

Supplementary data for:

Ambulacrarian insulin-related peptides and their putative receptors suggest how insulin and similar peptides may have evolved from Insulin-like Growth Factor

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Content

Spreadsheet 1 contains contains protein sequences for various insulin-like peptides and their putative precursors, as well as their genbank accession numbers or the terms Artemis or Trinity. Artemis indicates that the sequence in question was derived from a genome assembly, Trinity that the sequence was obtained using the Trinity program on a collection of transcriptome SRAs. In a few instances a combination of Trinity and Artemis was used to obtain a sequence.

Spreadsheet 2 contains the expression of some of these genes for a more limited number of species (there is little sense if the only transcriptome SRAs available for a species are from whole animals of unknown sex and unknown physiological status, or when then there are only very few such SRAs). The data contain the SRA identifier, the number of spots of each SRA and then for each protein of interest two numbers, one in blue, which is number of half spots that contains coding sequence of the protein of interest. The second number in black is the blue number multiplied by 1,000,000 and divided by the number of total spots, which yields a relative number.

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SRAs used in the analysis:

Anneissia japonica

SRR9663012, SRR9663013, SRR9663014, SRR9663015, SRR9663016, SRR9663017, SRR9663018, SRR9663019, SRR9663020, SRR9663021, SRR9663022, SRR9663023, SRR9663024, SRR9663025, SRR9663026, SRR9663027, SRR9663028, SRR9663029, SRR9663030, SRR9663031, SRR9663032, SRR9663033, SRR9663034, SRR9663035, SRR9663036, SRR9663037, SRR9663038, SRR9663039, SRR9663040, SRR9663041, SRR9663042, SRR9897705, SRR9897706, SRR9897707, SRR9897708, SRR9897709, SRR9897710, SRR9897711, SRR9897712, SRR9897713, SRR9897714, SRR9897715, SRR9897716, SRR9897717, SRR9897718, SRR9897719, SRR9897720, SRR9897721 and SRR9897722.

Antedon mediterranea

SRR6650067.

Apostichopus japonicus

ERR1193930, ERR1193931, ERR1193932, SRR166825, SRR414926, SRR414927, SRR414929, SRR414930, SRR771602, SRR771603, SRR771604, SRR771605, SRR771606, SRR863579, SRR934650, SRR934651, SRR1002331, SRR1002332, SRR1002333, SRR1657913, SRR1657914, SRR1657915, SRR1657916, SRR1657917, SRR1657918, SRR1657919, SRR1657920, SRR1657921, SRR1657922, SRR1657923, SRR1657924, SRR1657925, SRR1663411, SRR1663428, SRR1663429, SRR1663431, SRR1663432, SRR1663433, SRR1663436, SRR1663437, SRR1663438, SRR1663439, SRR1663440, SRR2006096, SRR2006097, SRR2006098, SRR2006099, SRR2006100, SRR2006101, SRR2006102, SRR2006103, SRR2006104, SRR2010219, SRR2012319, SRR2012383, SRR2012397, SRR2012405, SRR2014140, SRR2014144, SRR2014145, SRR2014150, SRR2014151, SRR2014153, SRR2014166, SRR2034609, SRR2089767, SRR2128001, SRR2128002, SRR5083072, SRR5083073, SRR5083074, SRR5083075, SRR5083077, SRR5083078, SRR5083079, SRR5083080, SRR5083082, SRR5083083, SRR5083084, SRR5083085, SRR5083086, SRR5083087, SRR5083088, SRR5817185, SRR5817186, SRR5817187, SRR5817188, SRR5817189, SRR5817191, SRR5817192, SRR5817193, SRR5817194, SRR5817195, SRR5817196, SRR5817197, SRR5817198, SRR5817199, SRR5817200, SRR5817201, SRR5817202, SRR5817203, SRR5817204, SRR5817205, SRR5817287, SRR5817295, SRR5839517, SRR5839518, SRR5839536, SRR5839538, SRR5839540, SRR5839546, SRR5839650, SRR5839684, SRR5839694, SRR5839713, SRR5839720, SRR5839725, SRR5839728, SRR5839730, SRR5839731, SRR5839732, SRR5839733, SRR5839734, SRR5839798, SRR5839799, SRR5839800, SRR5839801, SRR5839814, SRR5839840, SRR5839889, SRR5839890, SRR5839891, SRR5839892, SRR5839893, SRR5839897, SRR5839899, SRR5839900, SRR5839901, SRR5839902, SRR5839903, SRR5839904, SRR5839949, SRR5839950, SRR5839951, SRR5839952, SRR5839953, SRR5839954, SRR5840021, SRR5840022, SRR5840023, SRR5840024, SRR5840025, SRR5840027, SRR6004440, SRR6004441, SRR6004442, SRR6004443, SRR6004444, SRR6004445, SRR6004446, SRR6004447, SRR6004448, SRR6075435, SRR6075436, SRR6075437, SRR6075438, SRR6378158, SRR6856564, SRR6856565, SRR6856566, SRR6856567, SRR6856568, SRR6856569, SRR8258074, SRR8258075, SRR8258076, SRR8258077, SRR8258078, SRR8258079, SRR8258080, SRR8258081, SRR8258082, SRR8279868, SRR8801559, SRR8801560, SRR8801561, SRR8801562, SRR8801563, SRR8801564, SRR8801565, SRR8801566, SRR8801567, SRR9670443, SRR9670444, SRR9670445, SRR9670446, SRR9670447, SRR9670448, SRR9670449, SRR9670450, SRR9670451, SRR9670452, SRR9670453, SRR9670454, SRR9670455, SRR9670456, SRR9670457, SRR9670458, SRR9670459, SRR9670460, SRR9670461, SRR9670462, SRR9670463, SRR9670464, SRR9670465, SRR9670466, SRR9670467, SRR9670468, SRR9670469, SRR9670470, SRR9670471, SRR9670472, SRR9670473, SRR9670474, SRR9670475, SRR9670476, SRR9670477, SRR9670478, SRR9670479, SRR9670480, SRR9670481, SRR9670482, SRR9670483, SRR9670484, SRR9670485, SRR9670486, SRR9670487, SRR9670488, SRR9670489, SRR9670490, SRR11793939, SRR11793942, SRR11793943, SRR11793944, SRR12505006, SRR12505011, SRR12505013, SRR12505016, SRR12505017, SRR12830751 and SRR12830752.

Asterias rubens

SRR3087891.

Florometra serratissima

SRR3097584.

Holothuria scabra

SRR9125585.

Holothuria arguensis

SRR8889053, SRR8892978, SRR8893063, SRR8896868, SRR8896869, SRR8898365, SRR8898366, SRR8906597 and SRR8906598.

Lytechinus variegatus

SRR1139214, SRR1661401, SRR1661399, SRR1661397, SRR1661409, SRR1661406, SRR1661395, SRR1661363, SRR1661081, SRR1661075, SRR1661113, SRR1660833, SRR1661077, SRR1661079, SRR1660831, SRR1661112, SRR1661111, SRR1661090, SRR9673387, SRR9673388, SRR9673385, SRR9673386, SRR9673383, SRR9673384, SRR9673381, SRR9673382, SRR9673389, SRR9673390, SRR9673407, SRR9673408, SRR9673409, SRR9673410, SRR9673403, SRR9673404, SRR9673405, SRR9673406, SRR9673401, SRR9673402, SRR9673391, SRR9673392, SRR9673393, SRR9673394, SRR9673395, SRR9673396, SRR9673397, SRR9673398, SRR9673399, SRR9673400, SRR9673379, SRR9673380, SRR9673377, SRR9673378, SRR9673375 and SRR9673376.

Mesocentrotus nudus

SRR6438347, SRR6438348, SRR6438349, SRR6438350, SRR6438351 and SRR6438352.

Oligometra serripinna

SRR2845424.

Ophioderma brevispina

SRR10742213.

Patiria miniata

SRR1138704, SRR1138705, SRR1138706, SRR1138707, SRR1138708, SRR1139189, SRR1139190, SRR1139191, SRR1139193, SRR1139194, SRR1139195, SRR1139196, SRR1139197, SRR1139198, SRR1139199, SRR1139201, SRR1139214, SRR1139215, SRR1139455, SRR2454338, SRR5398132, SRR5398133, SRR5398134, SRR5398135, SRR5398136, SRR5398137, SRR5398138, SRR5398139, SRR5398140, SRR5398141, SRR5398142, SRR5398143, SRR5398144, SRR5398145, SRR5398146, SRR5398147, SRR5398148, SRR5398149, SRR5986254, SRR6054712, SRR8580044, SRR8580045, SRR8580046, SRR8580047, SRR8580048, SRR8580049, SRR8580050, SRR8580051, SRR8580052, SRR8580053, SRR8580054, SRR8580055, SRR8580056, SRR8580057, SRR8580058, SRR8580059, SRR8580060, SRR8580061, SRR8580062, SRR8580063, SRR8580064, SRR8580065, SRR8580066, SRR8926376, SRR8926377, SRR12983012, SRR12983013, SRR12983014, SRR12983015, SRR12983016, SRR12983017, SRR12983018, SRR12983019, SRR12983020, SRR12983021, SRR12983022, SRR12983023, SRR12983024, SRR12983025, SRR12983026, SRR12983027, SRR12983028, SRR12983029, SRR12983030, SRR12983031, SRR12983032, SRR12983033, SRR12983034, SRR12983035 and SRR12983036.

Patiria pectinifera

SRR1139200, SRR1141045, SRR5229423, SRR5229424, SRR5229425, SRR5229426, SRR5229427, SRR5229428, SRR8627925 and SRR8627926.

Pisaster ochraceus

SRR1139197, SRR2846074, SRR10982207, SRR10982208, SRR10982209, SRR10982210, SRR10982211, SRR10982212, SRR10982213, SRR10982214, SRR10982215, SRR10982216, SRR10982217, SRR10982218, SRR10982219, SRR10982220, SRR10982221, SRR10982222, SRR10982223, SRR10982224, SRR10982225, SRR10982226, SRR10982227, SRR10982228, SRR10982229, SRR10982230, SRR10982231, SRR10982232, SRR10982233, SRR10982234, SRR10982235, SRR10982236, SRR10982237, SRR10982238, SRR10982239, SRR10982240, SRR10982241, SRR10982242, SRR10982243, SRR10982244, SRR10982245, SRR10982246, SRR10982247, SRR10982248, SRR10982249, SRR10982250, SRR10982251, SRR10982252, SRR10982253, SRR10982254, SRR10982255, SRR10982256, SRR11293187 and SRR11293188.

Ptychodera flava

SRR1029584, SRR2033704, SRR2033705, SRR2033710, SRR2033711, SRR2033712, SRR2033714, SRR2033715, SRR2033716, SRR2033717, SRR2033718, SRR2033719, SRR2033720, SRR2033721, SRR2033722, SRR2033723, SRR2033724, SRR2033725, SRR2033726, SRR2033727, SRR2033728, SRR2033729, SRR2033730, SRR2033731, SRR2033732, SRR2033733, SRR2033734, SRR2033735, SRR2033736, SRR2033737, SRR2033738, SRR2033739, SRR2033740, SRR2033741, SRR2033742, SRR2033743, SRR2033744, SRR2033745, SRR2033746, SRR2079098, SRR2079099, SRR2079100, SRR2079101, SRR2079102, SRR2079103, SRR2079104, SRR2079105, SRR2079106, SRR2079107, SRR2079108, SRR2079109, SRR2079110, SRR2079111, SRR2079112, SRR2079113, SRR2079114, SRR2079115, SRR2079116, SRR2079117, SRR2079118, SRR2079119, SRR2079120, SRR2079121, SRR2079122, SRR2079123, SRR2079124, SRR2079125, SRR2079126, SRR2079127, SRR2079128, SRR2079129, SRR2079130, SRR2079131, SRR2079132, SRR2079133, SRR12736734, SRR12736735, SRR12736736, SRR12736737, SRR12736738, SRR12736739, SRR12736740, SRR12736741, SRR12736742, SRR12736743, SRR12736744, SRR12736745, SRR12736746, SRR12736747, SRR12736748, SRR12736749, SRR12736750, SRR12736751, SRR12736752, SRR12736753, SRR12736754, SRR12736755, SRR12736756, SRR12736757, SRR12736758, SRR12736759, SRR12736760, SRR12736761, SRR12736762, SRR12736763, SRR12736764, SRR12736765, SRR12736766, SRR12736767, SRR12736769, SRR12736770, SRR12736771, SRR12736772, SRR12736773, SRR12736774, SRR12736775, SRR12736776, SRR12736777, SRR12736778, SRR12736779, SRR12736780, SRR12736781, SRR12736782, SRR12736783 and SRR12736784.

Saccoglossus kovalewskii

SRR071700, SRR071701, SRR071702, SRR071703, SRR071704, SRR071705, SRR071706, SRR071707, SRR071708, SRR071709, SRR071710, SRR071711, SRR071712, SRR071713, SRR071714, SRR071715, SRR071716, SRR071717, SRR071718, SRR071719, SRR071720, SRR071721 and SRR071722.

Schizocardium californicum

SRR2921981 and SRR2922012.

Strongylocentrotus purpuratus

SRR409091, SRR409092, SRR409093, SRR409094, SRR409095, SRR409096, SRR505583, SRR505584, SRR505585, SRR505586, SRR505587, SRR505588, SRR505589, SRR531843, SRR531853, SRR531860, SRR531948, SRR531949, SRR531950, SRR531951, SRR531952, SRR531953, SRR531954, SRR531955, SRR531956, SRR531957, SRR531958, SRR531964, SRR531996, SRR532046, SRR532055, SRR532074, SRR532121, SRR532143, SRR532151, SRR533746, SRR1012313, SRR1012339, SRR1012340, SRR1012342, SRR1012401, SRR1012403, SRR1041572, SRR1041901, SRR1042009, SRR1043060, SRR1043069, SRR1139792, SRR1765910, SRR1765938, SRR1765978, SRR1765979, SRR1765980, SRR1765981, SRR1765982, SRR1765983, SRR1765984, SRR1765986, SRR1765988, SRR1765991, SRR2080791, SRR2080792, SRR2080793, SRR2080794, SRR2080795, SRR2080796, SRR2080797, SRR2080798, SRR2080799, SRR2080800, SRR2080801, SRR2080802, SRR2080803, SRR2080804, SRR2080805, SRR2080806, SRR2080807, SRR2080808, SRR2080809, SRR2080810, SRR2080811, SRR2080812, SRR2080813, SRR2080814, SRR2080815, SRR2080816, SRR2080817, SRR2080818, SRR2080819, SRR2080820, SRR2080821, SRR2080822, SRR2080823, SRR2080824, SRR2080825,

