATTGACGCA-3'			Rev 5'-TTTGTGACATTGACGCA-3'	
SRCR	XM_011436583.2	FW 5'-CCAAATTGCAAGATTGAGGTG-3'	58	BG624783.1	FW 5'-CACATGCGGCTTCTGTCTAA-3'	62
		Rev 5'-CAGATGCCTGCTATTGTCG-3'			Rev 5'-CGGTGATCGTGTGGTATATG-3'	
TNF	MGID91531	FW 5'-GCTTGTTAGGGTGTGATTG-3'	58	MGID91531	FW 5'-GCTTGTTAGGGTGTGATTG-3'	58
		Rev 5'-GTTGTACTTGCCGATGACTT-3'			Rev 5'-GTTGTACTTGCCGATGACTT-3'	
complement component 3 (C3)	KF927126.1	FW 5'-GGTATATCCTGTCCAAGCAG-3'	58	KF927126.1	FW 5'-GGTATATCCTGTCCAAGCAG-3'	58
		Rev 5'-TGTAGGCAGTCCTTGAGATA-3'			Rev 5'-TGTAGGCAGTCCTTGAGATA-3'	
Big defensing	JN251129	FW 5'-TTTGTGCTATAGCATCGT-3'	56	CV133156	FW 5'-TGGCAGCTGCTTACGGTATC-3'	60
		Rev 5'-GTATCTGTAAAGGGCGTAGG-3'			Rev 5'-CCCTGTTGGCACAGCTA-3'	
lectin	XM_011432477.2	FW 5'-TTACAAAACCGTGTACCTC-3'	56	CV088804.1	FW 5'-ATTTGCTCAGCCTTGAATGG-3'	55
		Rev 5'-GTATTGCTGTAAAACGCCAA-3'			Rev 5'-GTCCCTCCCACCCAGTAGTT-3'	
$\beta$ -actin	X75894	FW 5'- TTGGACTTCGAGCAGGAGATGGC-3'	55	X75894	FW 5'-CAC AGC CGC TTC CTC ATC CTC C-3'	55
		Rev 5'-ACATGGCCTCTGGGCACCTGA - 3'			Rev 5'-CCG GCG GAT TCC ATA CCA AGG-3'	

**Table S2.** Principal Component Analysis (PCA) of biomineralization-related genes in oysters.

Tissues were encoded as follows: 1- central mantle; 2- outer mantle edge; 3 - gills; 4 - hemocytes. Species were encoded as follows: 1 – *C. gigas*, 2 – *C. virginica*. CK – creatine kinase, CS – chitine synthase, CA – carbonic anhydrase, SLP - silk-like protein, VEGF - vascular endothelial growth factor, VEGF-R - vascular endothelial growth factor receptor, FN – fibronectin, FNAnk – fibronectin-ankyrin, NHX – sodium-proton exchanger, PM Ca<sup>2+</sup> ATPase – plasma membrane Ca<sup>2+</sup> ATPase.

PC	Eigenvalue	Percentage of		Cumulative
		Variance	Cumulative	
1	8,61749	41,04%	41,04%	
2	3,11565	14,84%	55,87%	
3	2,04403	9,73%	65,61%	
4	1,29895	6,19%	71,79%	
5	1,06344	5,06%	76,86%	
6	0,88823	4,23%	81,08%	
7	0,83594	3,98%	85,07%	
8	0,70519	3,36%	88,42%	
9	0,53363	2,54%	90,96%	
10	0,41985	2,00%	92,96%	

Loadings	PC1	PC2	PC3	PC4	PC5
species	0,21015	-0,11856	-0,32863	0,25598	0,02771
tissue	-0,02365	-0,42799	0,04893	0,06324	-0,17433
CK1	0,32375	-0,00357	0,01581	-0,02708	-0,09451
CK2	0,28498	0,0085	-0,03804	0,07719	-0,01627
CS2	-9,63E-04	0,46203	0,04119	0,22952	-0,01764
CS3	0,04843	0,2463	-0,42081	-0,15509	0,07272
CA1	0,26141	-0,08978	0,18878	-0,15123	-0,32732

CA2	0,18612	0,08529	0,14074	-0,22947	0,28101
CA14	-0,10233	0,35441	0,35062	0,01579	1,92E-04
VEGF	0,24633	0,20806	-0,24224	0,00434	-0,26342
VEGF-R	0,29119	-0,01567	0,11634	-0,11517	-0,27843
SLP	0,07634	0,31619	-0,30643	0,35547	-0,28692
NHX3	0,30943	-0,07496	0,18799	-0,18957	-0,06524
NHX9	0,33004	-0,01972	0,09116	-0,07965	-0,02703
Ca2+					
ATPase	0,23366	0,16476	0,187	-0,11612	0,2614
PM Ca2+					
ATPase	0,23663	-0,06606	-0,16949	0,13106	0,42184
V H+					
ATPse	0,09481	-0,26131	0,20689	0,52937	0,2529
Nacrein	-0,05897	0,0293	-0,26578	-0,51107	0,20816
FN3-2	-0,10338	0,35034	0,37273	0,07524	0,0142
FN3-3	0,26524	0,11025	-0,01402	0,0975	0,41358
FNAnk	0,3056	0,05037	0,06871	0,04597	-0,09432