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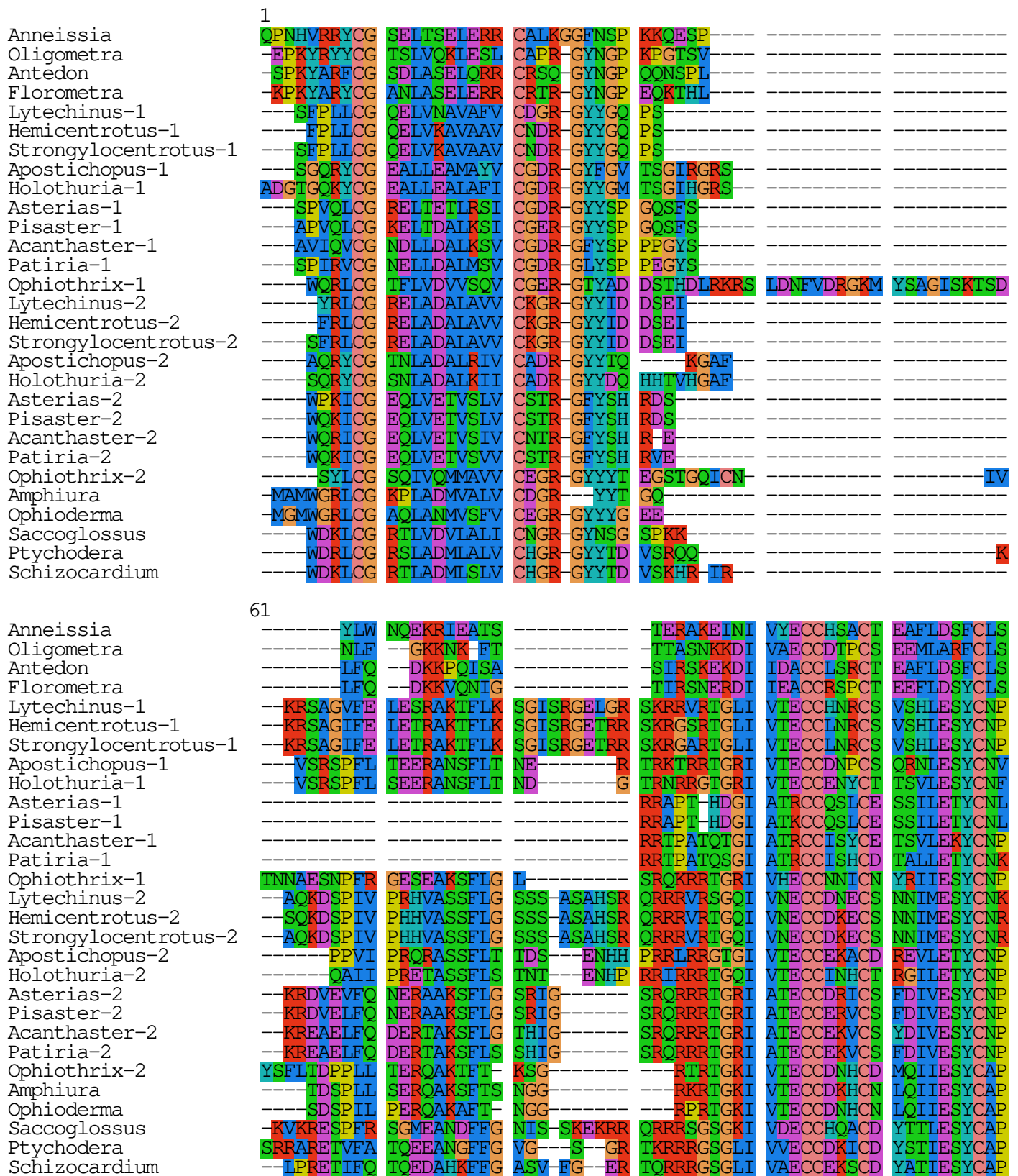


Figure S1. Sequences alignment of ambulacrarian IGFs. In order to illustrate the sequence similarities in the putative D- and E- domains of these molecules Seaview¹ was used.

¹ Gouy M, Guindon S, Gascuel O. 2010. SeaView version 4: A multiplatform graphical user interface for sequence alignment and phylogenetic tree building. Mol Biol Evol. 27:221-4. doi: 10.1093/molbev/msp259.

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Anneissia	SNKDEDLIVE	SDIV	ETTTITG	KRRKPTRKPK	N-PLKS	
Oligometra	PIPKDNLIVE	SEIM	ETTTIVN	TKKQRTKKP	K-PTRK	
Antedon	SNPEDDLIVE	SETI	ETTTIVG	SKKQLTKKP	K-TTRK	
Florometra	STPVDDITAE	LEIV	ETTTLIG	SKKPRTKKPK	S-DRRK	
Lytechinus-1	LPODAV	H	DPE	VH	IRLEK	SAEEDAD
Hemicentrotus-1	LQDAV	H	DAE	VH	IRLEK	SAEEDADET
Strongylocentrotus-1	LPPDAV	H	DAE	VH	IRLEK	SAEEDAD
Apostichopus-1	ATTQITEIPT	ELIT	EGT	TTEPA	ASPRRNSR	NIEADG TA
Holothuria-1	AT	ELPT	ERT	TTEPS	ASPRRNSR	HAGADI TP
Asterias-1	PAPPSQIOPS	TAAP	ITT	TKMAP	LTE-DRRTK	DVVVDY S
Pisaster-1	PAASQOTI	QASS	AAP	TKMAP	LTE-DRRTK	EVVVDY S
Acanthaster-1	PSTSQSQTA		AAP	PRITI	TPD-ERRAN	EIVVDE I
Patiria-1	PATPOSQIA		AAP	QRITS	TSD-DRRAN	EIVVDP P
Ophiothrix-1	WPLITI	L	ATI	TQSPE	PLPNEQ	EG GYLIDEIQMK
Lytechinus-2	RIPEVPS	ESAI	SEI		P	SG DRTEDSTVRI
Hemicentrotus-2	RIPEVPP	ESAI	SEN		P	SE EITEDSTLRI
Strongylocentrotus-2	RIPEVPP	ESAI	SEN		P	SE EITEDSTLRI
Apostichopus-2	HVTPTLALAS	LV	TSLM-TK	SPTPPSSEPS	SSSSSSSSSR	N-EDKFPMT
Holothuria-2	RVILEPIRPA	VISL	SPLN-PR	SOEPSGVQPO	ESPEEVHQN	S-RDNYPMG
Asterias-2	WPVAIE	S	RDP	PL-SP	VAPGRVREDK	SADVDMYNP
Pisaster-2	WPV-VE	S	RDV	SL-SP	VAPGRVREDK	SADVDMYNP
Acanthaster-2	WPVVED	R	DDP	ML-AP	VAPGRVRODK	SADADLLLRP
Patiria-2	WPVVED	R	DDP	MLIAP	VAPGRVRODK	SADADLLLM
Ophiothrix-2	LOEGQVKFTS	RNLD	FVNEAN-NV	VEEPSVRVPO	QVE-EN	KIVEETVPYV
Amphiura	LPEGQIRIQL	RHWFLLHEKEK	ESANEEN-NT	VEELPPPPPP	R	SE ERDEEQVPDV
Ophioderma	LPEGQIRGPE	RHEFLHEKER	ETIIDQN-NR	VEPPPLV-AE	E	AI VEEETVPVI
Saccoglossus	LPEGVVA	DDSL	KRF		L	SO SFGNDFKDTA
Ptychodera	WPKDIDP	AKKI	EGF		K	EG TWEEDY
Schizocardium	WPKDMDP	ALRE	AGF		K	YG SWEDEDY

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Anneissia	RK	KPKGSS			E INSE	Q SA	SNTE	
Oligometra	SGR	KNKDDP			D TSE	E SA	SNKD	
Antedon	SGK					SE	KNRD	
Florometra	DGR	KSKGGS			D MSD	D SA	SNRD	
Lytechinus-1	EGRPO	DG PS		OL	D			
Hemicentrotus-1	OGRPO	DG PS		OL	D			
Strongylocentrotus-1	EGRPO	DG PS		OL	D			
Apostichopus-1	AAA GGGSG	QGNRGRKKGK		RHGK	G NRRE	Q DQ	TV	
Holothuria-1	DGE TPR-Q	SNNGRNRGNP		RHSE	D N	P ED	NI	
Asterias-1	DQL AIEG	SQMSRVGVL	THDI		VI NRSKI-TTES	NE	GSYDNE	
Pisaster-1	DQL VIEG	SQMSRVDGAL	TQDI		VI NRSKSATTES	NE	GSYDNE	
Acanthaster-1	GQT GNIN	SQMLRGGNAM	GAGS		RA NGTKAPTEV	VD	GRSDDD	
Patiria-1	SGH TGDI	APRGESAKAP	GPSG		AA NATKIPVAEV	DE	GMSVDE	
Ophiothrix-1	HIT RQIE	D NS		V	D LLSE	G SD	LR	
Lytechinus-2	NDQSTERRID	DI DD	AT NLEVPSPDAD	APDA	T ATSDVERPLP	EE	TTAV	
Hemicentrotus-2	DGDSTEIRID	NINP	AT NLEVPSPEAN	APDA	T ATSDVEQSR	DN	TTAV	
Strongylocentrotus-2	DGESTEIRID	TNP	AT NLEVPSPDAN	TPDA	T ATSDVEQPRS	DN	TTAV	
Apostichopus-2	DNA LGEDY	EGPTNEGPL	TSGEPTPTEN	RIS	N GPRG	P SS	NASS	
Holothuria-2	DNV VREDY	EPPTINGGAL	TSGQPTPTEN	RIS	S GLRE	H SN	T-SI	
Asterias-2	DVV DVEEA	NS		VI	Q R	E ED	LI	
Pisaster-2	NAA DVEEA	NS		VI	Q R	E ED	LI	
Acanthaster-2	DIA EISE	DK SS		LI	R QAAE	K DE	PI	
Patiria-2	QEA AAGEQ	FAEE NS		LI	R Q	E EE	LI	
Ophiothrix-2	SQA IVGET	ISD	G FDWSDVSEI	HNILNGGGDM	YINDQPRDDP	S	ENDE	
Amphiura	SQD IIE	S D	HDWEDSIESE	TLINEAIVM	L-ADAPLIEQ		NTEE	
Ophioderma	NOE LVD-T	ISD	Q IDLEDSESE	TNLLNDALLM	L-SDQVRENS		EORIGTEEE	
Saccoglossus	NEDKLEI-VI	VVRP	SH		DE	M DGTE	TRI ED	NEHV
Ptychodera	HRKYHP-ES	VEQP	NA	NPEEPTPEPT	TIDL	D KSL	SES RD	NVDI
Schizocardium	YRKYHP-EE	FTQP	DL	TIWIASTDSA	NHDE	H FTTA	TPS E	

Figure S1-continued.

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Anneissia	---	KKN	---	---	---	KPT	---	---	RRPKRWDS	ET
Oligometra	---	NKN	---	---	---	KPT	---	---	RRPKRWDS	ET
Antedon	---	KKN	---	---	---	KPT	---	---	RRPKRWDS	ET
Florometra	---	KKN	---	---	---	KPT	---	---	RRPKRWDS	ET
Lytechinus-1	---	A-RREER	RRNRE-RSSG	GKSRSGRRKN	K	D	ND	RS	SRAKRQGLTL	
Hemicentrotus-1	---	A-RREER	RRNRE-RSSG	GRSRSGRRKD	K	D	ND	RA	SRAKRHGLNM	
Strongylocentrotus-1	---	A-RREER	RRNRE-RSSG	GRSRSGRRKD	K	D	ND	RA	SRAKRHGLNL	
Apostichopus-1	---	EVSSTDGL	-SREKSGSG	GGRNRG-N					GKGGKGSQR	
Holothuria-1	---	AATATEGA	-DRSSGSRGG	RGSNHQ-TGR	G	S	DRGSSRSNG		GKGGKGNRQD	
Asterias-1	---	SSSSRREK	RRRRO		RH	RERELREQRK	QSN	SKRKS	KDGKDHVS	
Pisaster-1	---	SSSSRREAK	RRRRO		RH	RERELREQRK	QSN	SKRKT	KDGKDHSA	
Acanthaster-1	---	LSSEKREDA	TRKLR		RK	EQLSRKQP	HS	NKRKS	KLE-KKGSE	
Patiria-1	---	LSIERKKDDA	TRRRR		K	EQLLRKQOO	SNS	SKRRT	KLE-KKGSE	
Ophiothrix-1	---	---	---	---	---	---	---	---	---	---
Lytechinus-2	---	KKRLESA	ERNR	GTDHMLSE	DSTLLAREPL	GID	VR		KRFH	
Hemicentrotus-2	---	KKRLESA	ERNR	GTDHMLSE	DSTLLAREPL	GID	VR		KRFH	
Strongylocentrotus-2	---	KKRLESA	ERNR	GTDHMLSE	DSTLLAREPL	GID	VR		KRFH	
Apostichopus-2	---	EEPAAGLNPT	EQOEDGGGGG	GGGGGGGGG	G	EPR	NNSNSDQPRN		NRGKVNESQR	
Holothuria-2	---	RGORINIK	-KOKSGERGS	ANPNPTRGGD	R	EPT	D	NEQSR	NRGKVNESQR	
Asterias-2	---	G-KSEGK	NKRRSGSREG	GRSSRRSRGK	S	S	RS	KK	QRDGRERSKR	
Pisaster-2	---	G-KSEGK	NKRRSGSREG	GRSSRRSRGK	S	S	RS	KK	QRDGRERSKR	
Acanthaster-2	---	G-KSEGK	SKRKS	GRSFRR-RGK	N	S	RR	KK	GRDGRERSKR	
Patiria-2	---	G-KSEGK	SRKKS	DRSSRR-RGK	S	S	RR	KK	GRDGRERSKR	
Ophiothrix-2	---	K-PKKNKNKH	DRRRKGRHG	GD	RD	DST	OPT			
Amphiura	---	K-SKNK	K	NRRRKN	R	HG	ED	DFI	OPT	
Ophioderma	---	K-PKHK	K	NRRRKP	K	HE	QD	DYT	OPT	
Saccoglossus	---	GTRKTKL	RHVVKVSKST	PI-QOI	E	TTTTM	KPF	FDV	D-ID	IIFYRFVNKT
Ptychodera	---	KSRAKSK	NSTKVKPT	-YVSSMTSD		EETLT	RPO	GDE	ARRET	DATRKIEDSS
Schizocardium	---	KSRTKKG	NNTKSKSIIIG	KLVENM				E	TESPT	NWQRDGTDER

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Anneissia	---	TTLSDFLFSQ	RFLQRAYDS	ID	VDEI	TTEFGVPEE	DISSSLSEEE	LSSNQVKSDD		
Oligometra	---	TTLSEF	---	LQDIYNSD	FADLSNIDKI	KTFGDTIPEG	DPSSSVSQEE	SSSNEVIPDA		
Antedon	---	STLSDFLLSQ	KLLQEIYDS	IDDRS	IDDI	ITQFDALPED	DLSSSLSQEE	SSSNEVIOEA		
Florometra	---	TTLSDFLLSQ	RFLQGVYDS	IGDQSTLDEL		APRFDAVQEG	DTSYSLSQE	SSSNEVISEA		
Lytechinus-1	---	WRN	MFSQ	KALSN						
Hemicentrotus-1	---	WRN	MFSQ	KGFNS						
Strongylocentrotus-1	---	WRN	MFSQ	KEFSD						
Apostichopus-1	---	REQSEELTVE		TTTG	CASQDQGN		CEESNAN	AGGAS		
Holothuria-1	---	RNQIDEDAER	NISSE	NGHG	SRQGGGG		EGEERN	NGGSSQGGT	SNSNIGIGNS	
Asterias-1	---	AATTP LAVQ					E-RPLK	NGGRNSTSGE	HS	SVN
Pisaster-1	---	AVTTP LAVQ					EP IHPLK	NGGRNSTSGE	LS	SVN
Acanthaster-1	---	SVTTP VAVQ					TADHPFK	HGAYNSTIGD	LS	LVN
Patiria-1	---	VITPV AIE					TAEHPFK	NGGYNSTSGD	LS	PVN
Ophiothrix-1	---	---	---	---	---	---	---	---	---	---
Lytechinus-2	---	HT	P	RSSRE		QAST	ATHSD	DD	PAT	SRQE
Hemicentrotus-2	---	HT	P	RSSRE		QAST	ATHALD	DD	SAT	SRQE
Strongylocentrotus-2	---	HT	P	RSSRE		QAST	ATHALD	DD	PAT	SRQE
Apostichopus-2	---	HPN								
Holothuria-2	---	PAE								
Asterias-2	---	WEG	LDTS	HPVKEPTARS	V	I GR		VDTRPFRNFL		YNRYTVDE
Pisaster-2	---	WEG	LDTS	HPEKEPAARS	V	FGG		IDTRPFRNFL		YNRYTVDE
Acanthaster-2	---	WEA	LVTS	HPPTKD IVDA	LR	SALRA		AGRSPSRVA		GSFAPDE
Patiria-2	---	WEG	LVTS	HPPTKEIVDA	LR	SALRA		AGRTPSLFAP		ANNFLLE
Ophiothrix-2	---	DEFITDIEVP	HPRIQAVAGM	PSSRSEPA			NIDDPD	PGTRSERSFV		
Amphiura	---	DELITDIEVM	HPQARVVSRS	EPVH			AVDDPD	PGSRERSFV		
Ophioderma	---	DQLITDIEVL	HPQOVVNAE	SPSRSEAG			NLDEAD	AGRSERSFV		
Saccoglossus	---	WRVIEE	P	EIMV		G GK		SESSRE	SDIDSSI	
Ptychodera	---	WWMVDN	R	EFEY		EGR		DRHNKS	KTRK	GGNAT
Schizocardium	---	WWTIVED	P	HFQI		GET		DENSSN	DKKINGNGT	

Figure S1-continued.

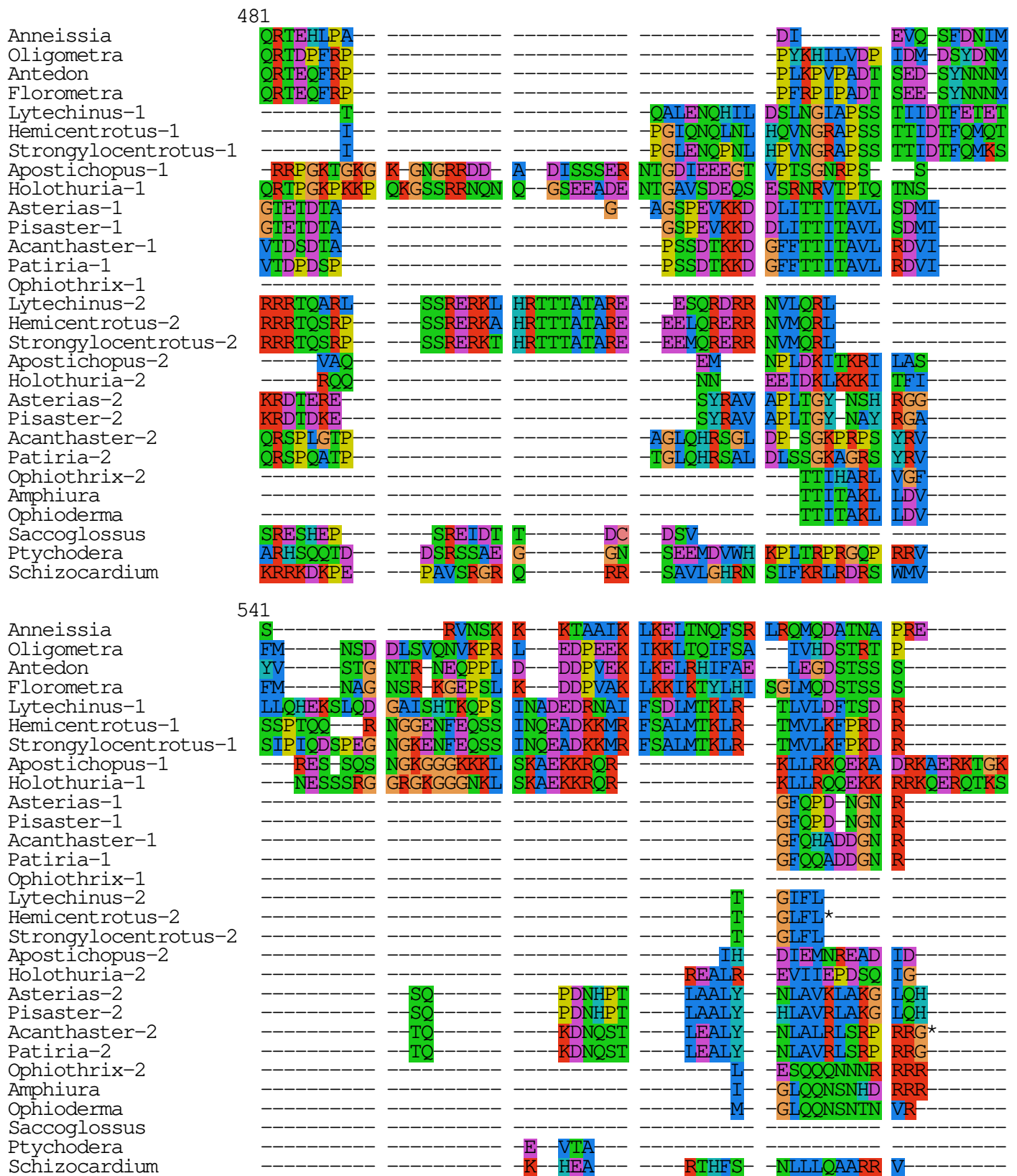


Figure S1-continued.

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Anneissia	-----	-----	-----	-----	-----	-----
Oligometra	-----	-----	-----	-----	-----	-----
Antedon	-----	-----	-----	-----	-----	-----
Florometra	-----	-----	-----	-----	-----	-----
Lytechinus-1	-----	-----	-----	-----	-----	-----
Hemicentrotus-1	-----	-----	-----	-----	-----	-----
Strongylocentrotus-1	-----	-----	-----	-----	-----	-----
Apostichopus-1	SKKSKSKNKN	ROTKGDRERR	ITVRWNSNDE	RSRROVPRDS	FSSVNGKYNS	GHPYRRVYSM
Holothuria-1	SKK---GKKG	SRTQGERERR	ITVRWNDGEE	RSRRHVPREQ	FSPNNPRTTY	HTDSR-TSLF
Asterias-1	-----	-----	-----	-----	-----	-----
Pisaster-1	-----	-----	-----	-----	-----	-----
Acanthaster-1	-----	-----	-----	-----	-----	-----
Patiria-1	-----	-----	-----	-----	-----	-----
Ophiothrix-1	-----	-----	-----	-----	-----	-----
Lytechinus-2	-----	-----	-----	-----	-----	-----
Hemicentrotus-2	-----	-----	-----	-----	-----	-----
Strongylocentrotus-2	-----	-----	-----	-----	-----	-----
Apostichopus-2	-----	-----	-----	-----	-----	-----
Holothuria-2	-----	-----	-----	-----	-----	-----
Asterias-2	-----	-----	-----	-----	-----	-----
Pisaster-2	-----	-----	-----	-----	-----	-----
Acanthaster-2	-----	-----	-----	-----	-----	-----
Patiria-2	-----	-----	-----	-----	-----	-----
Ophiothrix-2	-----	-----	-----	-----	-----	-----
Amphiura	-----	-----	-----	-----	-----	-----
Ophioderma	-----	-----	-----	-----	-----	-----
Saccoglossus	-----	-----	-----	-----	-----	-----
Ptychodera	-----	-----	-----	-----	-----	-----
Schizocardium	-----	-----	-----	-----	-----	-----

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Anneissia	-----	-----	-----	-----
Oligometra	-----	-----	-----	-----
Antedon	-----	-----	-----	-----
Florometra	-----	-----	-----	-----
Lytechinus-1	-----	-----	-----	-----
Hemicentrotus-1	-----	-----	-----	-----
Strongylocentrotus-1	-----	-----	-----	-----
Apostichopus-1	DPRRTAA-H	FRSKPKSVRO	IRRRPSSSSP	RKVEIKAR
Holothuria-1	DQTRTSKIDQ	HRGKHKMSR	NGKQLSRTRS	KSSLLKPR
Asterias-1	-----	-----	-----	-----
Pisaster-1	-----	-----	-----	-----
Acanthaster-1	-----	-----	-----	-----
Patiria-1	-----	-----	-----	-----
Ophiothrix-1	-----	-----	-----	-----
Lytechinus-2	-----	-----	-----	-----
Hemicentrotus-2	-----	-----	-----	-----
Strongylocentrotus-2	-----	-----	-----	-----
Apostichopus-2	-----	-----	-----	-----
Holothuria-2	-----	-----	-----	-----
Asterias-2	-----	-----	-----	-----
Pisaster-2	-----	-----	-----	-----
Acanthaster-2	-----	-----	-----	-----
Patiria-2	-----	-----	-----	-----
Ophiothrix-2	-----	-----	-----	-----
Amphiura	-----	-----	-----	-----
Ophioderma	-----	-----	-----	-----
Saccoglossus	-----	-----	-----	-----
Ptychodera	-----	-----	-----	-----
Schizocardium	-----	-----	-----	-----

Figure S1-continued.

IGF

0.2

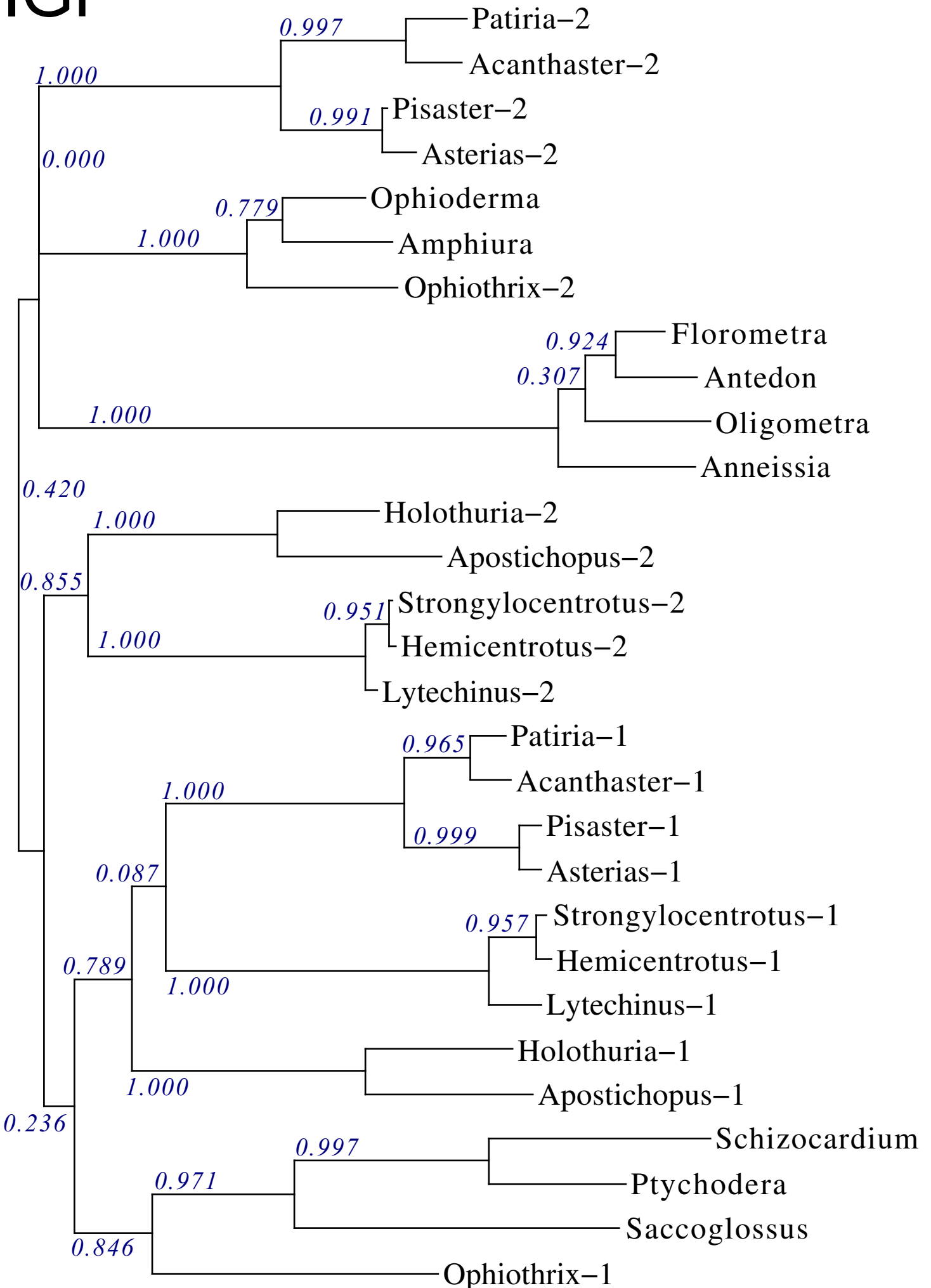


Figure S2. Sequence similarity tree of ambulacrarian IGFs.

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Lytechinus      --QHLTRVRLCGLEFARAVYNHCSRASKRSDPGTISDIPLADRYLAR
Hemicentrotus  --QQGPRNRYCGLEFARAVFSQSMANKRSDPGAVAESASAARYLAR
Strongylocentrotus --QQGPRNRYCGLEFARAVFTQSMANKRSDPGAVAESASAARYLAR
Apostichopus-1  -----IRLCGPDLSRAVYQICSHG-KRGYIPTFNS--E-----
Holothuria-1    -----VRLCGADLSRAVYRVCSHG-KRGYPMADL----E-----
Apostichopus-2  ----WSHQRLCGPDLVHALSLVGERG---YFGGSRLVER---D-VQ
Holothuria-2    -----HKLCGPALVDALAVVCRGRG---YGGTVSRTK---REAS
Asterias-1      -----AEKYCDEFHMAVYRTTEH-KRS-GRSAFSL--N-----
Pisaster-1      -----AEKYCDEFHMAVYRTCAEH-KRS-GRSTYSL--N-----
Acanthaster1    -----EKFCDNDFHLAVYQTSTH-KRGDGEPVLSL--K-----
Patiria-1       -----EKYCDDDFHMAVVRTCAVS-KRS--QPGMSL--S-----
Asterias-2      RSDHASVKHFCGLEFSYAVVTAGEA-KRS-IRSAFFF-----
Pisaster-2      SNDHGRVKQYCGLEFSYAVVTACAEA-KRS-IRSAFFY-----
Acanthaster-2   ---DSSSKHCGSAFPQFVWTASMA-KRS-NRSPRSL--D-----
Patiria-2       ---TETNRHCGAAFPDEFVLAACSMA-KRS-IRSSPSL--H-----
Ophiothrix-1   --DSARYQPLCGREFTRAVMEICATQVKRTEPLFQRFYNAN-----
Ophiothrix-2   ---QDSYKSCGREFTRRVMEVCATHVKRTEHF-----
Amphiura        ----DSAKYCGLAFSRAVMEICARQVKRTAPLWERLYTAS-----
Ophioderma     ----DSATYCGVAFSMAVYETCSMQVKRTDPVRQRLYSAA-----