**Table S3.** Pearson correlation analysis of mRNA levels of biomineralization-related genes in oysters.

Tissues were encoded as follows: 1- central mantle; 2- outer mantle edge; 3 - gills; 4 - hemocytes. Species were encoded as follows: 1 – *C. gigas*, 2 – *C. virginica*. CK – creatine kinase, CS – chitine synthase, CA – carbonic anhydrase, SLP - silk-like protein, VEGF - vascular endothelial growth factor, VEGF-R - vascular endothelial growth factor receptor, FN – fibronectin, FNAnk – fibronectin-ankyrin, NHX – sodium-proton exchanger, PM Ca2+ ATPase – plasma membrane Ca2+ ATPase.

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**Table S4.** Principal Component Analysis (PCA) of the transcriptomic profiles of oyster hemocytes.

Species: 1 - *C. gigas*, 2 - *C. virginica*. CK – creatine kinase, CS – chitin synthase, CA – carbonic anhydrase, SLP - silk-like protein, VEGF - vascular endothelial growth factor, VEGF-R - vascular endothelial growth factor receptor, FN – fibronectin, FNAnk – fibronectin-ankyrin, NHX – sodium-proton exchanger, PM, Cq3 - complement component 3, SRCR - scavenger receptor cysteine rich, TNF - tumor necrosis factor.

PC	Eigenvalue	Percentage of Variance		Cumulative	Species	PC1	PC2	PC3	PC4	PC5
1	13,63	43,96%	43,96%		lectin	<b>0,261</b>	-0,100	0,009	0,007	0,012
2	6,83	22,05%	66,01%		SRCR	0,095	<b>0,245</b>	<b>0,260</b>	-0,027	0,211
3	5,71	18,41%	84,42%		KC lectin like Rec	-0,087	<b>0,294</b>	-0,222	-0,056	-0,097
4	3,11	10,05%	94,47%		integrin	0,156	<b>-0,248</b>	-0,108	0,233	0,087
5	1,72	5,53%	100,00%		defensin	-0,116	<b>0,268</b>	0,010	-0,087	<b>-0,421</b>
					TNF	0,228	-0,121	-0,134	-0,150	0,103
					Mannose Rec2	0,211	0,016	0,188	-0,232	-0,105
					Cq3	0,062	<b>-0,262</b>	0,016	<b>0,392</b>	-0,026
					TLR2	0,121	<b>-0,310</b>	-0,058	-0,195	0,065
					TLR4	0,158	0,184	-0,184	<b>0,268</b>	0,084
					TLR3	0,141	0,193	-0,221	-0,168	<b>0,249</b>
					CK1	0,158	0,008	-0,179	<b>0,293</b>	-0,031
					CK2	<b>0,260</b>	0,031	-0,010	0,081	-0,174
					CS2	0,138	0,128	<b>0,331</b>	0,022	0,002
					CS3	0,106	<b>-0,288</b>	0,203	-0,108	-0,064
					CA1	0,224	0,164	0,028	0,197	0,068
					CA2	0,219	0,185	-0,108	0,109	0,053
					CA14	0,219	0,070	0,133	-0,260	0,037
					VEGF	0,108	<b>-0,281</b>	-0,192	-0,131	0,147
					VEGFR	-0,171	0,103	-0,094	0,195	<b>0,458</b>
					SLP	0,019	0,002	<b>0,349</b>	0,017	<b>0,416</b>
					NHX3	0,237	0,115	-0,151	0,048	0,073
					NHX9	0,225	0,034	0,166	0,206	-0,091
					Ca2+ATPase	0,216	0,227	0,018	-0,043	0,039
					PM Ca ATPase	0,189	-0,179	-0,186	0,153	0,118
					V H+ ATPAse	<b>0,254</b>	0,129	0,012	0,041	0,046
					SLP	-0,204	0,160	0,088	0,005	<b>0,354</b>
					FN3-2	0,143	0,168	-0,016	<b>0,375</b>	-0,228
					FN3-3	0,169	-0,143	<b>0,277</b>	-0,089	-0,081
					FNAnk	0,219	0,124	-0,081	0,256	0,029

**Table S5.** Pearson correaltion analysis of the transcriptomic profiles of oyster hemocytes.  
Species: 1 - *C. gigas*, 2 - *C. virginica*. CK – creatine kinase, CS – chitin synthase, CA – carbonic anhydrase, SLP – silk-like protein, VEGF - vascular endothelial growth factor, VEGF-R - vascular endothelial growth factor receptor, FN – fibronectin, FNAnk – fibronectin-ankyrin, NHX – sodium-proton exchanger, PM, Cq3 - complement component 3, SRCR - scavenger receptor cysteine rich, TNF - tumor necrosis factor.

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