Lytechinus      DTGYGQVQDTPFEWYDVAGQAEERLRP-----SL---SDIIFA
Hemicentrotus  DTGYEQAEDMPLEWYDIARQGAERLRP-----SL---TDIIFS
Strongylocentrotus DTGYEQAEDMPLEWYDVARQGAERLRP-----SL---TDIIFS
Apostichopus-1 DDQLNQEFGTDL-----EEYLAETIKEYLKPNLSLYDDVERELYPSLP
Holothuria-1   EEDFSQELDTEV-----DEFLAQALTGFLASRSFAADMESDRYITLP
Apostichopus-2 DDGLDEEITTLV-----VGAERT-----SILECLK--AWSFPF
Holothuria-2   QDKLDV-----HA--GGSMTH
Asterias-1     D--F-----FRS-NSKRTAGSPRP--DDDFFL
Pisaster-1     D--LLSMD-----SFRS-SPKRKAGSPLR--DDNSFL
Acanthaster1   D--VLTGS-----RLRG-NIKRSFGSTLE--DEAFFA
Patiria-1      D--VLTMN-----RFRGHNIKRSIDSTLE--DNAFFM
Asterias-2     D--MFPVF-----KSPE-----RIPAD--FDDSSM
Pisaster-2     D--MFPVF-----KSQE-----RIPAD--FDDSSM
Acanthaster-2 D--LLETf-----KSAR-----HLDIS--Y--RTP
Patiria-2      D--LLQAF-----KSDE-----YQANR--Y--TSP
Ophiothrix-1   ---LVKRSIDPAFWNNLLEANP-----DLMD-
Ophiothrix-2   ---MVKRSIDDEFWNDLMESGL-----GL-
Amphiura       ---RVKRFSDFEFWNAVLESDS-----DISM-
Ophioderma     ---RVRRFADPDFWEAVFNDS-----NNVM-

Lytechinus      PRYRRSLFARPNTPMGRHCCVTGCTSQELASVC-----
Hemicentrotus  SFRRSIQNRRLQPMGQLCCVYGCTLVELASVC-----
Strongylocentrotus SFRRSIHNRGQLPMGQLCCVYGCTLVELASVC-----
Apostichopus-1  RG---FRRVTRTGGIARRCCSTGSSSDIAKLC-----
Holothuria-1    QR---FRRNA-RGGGIARRCCASGSSSDIAKLC-----
Apostichopus-2  -----RRRTRGIVEECCFRRCTWENLESYCSKTTAYKKADNMI
Holothuria-2    -----VRFTRGIVEDCCFKGCTWSYLENYCLLS-----
Asterias-1      TM---QKRPETYVGMGSYCCLVGCTRDQLSQVC-----
Pisaster-1      AL---QKRTETYVGMGSFCCLVGCTTEQLSQVC-----
Acanthaster1    SR---LVKRSEYDGIASYCCIHGCTPSELAVC-----
Patiria-1       SG---LEKRSEYTGIASYCCLHGCTPSELSVVC-----
Asterias-2      IH---VRKRQDYQGMATYCCTNGCTISQLTSNGIC-----
Pisaster-2      IH---VRKRQDYQGMATYCCTNGCTISQLTSNGIC-----
Acanthaster-2   IR---LSKRQDYDGMADYCCIIGCTNELIASGIC-----
Patiria-2       IH---LRKREEYMTIADYCCSVGCTSPDLVASGIC-----
Ophiothrix-1    ---KRQSSAGVMATHCCQSGCTSQEISMVC-----
Ophiothrix-2    ---DKR--SETGMAEHCCQNGCTDQEISMVC-----
Amphiura        ---DKRQPAGVGMATYCCNHGCTDTELSLVC-----
Ophioderma     ---DKRQTAMGMAQYCCSHGCTPQELSLVC-----

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Figure S3. Sequence alignment of ambulacrarian GSSs.

GSS

0.5

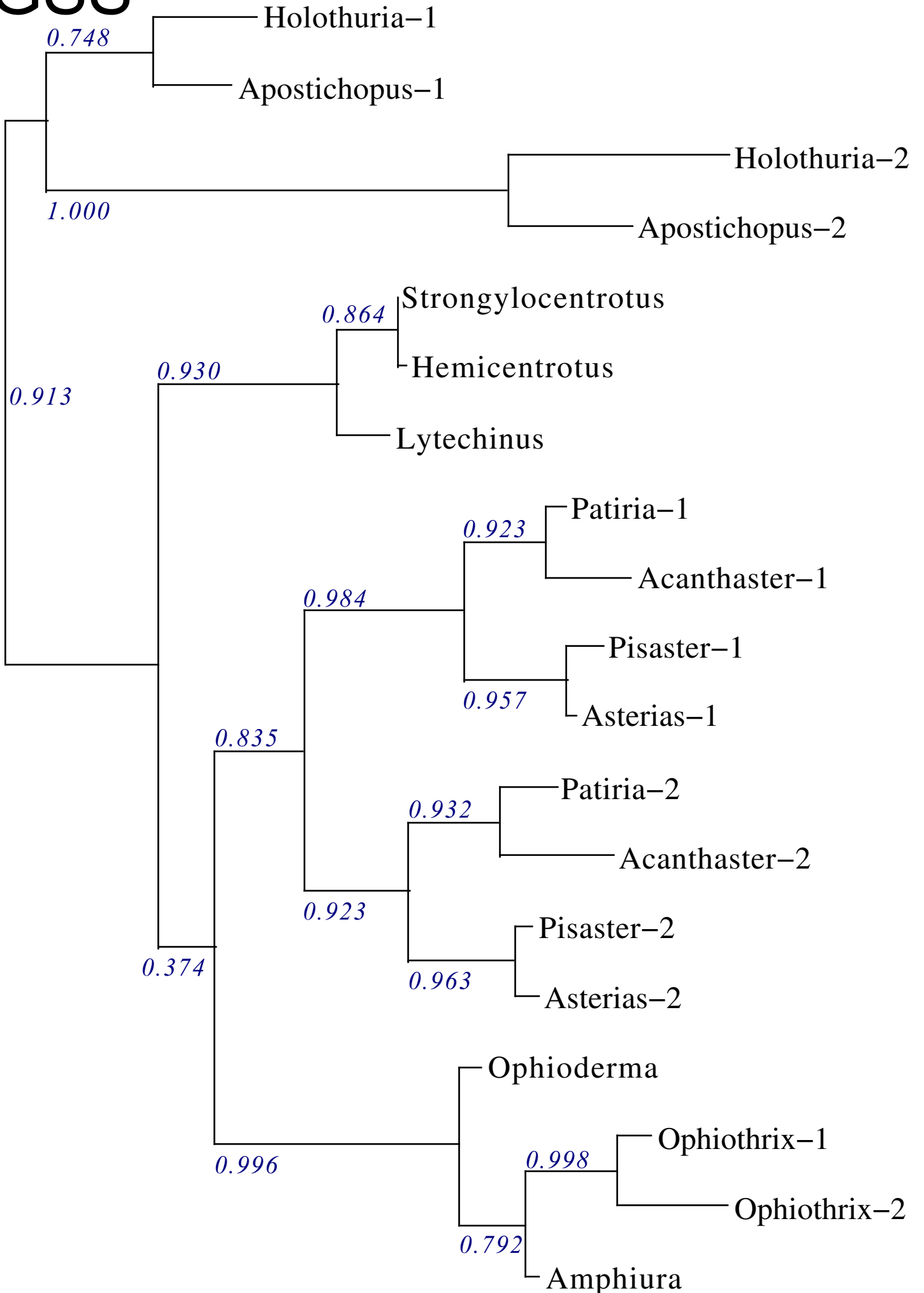


Figure S4. Phylogenetic tree of ambulacrarian GSSs.

Drosophila -----LQHTTEGLEMLFRERSQSDWENVVHQETHS-R--C-RDKLIVRQLYWA
 Periplaneta -----TKTENELEEMFKARSEEDWENAWHREHRT-R--C-QETLLRHLIYWA
 Stegodyphus -----EVDVDPAWENIFKARSDWDWRSVWHTERHR-R--C-YHDLVHMDWV
 Oligometra -----QDYSHRSRQEWARVWTVESMR-Q--C-HEDLREMVHIS
 Anneissia -----LRDYSRSHNDWARVWTVESMR-Q--C-HENLREMVHVS
 Antedon -----LQDYSDRSHHDWARVWTVESMR-Q--C-HEDLREMVHIS
 Florometra -----LQDYSDRSHYDWARVWTVESMR-Q--C-HEDLREMVHIS
 Lytechinus -DNLNCNQVIPQETMDEYELRTPPEEWRENWLLDSLY-T--CVGPQLQRLGELA
 Hemacentrotus TEKFCNCMVIPELTMEDYEDRTPPEEWRESWTMDTLR-T--CVGPQLQRVGELA
 Strongylocentrotus -EKFCNCMVLPELTMEDYEDRTPPEEWRESWNMDTLR-T--CVGPQLQRVGELA
 Apostichopus -----TLQELNSRTQPSWEQLWIVENV-PTVDCTV-DAVQLHIIA
 Holothuria -----DTTGLPETTIETLNAWTASEWVIAWASGSLVPEGC-TTLSVQQLFEYA
 Asterias -----AKPHLPVDQWRSRSKADWIRLWNTERHVNV--C-NEHLQPVFDDAA
 Pisaster -----AKPHLPVDQWRSRSKADWIRLWNTERHVNV--C-NENLQPVFDDAA
 Acanthaster -----APHLPVEQWNSRSKADWVKLWNTERHVNT--C-NEALLPVWDVA
 Patiria -----AAPHLPVEQWKSRSKADWVKAWNTERHVDT--C-NEALLPVWDIA
 Ophiothrix -----KITDYSSRTKADWQRLWLWLTESHQ-K--C-NEDLPLWKIA
 Amphiuira -----RNTDYSSRTRADWQRLWVLTESHQ-K--C-NEDLIPLWKIA
 Ophioderma -----KTTYDYSSRTTADWQRLWVLTESHQ-K--C-NEDLIPLWKIA
 Saccoglossus-1 LTVENEETITFSELNTMYGTRTLTDWQGWKWTSETH-A--C-GSNLYRISEYV
 Ptychodera -----AKDYDTVEDLILKYGTRTEDDWRNVWHTESHN-K--C-RNSLYSYVIFA
 Schizocardium -----ENAYETVESLKAKYSGRTFNDWRAAWNTETHN-K--C-RNSLYSYVIFA

Drosophila CEKDIYRLTRRNKKRTGNDEAWIKKTTTEPDGSTWLHVNYANMFLRSRR----
 Periplaneta CEKDIYRLSRRNDYQOKENL-FLDE---GEPYPELSVVEARVFLDRRRQR-
 Stegodyphus CQKDIYAVRRKKRST-----DPEFLDDQKAHSFLGRRLKKS
 Oligometra CRNDPRK-ITSKRN-----IEIPRSEATGFLSRFL----
 Anneissia CRNDPRK-ISSKRS-----IEIPRNEATGFLSRFL----
 Antedon CHNDPRK-ITSKRS-----IEIPRNEATGFLSRFL----
 Florometra CHNDPRK-ITSKRS-----IEIPRNEATGFLSRFL----
 Lytechinus CMNDPRKSVVVKRSN-----SGREIFLPAKLAKAFLHYRHRHD-
 Hemacentrotus CINDPRKTIVVKRSN-----SDRDLELPAKLAKAFLQYRHRKD-
 Strongylocentrotus CINDPRKTIVVKRSN-----SDRDLELPAKLAKAFLHYRHRKD-
 Apostichopus CSNDVYKDEHGSRRRRF-----SDKRRRS--IEFLNFSEANNFLA-KTKRT-
 Holothuria QONDFYDAEASTGL-----GSGTGRRRRQSSIEFLTHREASNFLHRSKRFR
 Asterias QONDIRK-IT-KRT-----GEEFVKEWAAKDFLIGS----
 Pisaster QYDVRK-IT-KRT-----GEEFVKEWAKDFLIGS----
 Acanthaster QONDIRK-IT-KRM-----GREFLNEWTAKNFLAGS----
 Patiria QONDIRK-IS-KRT-----DREEVKEWNAKNFLAGS----
 Ophiothrix CTYDIRK-IN-KRA-----PEEVEDSEAKAFLIGP----
 Amphiuira CTYDIRK-IT-KRS-----PEEIAEPDAKNFLLGP----
 Ophioderma CTYDIRK-IN-KRS-----PEEVAEPEAKNFLLGP----
 Saccoglossus-1 CYVDIHKSPDRKRTD-----DAFVDSAVAHDFLRLGLMEKRT
 Ptychodera CMVDIYATGDKKRAE-----PPEVEHSIANSFLAGHRAEKR
 Schizocardium CMKDIHASGDRKRGQ-----FPFLDHEVADKFLSGSL-GKR

Drosophila --SDGNTPSISNECCT-KAGCTWEEYAEY-CPSNKRNRNHY-----
 Periplaneta --RRGPGSSITEECCHNTAGCTWEEYAEY-CPANKRLRKFV-----
 Stegodyphus PHHTLVKRGIIIDECCHGSAGCSWEEYAEY-CPANSRMRS-----
 Oligometra --RTRRPSELHEDCCLDSRGC TWEEVAEIA CINNRRAHRPGSPIGR----
 Anneissia --RTRRPSELHEDCCLDSRGC TWEEVAEIA CINNRMRHRPGSPVGR----
 Antedon --RTRRPSELHEDCCLDSRGC TWEEVAEIA CINNRMRHRPGSPVGR----
 Florometra --RTRRPSELHEDCCLDSRGC TWEEVAEIA CINNRRIHRPGSPVGR----
 Lytechinus --SRRRRVTGKDEECCLESNGCHLEELGEY-CTLHSRAYHVSQSQP----
 Hemacentrotus --SRRRRVTGKDEECCAEAQGRWEEELGEY-CTLHTRAYHQSQGP----
 Strongylocentrotus --SRRRRVTGKDEECCAEAQGRWEEELGEY-CTLHTRAYHQSQGP----
 Apostichopus HSRVRRTTTTFSTECDD--KLCIWEEVGEY-CWH-SRVYH-----
 Holothuria RGRTRRSTTISAECCG-TQEC KWEEIGEY-CVH-PREWHLP-----
 Asterias ----KRRKRLNEECCHEDTGCWEEVAEY-CKKHGREKHKPGSTVAQKQGR-
 Pisaster ----KRRKRLNEECCHEDTGCWEEVAEY-CKQHGREKHKPGSPMVPGMQGR-
 Acanthaster ---KRRKRLNEECCHEDLGCWEEVAEY-CVMHGREKHEDGSPVRGKPGRRR
 Patiria ---RRKRLNEECCHEDLGCWEEVAEY-CVMHGREKHEDGSPVRRRPGRRR
 Ophiothrix ---RRHKRRLNEECCHESKGCWEEIGEY-CRMHSRASHVDSRIDSR----
 Amphiuira ---IRHKRRLNEECCHESKGCWEEIGEY-CRMHSRASHVSGKVDAR----
 Ophioderma ---RRHKRRLNEECCHESKGCWEEIGEY-CRMHSRASHIDGRVDSR----
 Saccoglossus-1 L-RRYRRTSATSECCADDGCVWEEELAEY-CTHQREVRTMDE-----
 Ptychodera M-TRFRRASPTEECCSNAHGCNWEEELAEY-CSHQRDDTRRR-----
 Schizocardium M-ARFRRANPSEECASNRRNGCTWEEELAEY-CNHQRDDIDGR-----

Dilp7

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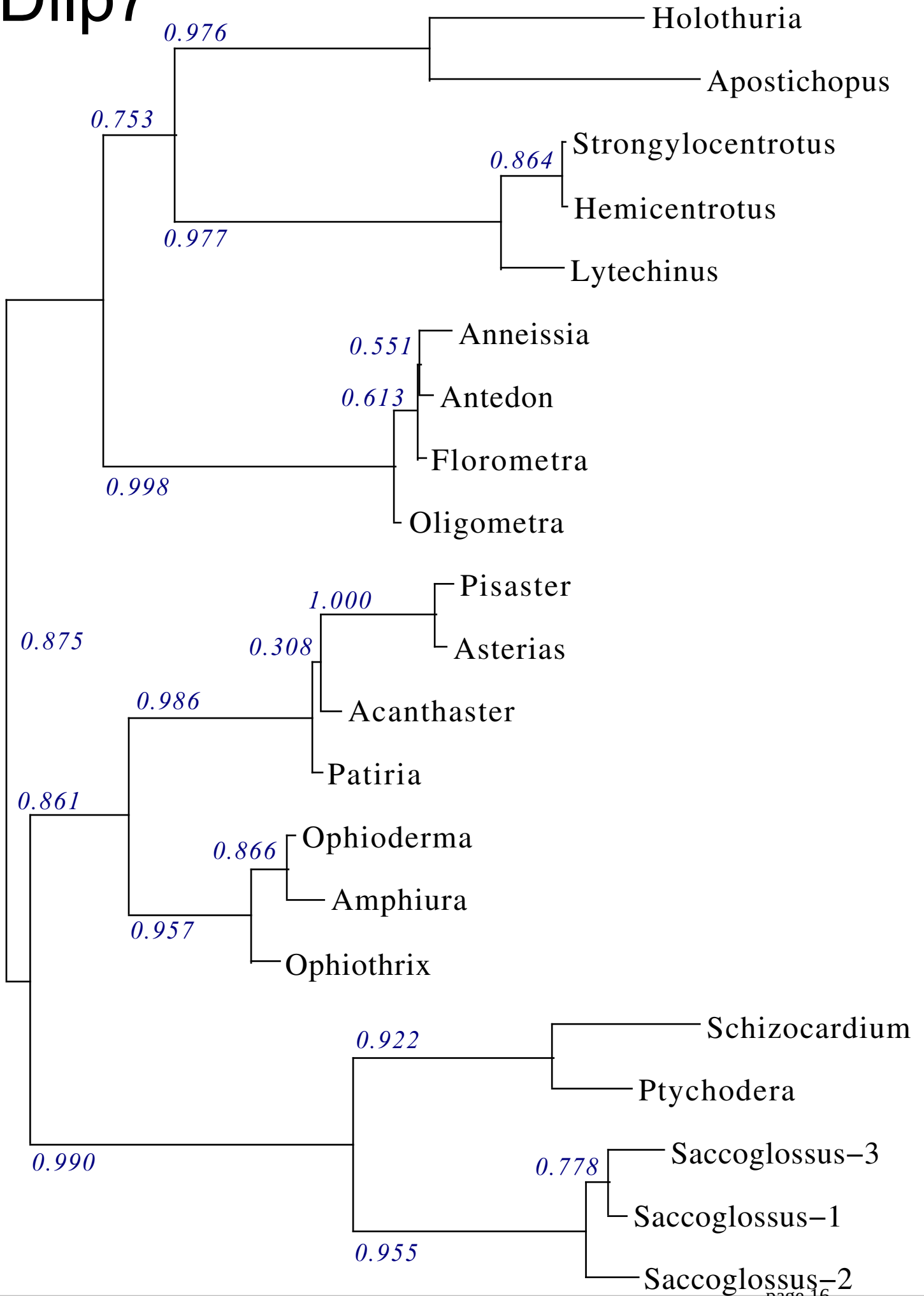


Figure S6. Phylogenetic tree of ambulacrarian dilp7 orthologs.

Anneissia E C C Y N P C S S F E M I K Y C C P T R Q I E L H N R N P N S S E D K -----
 Oligometra E C C Y N P C S R F E M V K Y C C T S R Q I E F H E S E G K K -----
 Antedon E C C Y N P C T R F E M I K Y C C T S R Q I E F N D T E G K K -----
 Florometra E C C Y N P C S R F E M I K Y C C T S R Q L E F N D T E G K K -----
 Lytechinus E C C N K F C D P G E M I L Y C C E K R Q I E W A H F H N L L K A -----
 Hemicentrotus E C C N K F C D P G E M V L Y C C E K R Q I E W A Q F H N L L K A -----
 Strongylocentrotus E C C N K F C D P G E M V L Y C C E K R Q I E W A Q F H N L L K A -----
 Apostichopus E C C E K N C E I R E M V F Y C C A E K Q R E Y A S F F P E I F R N R I R H T -----
 Holothuria E C C R R S C D I F E M I F Y C C A A Q Q Q F Y A E F F K L V K R S -----
 Asterias E C C L K R C T T N E L M L Y C C E E K Q R E Y F S F V G W L S R R -----
 Pisaster E C C L K R C T T N E M M L Y C C E E K Q R E Y F S F V G W L A R R -----
 Acanthaster E C C H R Q C A V S E M M L Y C C E Q K Q R E Y Y T F V G W L K R R -----
 Patiria E C C H R P C S V N E M M L Y C C E Q K Q R E Y Y T F V G W L K R R -----
 Amphiuira E C C T S Q C E A G E M I L Y C C Q E R Q R E W H S V R G F F N K -----
 Ophioderma E C C T Q Q C E I G E M V L Y C C Q E R Q R E W H S M M G F F N K -----
 Ophiothrix E C C T Q Q C D T G E M I L Y C C Q E R Q R E W H I M M G L Y N K -----
 Saccoglossus-1 E C C Y S Q C S L T H M I T Y C C A E V Q N E F Q V F I N I L G N T D E S S E N D G D D G E E S S S V H E D ---
 Ptychodera-1 D C C Y R R C N L Q K M M T Y C C A E R Q R E L N N F F S L L N Q K D N G S T -----
 Schizocardium-1 H C C N H H C S F T E L L I Y C C E E R S E E F Y S F I G L L R M D D E D T D A S L E K G N G D V E A E D N T D L
 Saccoglossus-2 A C C K E Y C P L P K I T E F C C D E R Q Q E F H Q F M S S F A S T E E -----
 Ptychodera-2 K C C N R R C T I H K M M Q F C C E A R R N E F H K F L A L M G N T D N -----
 Schizocardium-2 V C C D N Y C S L D K I T E F C C E D L Q Q E F R Q F M S F V S N S K -----
 Saccoglossus-3 D C C Y H T C P T E R K T I Q Y C C F E V Q A Q Y R L F M E S A I -----
 Ptychodera-3 E C C R N R C S V E R K T I Q Y C C D E I Q K E F A F F F S L F G S -----
 Ptychodera-4 E C C R R Y C T L S R R I Q Y C C Y E V Q L E Y Q I Y Y E S R N E E -----
 Ptychodera-5 E C C R S F C S L E R R I Q Y C C Y N V Q A R F A I F K E M S K E M S K E R G M -----
 Ptychodera-6 E C C R G T C S L E R K T I Q Y C C Y E I Q K E F A L F K Y G Y R S -----
 Ptychodera-7 E C C H T Y C S F E R K T I Q Y C C N A V Q Q E F A L F K S G Y R S -----
 Ptychodera-8 E C C H S R C S L Q R K T I Q Y C C D E I Q E E L A L F L S L F G S -----
 Schizocardium-3 E C C L R T C T V I E K T H Y C C R E K Q I E L Y I I I Q S A P W L V D N Q R -----

Anneissia -----
 Oligometra -----
 Antedon -----
 Florometra -----
 Lytechinus -----
 Hemicentrotus -----
 Strongylocentrotus -----
 Apostichopus -----
 Holothuria -----
 Asterias -----
 Pisaster -----
 Acanthaster -----
 Patiria -----
 Amphiuira -----
 Ophioderma -----
 Ophiothrix -----
 Saccoglossus-1 -----
 Ptychodera-1 -----
 Schizocardium-1 D Q G D D D D N T Q N N E G G S I D V V V E R D V G D V L L K T D K S K P
 Saccoglossus-2 -----
 Ptychodera-2 -----
 Schizocardium-2 -----
 Saccoglossus-3 -----
 Ptychodera-3 -----
 Ptychodera-4 -----
 Ptychodera-5 -----
 Ptychodera-6 -----
 Ptychodera-7 -----
 Ptychodera-8 -----
 Schizocardium-3 -----

Figure S7-continued.

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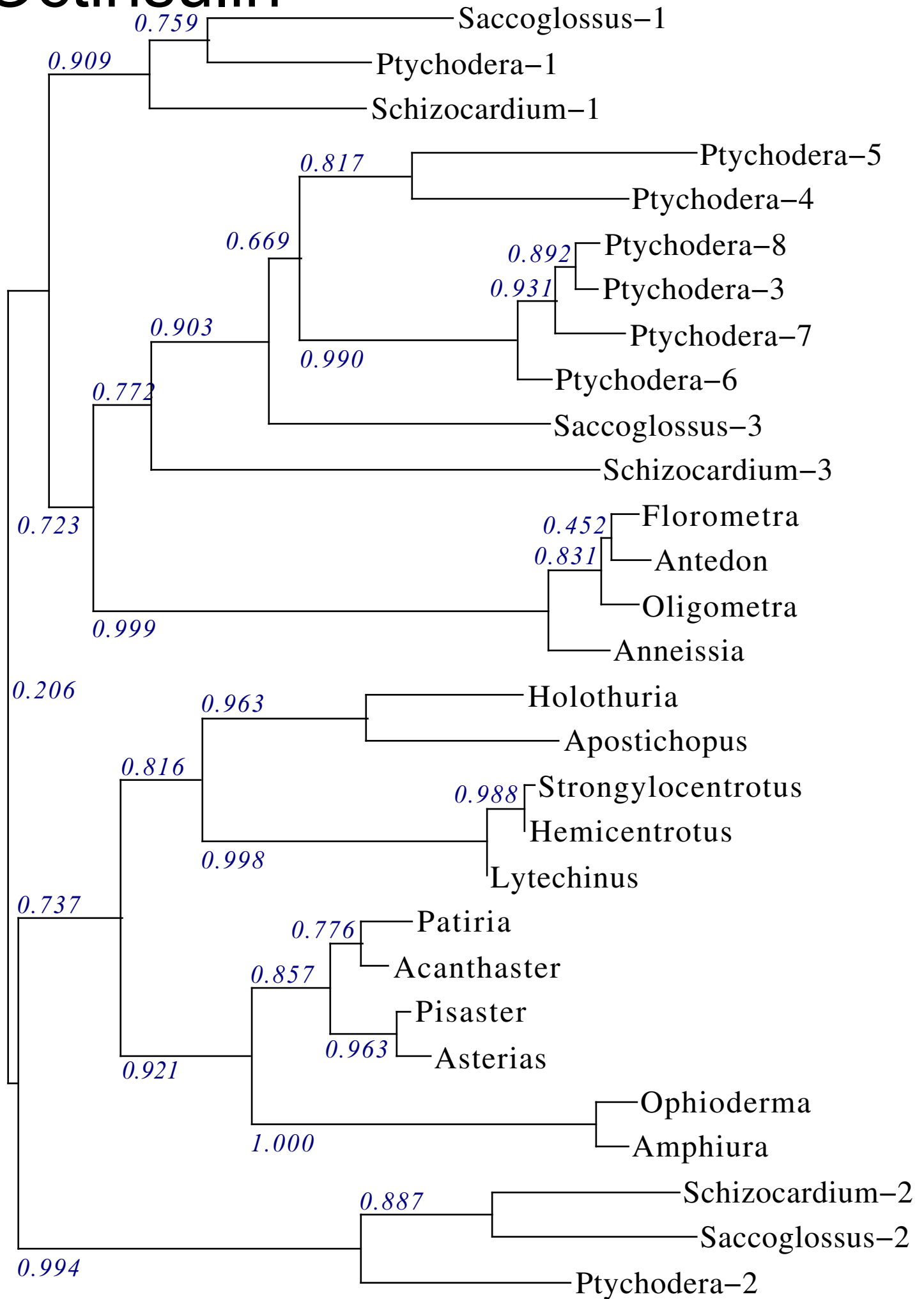


Figure S8. Phylogenetic tree of ambulacrarian octinsulins.

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Amphiura-1 -----
Amphiura-15 -----FD-----LP-----GREPGP
Amphiura-16 -----FLSDATSKKT-NEEALY-----AQAMKR
Amphiura-2 -----YLTDAEH-----AER
Amphiura-3 -----YLTDAEH-----AER
Amphiura-7 YQDSDLRRTLLDALEQSLRADSGDAPS-----MKT-----SKRA
Amphiura-6 IPDGYLRSLMDALQQIERADSGHAGV-DA-----TAMKT-----AERE
Amphiura-8 YQDSDLRRTLLDELKQ--RADSRDAAA-----IDT-----NKRD
Amphiura-9 YQETDLRRTLLEALKQ--REDSGDAPA-----INT-----NKKG
Amphiura-5 -----YP-----GALTRGTN
Amphiura-10 YPDTYLRTLLDQIVDSDATSKKT-NERAPDAYAMK-----
Amphiura-11 YPDTYLRTLLDQIVDSDATSKKT-NERAPDAYAMK-----
Amphiura-4 FPDNYLRTLLDALEKISDSDATGKRQ-MYADPDIARPPA-----
Amphiura-14 FPDNYLRTLLDALEKIADSDATAKRQ-LYDDEDLVRKPG-----
Ophioderma-10 -----DTETT-SSEEPDEWDEINP-TAIA-----ETKD
Ophioderma-3 -----TKS-DNEEPDEWEVLHP-GE-----IREQSPD
Ophioderma-8 -----TKS-ADEEPDEWEVLHP-GE-----PREPVS
Amphiura-13 -----KS-NSEEPDEHTT-----TTAPTTVGTDD
Amphiura-17 -----TKS-IDEEPDELVSQGT-TTTGTTTAAVGRRDD
Amphiura-18 -----TKS-IDEEPDELSMQAT-T-----TVAARRRDD
Ophioderma-1 -----DEIGAMKS-QNEEPDEHDSHIG-TT-----PVIN
Ophioderma-2 -----TKT-ANEPPDEWGLIPT-MP-----PAPTDSL
Ophioderma-4 -----TNP-VNEEPDEGGLAP-----
Ophioderma-7 -----TTT-INEEPDEGGQAK-----
Amphiura-12 -----APNLFEDL-LRR-----DHVEQSGNITCM--
Acanthaster-5 -----VPRKPEEP-----SISAHCGMLLELRQ
Patiria-6 -----VPRKPGE-----ISAHCGMLVELRQ
Asterias-4 -----KLNKPEETIDV-----TSSEHCGFVKEFRQ
Pisaster-2 -----KLNMPKDEVLSV-----ESEHCSAVKEFRQ
Pisaster-5 -----AQ-----QKSGHGPLLREVRQ
Asterias-1 -----ELRSQDGLMREVRQ
Pisaster-3 -----EPRPDGLLREVRQ
Asterias-2 -----APNHNGLLREAKR
Pisaster-4 -----EPNHYGLLKETKR
Patiria-2 -----DVPKPLA--DSE-----IDSNEDGEME----
Acanthaster-6 -----DDPKPSESAAIAE-----DDSNKGDIE----
Acanthaster-7 -----DGPKLSES-----TAIDSDIE----
Patiria-1 -----APPANDGIEVLTGGKIEE-----DDFEG---D-DFD
Acanthaster-2 -----LL-DLH
Acanthaster-1 -----HP-DAD
Acanthaster-8 -----HS-GAD
Acanthaster-9 -----HP-GAD
Patiria-5 -----EP-----ADFNKDDKID-DLD
Patiria-8 -----DKTD-DWH
Ophioderma-5 -----NSLTRDADDAPVAMDDKPTSPRPIDI I KRSRHLRCAQFKDMAL
Ophioderma-6 -----AAVSPVHGSCVELK----
Ophioderma-9 -----AAFNSVPVSCADFQ----
Asterias-3 -----ELNVASCQQQLADQVK
Pisaster-1 -----TELDEASCKQLADQVK
Acanthaster-3 -----DKTPSTASCEALAAQIS
Patiria-7 -----DKAPSAATCEALAAATVK
Acanthaster-4 -----SDTG--ADD-----DKVHIDDATCQALANQVK
Patiria-3 -----DDAE--FKD-----GAIVIDDEVCEKLAQVK
Patiria-4 -----DDAE--FKD-----GAIVIDDEVCEKLAQVK

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Figure S9. Sequence alignment of ambulacrarian multinsulins.

Amphiura-1 -----DWVGFRTI**C**DPP-FTPSLYIEDF**C**GVT---VKR-----
 Amphiura-15 ASYV--ADNTWTGKTNI**C**NYE-Q-QVVYHREL**C**GH---QKR-----
 Amphiura-16 YILN--PWSGWAGGKTE**C**NTQ-TQESDF-DHAC**R**-----
 Amphiura-2 IDLA--KRKDW-----**C**NNA--AHEF-SRL**C**N-----
 Amphiura-3 IDLA--KRKDW-----**C**NNA--AHEF-SRL**C**N-----
 Amphiura-7 WEKE----FRSR---AE**C**ERQ-WK-LEL-DGH**C**ISH-----
 Amphiura-6 EGVK--RG---GVTP**L**CKSA-K--DRA-GKF**C**VYW-----
 Amphiura-8 EGNE--KRFVSMHSQA**C**YSD-**I**YTYRK-PGI**C**PTR-----
 Amphiura-9 TDAR--D-----G**C**EAN-**I**N--VKV**S**QL**C**-----
 Amphiura-5 --DS--MNLRADFKLKL**C**GTE-**I**TLER--YYA**C**GKR--DLK-----
 Amphiura-10 ---R--GEYNWSGKT**L**CGGT-**I**QTYK--GNI**C**WGK--REAK-----
 Amphiura-11 ---R--GEYNWSGKT**L**CGGT-**I**QTYK--GNI**C**WGK--REAK-----
 Amphiura-4 --VF--DWQDWSGKKKI**C**TAF-DQQQH**F**-NGV**C**Q-----KRR-----
 Amphiura-14 --VF--DWEDWSGNKNI**C**GRH-TQNQYY-NGV**C**QQYEGTGKRR-----
 Ophioderma-10 PVMM--RDKKWR-TSW**F**CGSD-**I**FRAK--KFI**C**SPR--SYVRHIPY-----RKR-----
 Ophioderma-3 IELD--HVKRWHSSVRI**C**SS--KYRVQ--EAI**C**DPR--NAKREVS-----
 Ophioderma-8 TELD--HVKRWHSSVRM**C**SS--MHRVK--ETI**C**DPR--NAKREVS-----
 Amphiura-13 NAIL--MKRSWSG**T**KKHL**C**G**Y**Q-**I**NNER--SSV**C**GFK-----RD-----
 Amphiura-17 DSST--LMKRWYG**T**VQ**L**CGSH-**I**TKVK--SVI**C**NP**G**--RPFKREE-----
 Amphiura-18 DSST--LMKRWNGYVQ**L**CGSH-**I**TKVK--GVI**C**NP**G**--APFKRDE-----
 Ophioderma-1 RSGT--MEKRWRGYVYI**C**EPQ-**I**TRLK--NVI**C**NPA--SVKRS-----
 Ophioderma-2 RSNM--LEKRWRGATKI**C**GST-**I**NTVQ--SVV**C**HPN--NYKRD-----
 Ophioderma-4 -----LGKRWSGSNKL**C**GEA-**I**SRAT--KNL**C**NPL--SAKRD-----
 Ophioderma-7 -----KGWSFTTGEKI**C**GDD-**I**HTAT--TDV**C**FPD--SEKRD-----
 Amphiura-12 AYATMLEYEPNEEAY**T**W**C**DAN-**I**EHQR--EGI**C**SCV--EYI**K**EHNK**R**SL**F**-----
 Acanthaster-5 MLDN**P**GLD-KRSPRNYW**C**GTT-**I**NNRK--SAL**C**SCN--H-----H-----
 Patiria-6 MLDN**P**GLE-KRSPRNYW**C**GTA-**I**NNRK--STL**C**SCN--H-----H-----
 Asterias-4 LSDN**P**TLM-KRSPRNYW**C**SST-**I**ERRK--EAL**C**SCP--W-----H-----
 Pisaster-2 LADN**P**GVV-KRSPRNYW**C**NTA-**I**SQRK--TAL**C**GCT--H-----H-----
 Pisaster-5 LFKGRNSQ-VRSE**T**HYW**C**WEV-**I**EKNR--ESI**C**NGP-----PQPTQ**H**-----
 Asterias-1 LARNGRH**F**-RAAEDHIY**C**GVV-**I**EQNR--ESV**C**GVI-----PGS-----
 Pisaster-3 LGRK**P**GH-TRAEDHIY**C**GAV-**I**EQNR--EQV**C**GIV-----PAS--R-----
 Asterias-2 ILGRR**G**HQSRWDE**T**HFY**C**DDA-**I**EQQR--EVI**C**DPN--HTHAPVQ**P**T**P**TGG**P**LP**P**TV**S**-----
 Pisaster-4 VFRRR**G**FQ**P**TN**C**EEAVEY**C**DA-**I**GQKR--EVL**C**QHN--HGTDAPRDSAV**G**-----A-----
 Patiria-2 TKSG**F**SVA-WTGPQMWV**C**SSST**A**ARK--HYV**C**HP**P**--GRHHH**H**KRE-----DE-----
 Acanthaster-6 AKG**D**FSVA-WSGPQMWV**C**RGR-**I**RRRR--RYA**C**HP**P**--GRH**H**Y**K**KRN-----DVQ-----
 Acanthaster-7 AKG**D**FSVA-DNGPKLWV**C**QGN-**V**TNTL--KNV**C**THT--GR**P**HS**D**TRD-----DVQ-----
 Patiria-1 KNKNQYYS-RSGPRFRV**C**GTT-**T**HSWS--SFV**C**HP**S**--GLI-----HH-----
 Acanthaster-2 AKEGR**I**LV---RYPHY**C**NGI-**I**QIKY--NQL**C**HP**Q**--P-----P-----
 Acanthaster-1 AKHG**G**NLA---YRANY**C**GAT-**I**YEKV--RET**C**HAV--R-----R-----
 Acanthaster-8 TKEG**G**RVV---RYPHY**C**GAT-**I**QEKY--REI**C**HAL--R-----R-----
 Acanthaster-9 TKEG**G**RVA---RYPHY**C**GAS-**I**QEKY--REI**C**HAF--R-----R-----
 Patiria-5 EDDG**Q**LET---RKPHY**C**GHR-**I**LRKY--AKI**C**HHV--TLHRR**P**H--H-----LAA-----
 Patiria-8 ADLG--QK---RSPHY**C**GRH-**I**GTKI--GOI**C**GWH--L-----L-----EAW-----
 Ophioderma-5 DHFRR-LVGKER**V**FAKY**C**SPT-**P**QTVM--DNY**C**QCD--VVPR**S**I-----D-----
 Ophioderma-6 -----KARELGAKHR**F**CGEE-**I**TYVR--NSY**C**SCR--VIPR**D**M-----N-----
 Ophioderma-9 -----SAQKRGNLHKL**C**GSE-**I**TAAV--DNY**C**QCK--VIPR**D**M-----S-----
 Asterias-3 EGKKRWD----G**P**SHK**F**CGET-**I**NEKR--YAY**C**TCG--LVPR**K**R-----E-----
 Pisaster-1 EGKKRWT----G**S**W**H**T**F**CGET-**I**NEK**K**--YAY**C**TCG--LVPR**K**R-----E-----
 Acanthaster-3 EGKKRWD----G**P**S**H**T**F**CGED-**I**NERR--NAY**C**NCQ--VVPR**K**R-----E-----
 Patiria-7 EGKKRWD----G**P**A**H**T**F**CGET-**I**TEKA--NAY**C**HCQ--VVPR**K**R-----E-----
 Acanthaster-4 ERGRR**P**WSRTG**P**KHY**F**CGPT-**I**EKK**K**--EAY**C**NC**K**--VVPR**K**R-----D-----
 Patiria-3 EKS----ILGV**G**P**K**HWY**C**NP**T**-**I**ER**K**K--EQY**C**TC**S**--VVPR**E**R-----D-----
 Patiria-4 EKS----ILGV**G**P**K**HWY**C**NP**T**-**I**ER**K**K--EQY**C**TC**S**--VVPR**E**R-----D-----

Figure S9-continued.

Amphiura-1 -----EYE-ATDPLGFLK-----MRGMVK---RLNP---NWRELMSEECYEST
 Amphiura-15 -----EIE-AEDALGFLK-----MKLRGM---EKRG---GWQEYMNEECIEWCT
 Amphiura-16 -----LY-GRDALDFLK-----LRDVVK---RA---SFNDIKEWIHEECLERCI
 Amphiura-2 -----N-RRDALDFLN-----LRDVRN---KVHAFTNYIKEAVHEECCESCI
 Amphiura-3 -----N-RRDALDFLN-----LRDVRN---KLHAFTQYIKEGVYEECCDETCI
 Amphiura-7 --PYRRDMP-DVDALAFLN-----KRG-----KSLNGLYHECCDESCS
 Amphiura-6 INRRDIEVS-MPDALGFL-----KTE-----VQARDLNHECCVETCS
 Amphiura-8 RSEDIQQLG-MQGALAFLN-----KRE-----MVKRDLFHECCVETCT
 Amphiura-9 RREDIQQLD-TPDAFAFL-----KRE-----LVQRDLYHECCVEQCD
 Amphiura-5 --DALTFLE-DGA-----NRKRD LHEECCVETCS
 Amphiura-10 --DALAFLE-TDDRQ-----TDADP-LGIWALISTTLNEECCGEACY
 Amphiura-11 --DALAFLE-TDDRQ-----MDPLSTFISLALISTTLNEECCGEACY
 Amphiura-4 --DIPQQLD-TPDALGFLQ-----AKRI-----AGFEKDVYESMTEECCLEGCT
 Amphiura-14 --DIPQQLD-TPDALGFLQ-----AEK-----RKDVVFESINEECCAEQCS
 Ophioderma-10 RSVGDATLI-KQDADMFLN-----RQKR-----RKSSYSLYEECCGEFCS
 Ophioderma-3 DNGVPGGVA-KETAKRFLK-----RQRR-----GEWGKGDLEEECCHEGCS
 Ophioderma-8 DNGVPGGVA-KETAKRFLK-----RQRR-----GEWGKGDLEEECCHEGCS
 Amphiura-13 AEDALDFLK-QDIV-----KRS LTEECCHEGCS
 Amphiura-17 SEAALAFLK-EERAKRFLQ-----ADQQLLHQQLHQP SLRLWGG LTEECCNEHCS
 Amphiura-18 GEAALAFLN-EERAKRFLQ-----PDQQ-----QLDQPNRLWGG ISEECCNEHCS
 Ophioderma-1 DTAGLEFLT-EHQAKRFLM-----QNKR-----IWGGGLSEECCNEGCS
 Ophioderma-2 --ETAALVG-EQQAKRFLR-----KR-----WWGGAGGLTEECCNEGCS
 Ophioderma-4 --ETTAVME-ERRAKRFLI-----EKRSS LNEECCNEGCA
 Ophioderma-7 --A---IIQ-EKGAKRFE-----NKRLW-----GWSWSTHGS LNEECCNEGCV
 Amphiura-12 --KRMAEVT-EDVAKRFE SLLVLEVERAR-----RPKTS LQEECCNESCY
 Acanthaster-5 SLLSDELIE-SKEANSFL-----KRG I-----EK-RS LTEECCHEGCV
 Patiria-6 TFL-----K-SDEANFEL-----KRGV-----EK-RS LSEECCHEGCV
 Asterias-4 TLRDDDFMEEKKDATNFL-----ERGV-----EK-RS LHEECCNEGCV
 Pisaster-2 TLRDDDFMEEKKDATNFL-----ERGI-----EK-RS LSEECCHEGCV
 Pisaster-5 YDSTTEFVG-AREAKGFL-----GKD-----FTNLHEECCFEGCT
 Asterias-1 --KRNLFVR-KEAASEFL-----ERG-----VQGLAEECCGEGCT
 Pisaster-3 LSKRNVFVG-KEAASDFL-----KRG-----VQGLGEECCGEGCT
 Asterias-2 PGHQDAFVG-KNEASRFL-----GRGV-----VQGLIEECCFEGCH
 Pisaster-4 IRSQDEFVK-RREASKFL-----GRGA-----FQGLLEECCHEGQ
 Patiria-2 -DNSDAFLT-EDDANTEFLA-----SPSK-----RKANI IHEECCHEGCF
 Acanthaster-6 EESNPEFLD-EAEANFFLR-----R-----HKRNHI SEECCHEGCV
 Acanthaster-7 EENNPEFLD-EADANFFLR-----Q-----QNSKQ ISEECCHEGCV
 Patiria-1 KRDNDEFLS-AGEANTEFLM-----SEGV-----GK-RGMHEECCHEGCV
 Acanthaster-2 EVFDQDFLD-SKEANTEFL-----KQRI-----GK-RS LIEECCFEGCT
 Acanthaster-1 GVSNQEF LD-SKDASTFLF-----GRGI-----EK-RGLHHECCTEGCS
 Acanthaster-8 GVSNQEF LD-SKDANTEFLF-----GRGI-----GK-RNLNEECCSEGD
 Acanthaster-9 GVSNQEF LD-SKDANTEFLF-----GRGI-----GK-RNLNEECCGEGCD
 Patiria-5 NEAPSAFVE-SDEANSFLD-----NRGI-----SK-RGLHEECCHEGCS
 Patiria-8 DDVHPAFVE-SDEANSFLA-----DRRI-----SK-RS LGEECCHEGCS
 Ophioderma-5 --DKRAEVD-KSSAKSEFLN-----HRA-----ST-RS LDEECCNEGCV
 Ophioderma-6 P-----G-LEDAKAFK-----MRSP-----ST-RS ISEECCYETCY
 Ophioderma-9 P-----G-LEDAKAFK-----MRSP-----ST-RS ISEECCYETCY
 Asterias-3 -LELSEFLN-RGKANGFLS-----ARNV-----QK-RS LSEECCHEGCV
 Pisaster-1 -LDLSEFLN-RGKANGFLS-----ARNL-----QK-RS LSEECCSEGCY
 Acanthaster-3 -LDLSEFLP-SGKANAFLS-----GRRI-----TK-RS LSEECCHEGCV
 Patiria-7 -LELSEFLT-PVKANSEFLS-----GRNI-----AK-RS LTEECCHEGCV
 Acanthaster-4 DGDQSEFLK-PEKAGSFLE-----SSI-----GK-RDFNHECCKEGCV
 Patiria-3 -ADRAEFLE-PEEAGGFLN-----R-----SK-RD LNHECCDEGCV
 Patiria-4 -ADRAEFLE-PEEAGGFLN-----R-----SK-RD LNHECCDEGCV

Figure S9-continued.

Amphiura-1	S	E	E	I	K	E	L	C	-----																
Amphiura-15	M	E	E	V	K	E	L	D	C	-----															
Amphiura-16	V	E	E	V	V	E	L	C	-----																
Amphiura-2	N	E	E	V	L	E	F	C	-----																
Amphiura-3	D	E	E	V	L	E	F	C	P	-----															
Amphiura-7	M	E	E	F	G	E	H	C	T	Q	R	P	E	S	Q	E	G	F	N	P	F	K	L	G	K
Amphiura-6	D	E	E	V	K	E	H	C	V	M	T	K	-----												
Amphiura-8	T	E	E	I	Q	E	T	C	-----																
Amphiura-9	A	E	E	I	E	E	T	C	-----																
Amphiura-5	M	N	E	I	E	E	D	C	-----																
Amphiura-10	R	E	E	I	A	E	T	C	-----																
Amphiura-11	R	E	E	I	A	E	T	C	-----																
Amphiura-4	K	G	E	V	Q	E	L	C	P	-----															
Amphiura-14	K	H	E	I	Q	E	L	C	-----																
Ophioderma-10	M	E	E	L	D	E	T	C	-----																
Ophioderma-3	M	E	E	V	N	E	T	C	-----																
Ophioderma-8	M	E	E	V	N	E	T	C	-----																
Amphiura-13	W	E	E	I	K	E	T	C	-----																
Amphiura-17	V	E	E	I	N	E	V	C	-----																
Amphiura-18	L	E	E	V	N	E	Y	C	-----																
Ophioderma-1	V	E	E	I	D	E	V	C	-----																
Ophioderma-2	N	E	E	V	N	E	S	C	-----																
Ophioderma-4	S	E	E	I	S	E	H	C	-----																
Ophioderma-7	T	E	E	I	R	E	H	C	-----																
Amphiura-12	V	Q	E	V	Y	D	H	C	D	K	H	F	D	G	S	I	-	Y	D	L	F	R	S	-	-
Acanthaster-5	Y	E	E	V	Y	E	L	C	-----																
Patiria-6	Y	E	E	V	Y	E	L	C	-----																
Asterias-4	Y	E	E	V	Y	E	L	C	-----																
Pisaster-2	Y	E	E	V	Y	E	V	C	-----																
Pisaster-5	V	E	E	V	N	E	S	C	-----																
Asterias-1	I	E	E	I	S	E	S	C	-----																
Pisaster-3	V	E	E	I	S	E	S	C	-----																
Asterias-2	S	E	E	I	H	E	H	C	P	-----															
Pisaster-4	A	E	E	I	H	E	H	C	P	K	V	Y	-----												
Patiria-2	W	E	E	I	L	E	Y	C	-----																
Acanthaster-6	W	E	E	I	L	E	Y	C	-----																
Acanthaster-7	W	E	E	V	L	E	Y	C	-----																
Patiria-1	W	E	E	M	L	E	H	C	-----																
Acanthaster-2	N	E	E	I	Y	E	V	C	-----																
Acanthaster-1	I	E	E	I	Y	E	S	C	-----																
Acanthaster-8	D	E	E	I	Y	E	T	C	-----																
Acanthaster-9	D	E	E	I	Y	E	I	C	-----																
Patiria-5	N	R	E	V	R	K	H	C	-----																
Patiria-8	N	E	E	V	R	E	H	C	-----																
Ophioderma-5	L	E	E	I	V	E	L	S	K	T	M	C	S	S	S	-----									
Ophioderma-6	Y	E	E	I	E	E	V	C	-----																
Ophioderma-9	Y	E	E	I	E	E	V	C	-----																
Asterias-3	W	E	E	I	E	E	V	C	-----																
Pisaster-1	W	E	E	I	E	E	V	C	-----																
Acanthaster-3	W	E	E	I	E	E	V	C	-----																
Patiria-7	W	E	E	I	E	E	V	C	-----																
Acanthaster-4	W	E	E	V	E	E	Q	C	H	-----															
Patiria-3	W	E	E	V	E	E	H	C	H	-----															
Patiria-4	W	E	E	V	E	E	H	C	H	-----															

Figure S9-continued.

Multinsulin

0.5

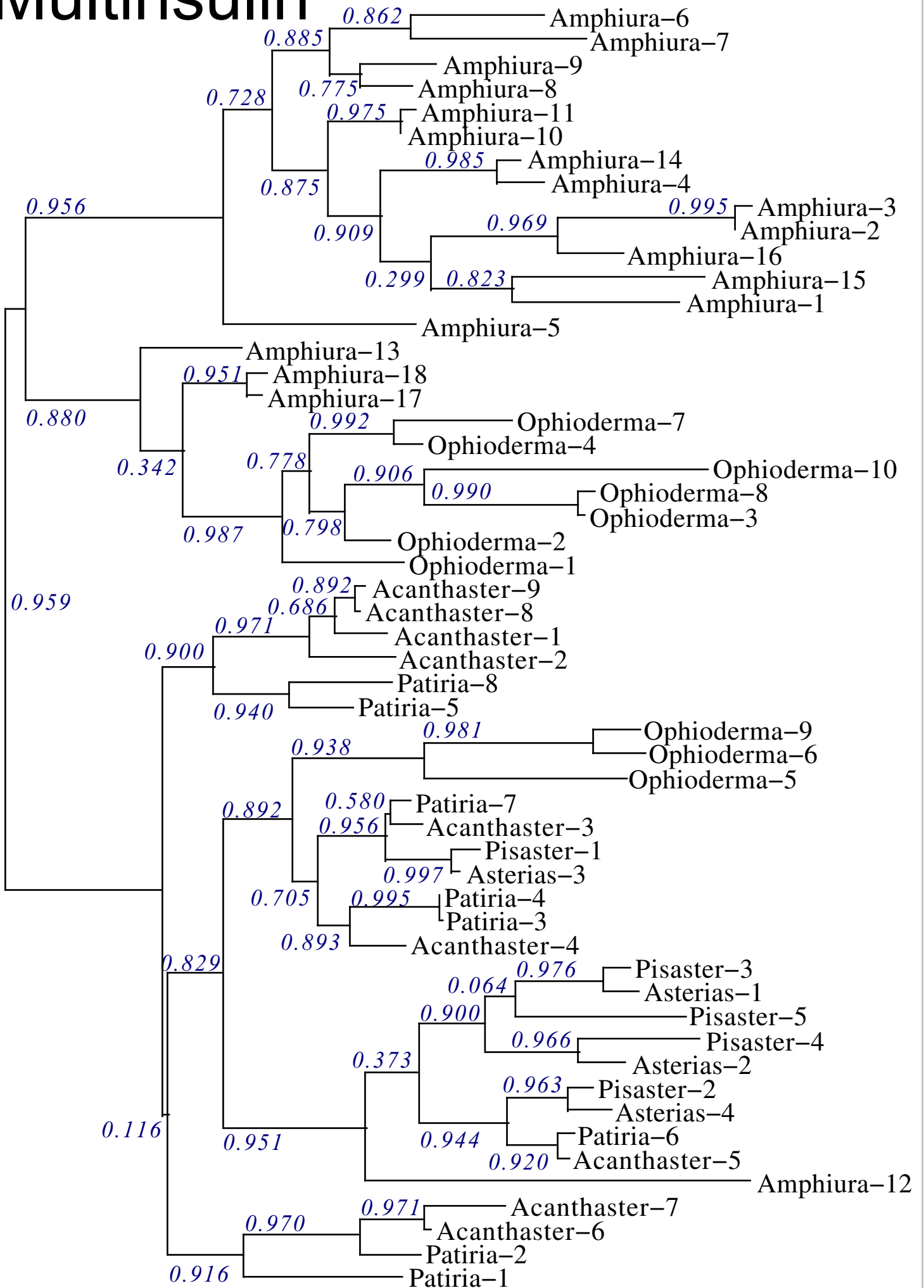


Figure S10. Sequence similarity tree of ambulacrarian multinsulins.

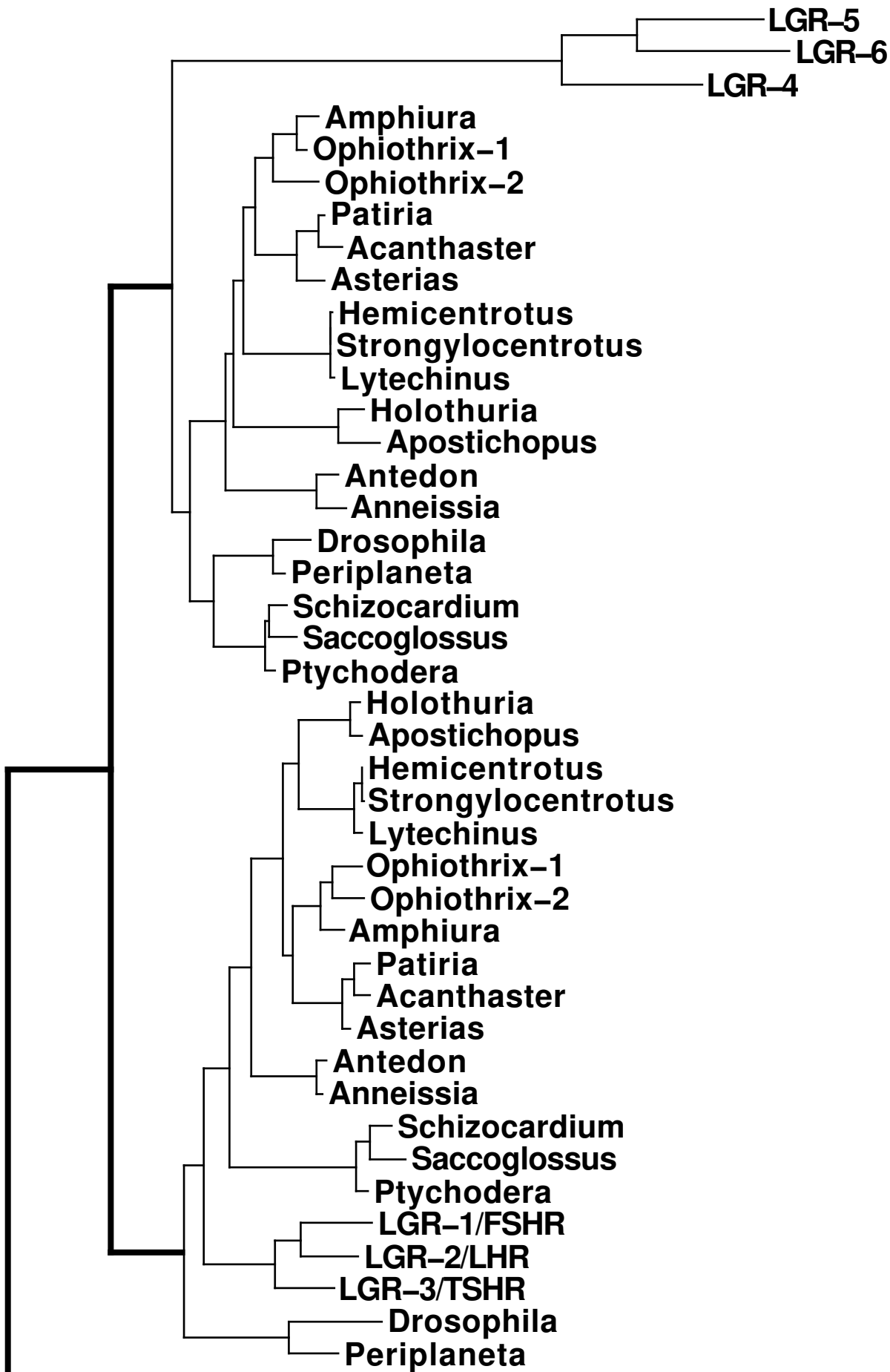


Figure S11. Phylogenetic tree of bursicon and GPA2/GPB5 receptors.

Ptychodera
 Periplaneta
 Anneissia
 Apostichopus
 Strongylocentrotus
 Patiria
 MEMKEPAEDGNKTKIRAGSDGTPRPRNILTSSRSRASRSRSGDGRGVSWSAASSMLH

Ptychodera
 Periplaneta
 Anneissia
 Apostichopus
 Strongylocentrotus
 Patiria
 -----MFIVITL~~LA~~TLPG-----VTSNE
 ---MQCRRSVACGLAV~~AVVLA~~-----LAALTFLL
 -----MCSSKLAGLICIFVL
 -----MLTRT~~GK~~WILLSVTM-----IALTS
 -----MKMEI~~I~~LRVV~~T~~FTSA-L--AAMSRT~~G~~SCQ-----W
 RLRTRQCKVLVLCVL~~LL~~ILV~~LAV~~TFIGVSLTGNDVAQPGNNEFIPATVKTEYEELIG

Ptychodera
 Periplaneta
 Anneissia
 Apostichopus
 Strongylocentrotus
 Patiria
 LPOSFS~~C~~PDGY~~F~~Q~~C~~GNV--TE~~C~~VHOKY~~F~~~~C~~DGKAD~~C~~VDGFDEIPTK~~C~~RDNFGWANLISRI
 SQTHGAC~~A~~EGET~~F~~~~C~~GNSS--SI~~C~~LPORFI~~C~~NGHID~~C~~PNGEDES~~K~~YTDVHGSNFNQDI~~V~~
 LPFTYC~~C~~QSGT~~F~~~~C~~GDDKEQ~~C~~FPQEF~~Q~~CNDVVD~~C~~TNAADEQ--D~~C~~EKAGFGDDFDRR
 PCWAFE~~C~~PKGE~~F~~~~V~~~~C~~GNL--TK~~C~~VKOKY~~Q~~CNEIDD~~C~~GNNADE~~E~~EEV~~C~~RNFE~~G~~VWKSMDKV
 ANDLIE~~C~~DPGF~~F~~~~C~~GNSS--TE~~C~~VAQ~~Q~~F~~Q~~DDIAH~~C~~QNADES--G~~C~~AIDGWLAFD~~V~~
 FSSEYT~~C~~PKGE~~F~~~~R~~~~C~~GNL--TH~~C~~VAQ~~K~~Y~~Q~~CNGEDD~~C~~GNNADE~~T~~--E~~C~~EHNEGWI~~K~~TFDEQ

LDLa

Ptychodera
 Periplaneta
 Anneissia
 Apostichopus
 Strongylocentrotus
 Patiria
 TTFDKSNNDTLQPRNFIRRCETDDYPEACECT-FTSVSCANANLTGIP~~TN~~ISGSVTHL
 IN---RNY---SQAFND~~C~~LES~~L~~PRGCLCRDKT~~W~~VFCRELGLTH~~V~~POD~~I~~STNV~~TR~~L
 HNTTIVLKYD-VGNYNTNVCLIPVYPPVCKCGNKTEVDCSATG~~M~~TTIPQA~~I~~SRN~~I~~SR
 F---DEKD---NIERECET~~T~~NYPVCD~~C~~VNGEK~~L~~CSNKG~~L~~TE~~V~~PSVPPNT---
 HPVSVGETK-----ALNECALAQY~~P~~DGCV~~C~~SKLT~~Q~~LD~~C~~SEFN~~L~~NE~~V~~PPN~~L~~PENIT~~R~~L
 NPVPVDLDW-----QINQ~~E~~CGLY~~G~~FPDVCV~~C~~FEETELKCIQVN~~L~~TQ~~V~~PSV~~S~~ANL~~T~~R

Ptychodera
 Periplaneta
 Anneissia
 Apostichopus
 Strongylocentrotus
 Patiria
 YVSGNK~~I~~KR~~L~~EPGIF~~F~~KEY~~P~~NLL~~T~~LS~~L~~FDNA~~V~~EK~~L~~EEDTF~~Q~~GL~~P~~RI~~E~~K~~L~~YL~~N~~DNK~~I~~KE~~I~~
 ILSNN-SIT~~L~~SQDS~~F~~KKY~~H~~NLE~~L~~HL~~G~~WNO~~T~~SD~~I~~ENG~~M~~F~~K~~G~~Q~~RT~~L~~RR~~L~~F~~L~~SK~~N~~S~~L~~TE~~L~~
 TLLGND~~I~~Q~~T~~ILNNS~~F~~VNFE~~Q~~LHK~~L~~T~~L~~AQNG~~L~~VR~~M~~E~~I~~NA~~F~~NG~~L~~TE~~L~~K~~Q~~LY~~L~~SEN~~N~~IK~~E~~I
 -----SH~~L~~I~~L~~MNN~~Q~~I~~H~~D~~I~~EL~~T~~A~~F~~E~~G~~L~~T~~N~~L~~K~~V~~LY~~L~~SEN~~P~~IST~~L~~
 YLKSNN~~I~~VNIGSELLAN~~Y~~SS~~L~~VY~~L~~NLMGN~~R~~I~~H~~E~~I~~A~~E~~NS~~F~~R~~N~~L~~R~~N~~L~~K~~R~~L~~F~~L~~S~~EN~~N~~I~~S~~R~~I~~
 NLNGN-MV~~H~~L~~E~~DGAF~~E~~RY~~T~~K~~L~~GS~~L~~NLM~~O~~NG~~I~~RE~~L~~RD~~V~~ER~~G~~L~~T~~D~~L~~K~~L~~Y~~L~~S~~T~~NR~~I~~ST~~I~~

LRR

Ptychodera
 Periplaneta
 Anneissia
 Apostichopus
 Strongylocentrotus
 Patiria
 EDGAFRS~~L~~Q~~K~~LAW~~L~~M~~L~~NN~~N~~H~~L~~KS~~L~~EG~~G~~ME~~F~~E~~G~~LES~~V~~Y~~L~~N~~L~~KD~~N~~E~~V~~TEAD~~F~~G~~L~~T~~F~~TH~~M~~
 R~~P~~G~~V~~L~~Q~~D~~L~~P~~H~~L~~S~~W~~L~~V~~L~~Q~~D~~N~~C~~I~~S~~D~~I~~D~~L~~D~~T~~E~~Q~~Y~~L~~-N~~L~~T~~W~~L~~D~~M~~T~~R~~N~~N~~L~~T--L~~K~~G~~K~~-I~~F~~P~~D~~L
 P~~S~~G~~V~~F~~L~~P~~L~~K~~R~~L~~E~~W~~L~~V~~L~~D~~Y~~N~~E~~L~~T~~T~~L~~L~~G~~N~~P~~E~~K~~G~~L~~L~~S~~L~~Y~~W~~L~~S~~V~~R~~H~~N~~K~~I~~N~~D~~A~~N~~I~~R~~T~~-V~~L~~E~~N~~L
 R~~A~~G~~V~~F~~R~~D~~L~~I~~N~~L~~E~~W~~L~~F~~L~~V~~N~~N~~T~~L~~R~~S~~L~~D~~D~~D~~A~~E~~I~~G~~L~~R~~K~~V~~Y~~W~~L~~R~~L~~N~~S~~N~~L~~L~~E~~D~~L~~S~~D~~G~~T~~-P~~F~~R~~H~~M
 Q~~T~~G~~A~~F~~N~~G~~L~~S~~G~~L~~H~~W~~L~~F~~L~~N~~D~~N~~K~~M~~R~~T~~L~~E~~P~~G~~I~~E~~L~~G~~L~~E~~G~~L~~Y~~W~~L~~D~~M~~R~~N~~N~~E~~I~~R~~D~~L~~Q~~E~~G~~E~~-A~~L~~K~~D~~L
 T~~P~~G~~T~~F~~R~~E~~L~~Q~~N~~L~~T~~W~~L~~F~~L~~N~~E~~N~~E~~I~~E~~T~~L~~D~~E~~D~~V~~E~~E~~G~~L~~H~~K~~V~~Y~~W~~L~~M~~L~~Q~~N~~K~~I~~G~~D~~L~~N~~H~~G~~V-A~~F~~R~~D~~L

LRR

Ptychodera
 Periplaneta
 Anneissia
 Apostichopus
 Strongylocentrotus
 Patiria
 P~~S~~L~~E~~W~~L~~N~~L~~G~~D~~N~~D~~I~~K~~H~~L~~H~~T~~G~~M~~F--P~~N~~N~~S~~A~~L~~K~~V~~L~~F~~L~~G~~S~~N~~L~~I~~Q~~S~~I~~H~~E~~D~~T~~L~~R~~G~~L~~D~~T~~L~~E~~D~~L~~D~~L
 P~~E~~L~~K~~Q~~L~~I~~L~~E~~D~~N~~T~~I~~E~~T~~I~~G~~E~~F~~T~~L--T~~N~~L~~K~~A~~L~~Q~~A~~L~~D~~L~~T~~K~~N~~R~~I~~Y~~I~~H~~P~~K~~A~~F~~A~~N~~L~~W~~N~~L~~E~~E~~L~~L
 P~~S~~L~~A~~W~~L~~E~~L~~D~~H~~N~~K~~I~~T~~R~~I~~E~~A~~E~~D~~F--A~~R~~D~~T~~P~~M~~S~~T~~L~~S~~L~~K~~N~~N~~E~~V~~S~~Y~~V~~H~~P~~L~~A~~F~~T~~S~~L~~I~~N~~L~~D~~L~~D~~L~~
 Q~~E~~L~~K~~W~~C~~D~~L~~G~~S~~N~~K~~I~~T~~K~~I~~T~~S~~G~~T~~F--Q~~G~~E~~T~~G~~L~~Q~~T~~D~~L~~S~~N~~N~~K~~I~~H~~T~~I~~S~~K~~G~~A~~F~~L~~G~~Q~~D~~N~~L~~T~~V~~L~~N~~L~~
 K~~S~~L~~V~~W~~L~~D~~F~~E~~G~~N~~D~~I~~R~~S~~I~~N~~A~~R~~S~~F--A~~G~~N~~T~~S~~L~~T~~V~~L~~I~~L~~R~~N~~S~~I~~E~~S~~I~~E~~R~~D~~A~~F~~T~~S~~L~~G~~T~~L~~V~~E~~L~~D~~L~~
 P~~K~~L~~M~~W~~L~~D~~M~~S~~N~~N~~P~~L~~H~~H~~L~~S~~A~~D~~N~~F~~S~~A~~S~~G~~N~~P~~P~~L~~S~~I~~L~~M~~L~~S~~N~~C~~N~~I~~S~~T~~I~~Q~~K~~D~~T~~E~~Q~~A~~F~~R~~E~~L~~T~~A~~L~~H~~V~~

LRR

Ptychodera
 Periplaneta
 Anneissia
 Apostichopus
 Strongylocentrotus
 Patiria
 S~~D~~N~~L~~I~~S~~T~~I~~P~~A~~K~~T~~F~~H~~E~~L~~I~~S~~L~~A~~K~~L~~N~~L~~C~~N~~N~~R~~K~~L~~R~~R~~L~~P~~L~~E~~L~~F~~S~~N~~L~~H~~Q~~L~~R~~T~~L~~N~~L~~T~~G~~V~~K~~I~~T~~N~~I~~D~~
 S~~G~~N~~Q~~L~~V~~S~~L~~S~~S~~S~~V~~E~~F~~N~~L~~T~~F~~L~~M~~K~~L~~S~~L~~S~~N~~N--P~~F~~R~~L~~L~~P~~T~~Q~~L~~F~~R~~R~~L~~E~~N~~L~~R~~S~~L~~G~~L~~V~~D~~T~~D~~I~~Q~~N~~I~~D~~
 C~~G~~N~~K~~I~~S~~E~~L~~S~~P~~M~~Q~~E~~K~~N~~L~~T~~K~~L~~D~~R~~L~~A~~L~~G~~F~~N--L~~F~~D~~S~~L~~P~~L~~N~~I~~F~~D~~D~~L~~V~~N~~L~~Q~~S~~L~~R~~L~~E~~G~~I~~T~~I~~N~~N~~I~~D~~
 T~~L~~N~~N~~I~~S~~S~~V~~P~~K~~G~~L~~S~~S~~E~~L~~P~~M~~L~~T~~T~~L~~S~~L~~S~~F~~N--P~~I~~Q--L~~D~~E~~L~~S~~F~~S~~G~~F~~H~~N~~L~~K~~E~~I~~D~~L~~V~~G~~V~~D~~I~~P~~N~~I~~N~~
 S~~H~~N~~Q~~I~~S~~H~~L~~P~~E~~G~~I~~E~~D~~G~~L~~H~~T~~L~~E~~I~~L~~R~~L~~R~~N~~N--P~~L~~F~~S~~L~~P~~V~~D~~V~~F~~R~~G~~M~~K~~L~~V~~D~~L~~D~~L~~A~~E~~I~~I~~I~~G~~N~~I~~
 S~~G~~N~~K~~I~~G~~H~~F~~P~~S~~G~~L~~E~~R~~N~~M~~A~~N~~L~~T~~V~~L~~T~~I~~A~~N~~N--P~~A~~T~~S~~L~~P~~E~~D~~L~~F~~D~~D~~L~~V~~L~~D~~D~~L~~N~~L~~G~~G~~L~~V~~I~~N~~N~~I~~S

LRR

Ptychodera
 Periplaneta
 Anneissia
 Apostichopus
 Strongylocentrotus
 Patiria
 T~~K~~M~~F~~N~~S~~M~~O~~K~~L~~E~~H~~L~~Y~~F~~A~~K~~F~~H~~Y~~C~~S~~Y~~A~~S~~H~~V~~R~~D~~C~~S~~P~~K~~S~~D~~G~~I~~S~~S~~L~~E~~N~~L~~L~~A~~N~~K~~V~~L~~R~~C~~F~~I~~W~~I~~V~~A~~A~~
 V~~E~~L~~F~~A~~H~~C~~P~~K~~L~~E~~F~~L~~Y~~F~~S~~K~~E~~Y~~Y~~C~~T~~Y~~A~~P~~A~~V~~R~~I~~C~~R~~P~~N~~T~~D~~G~~V~~S~~S~~L~~K~~H~~L~~L~~V~~K~~P~~A~~L~~R~~V~~T~~V~~W~~V~~V~~A~~A~~
 Q~~R~~M~~F~~E~~K~~M~~E~~K~~L~~S~~I~~V~~F~~S~~S~~E~~F~~Q~~Y~~C~~S~~Y~~A~~P~~H~~V~~R~~N~~C~~N~~P~~K~~T~~D~~G~~I~~S~~S~~I~~Y~~N~~L~~L~~E~~S~~T~~A~~L~~R~~V~~S~~W~~T~~I~~A~~
 N~~A~~M~~F~~E~~Q~~I~~N~~S~~L~~I~~L~~H~~F~~E~~R~~F~~E~~Y~~C~~K~~F~~A~~H~~V~~R~~N~~C~~N~~P~~K~~T~~D~~G~~I~~S~~S~~T~~E~~N~~L~~L~~E~~G~~A~~L~~I~~R~~V~~S~~W~~T~~I~~A~~
 V~~D~~M~~F~~Q~~L~~T~~R~~L~~E~~K~~V~~A~~F~~D~~K~~E~~Y~~C~~R~~Y~~A~~P~~H~~V~~R~~T~~C~~T~~P~~R~~S~~D~~G~~I~~S~~S~~F~~E~~N~~L~~L~~K~~N~~V~~L~~R~~V~~E~~V~~W~~T~~I~~G~~I
 A~~R~~M~~F~~K~~G~~M~~T~~N~~L~~Q~~H~~I~~E~~F~~F~~K~~E~~Y~~C~~R~~Y~~A~~A~~H~~V~~R~~T~~C~~K~~P~~R~~S~~D~~G~~I~~S~~S~~F~~E~~N~~L~~L~~K~~D~~G~~I~~L~~R~~V~~S~~W~~T~~I~~A~~L~~

Hinge region

Figure S12. Sequence alignment of various gonadulin receptors.

Ptychodera TLVLCNLA VILGRMCIMK IENKVHSLLIK NLCCGAD LLMGIYLV IIGSHDLMYRNHY YI
 Periplaneta VTCAGNALV LWGRF-SSRDENRVHSLVIRNLAVSD LLMGVYLLVIGTQDCQFRDRYHK
 Anneissia MTFIGNEGVFISRL-LMKAHRVYSLFIMNLCAADFLMSIYLF TIAAODYRFRD VYNQ
 Apostichopus LTTCCGNLNVFISRI-AIHAENKVH SIVVSNLCAADFMMGLYLF AIGIQDAREFN NYID
 Strongylocentrotus ITSVGNLGVLVSR A-FMKAENKVH TVVVINLCTADFLMGIYLL IIGTHDVKYRDN YNQ
 Patiria LCFLGNIGVLISRY-LMKAENRIHSLV VVNLCTADFCMSIYLFVIGYHDAKERNQFNT

■ TM1 ■ TM2 ■

Ptychodera YSHKWMTSWTC SLCGFLAVFSSETLLVLT VVISVQRFCLIA FQTRMIH-FKYSYGVIS
 Periplaneta EAHSWMTSWKCTV VGMVAMTSSEVSVL IILVFLSMERFLLI AVPFGGHQ NMSMRTTCLS
 Anneissia NARQWVESTGCKMS GFLAMVSSEVSVL L LALISVERFLCIVFPYEFHR-LKVKEAAVI
 Apostichopus YALDWSESWGCHFV GFLALLSTEASVLT LTFISLERFFIVAFPYRFHR-LNIKEVVS V
 Strongylocentrotus HALEWTNGITCKV SGLLAMI SSEVSVL TLMFISLERFY IIVYPYSEQR-IKTRRAIMV
 Patiria HALEWMOGSACKFAGFMAMF SSEVSVFMLTFISLERFICIVPYRLHR-LTSKEALVI

■ TM3 ■

Ptychodera TAAAWITAAALAA FPLTM-SSENFHYGKNGACFP LDPNDFEAGWQYSVAMFLGLNA
 Periplaneta LAVIWEIGVCLAA VPMYWINSTRFYGTNGMCFPL-HIDDPFLLGWEYSAFIFLGVNF
 Anneissia ISSIWA VAGILIAWI PPLAEGYFGNFYGTNGVCFPL-HIHGPRIKGWEYSVAIFLGMNL
 Apostichopus LILIWIVAFVLAAS PLIFTEYFKNFYGANVCVCFPL-HIHDPRLGWEYSIFIFLGIN T
 Strongylocentrotus LAFIWEFGTLLAVVPIIPVDYFGNFYGSNGVCFPL-HLHEPRMRGWEYSVVVFLGINS
 Patiria MTIIWFLGALVAWI PPLISVGYFVDFYGSNGVCFPL-HIHDPWLOGWEYSAFIFLGLNA

■ TM4 ■

Ptychodera VCFCLIVCSYVGMFYSIRETRNAAFK DINLRRRGDMNFAKRFFV FIVLSNALCLVPIML
 Periplaneta SSLLLI AVL IYAWMFVSIWRTRHATP---ISSV GDFEFVIRFFFIVLTDAGCWAPIFA
 Anneissia LALILII VSYIGMFISIRTRKAAV---QIGYK GDMTYARRFFFIVLTD SLCWIP III
 Apostichopus F S F M V I I F S Y C G M F Q S I Q K T R K R T T --- T - L L P G D I N Y A K R F F F I V L T D C I C W L P L A V
 Strongylocentrotus TAFVAIALSYTGMF LSIRKTRRAAA---QCGMK GDMAYAKRFFFV I L T D S L C W L P I A V
 Patiria TCFTAIAI SYTGMF ISIQQTRKAAT---HLGRR GDMNYAKRFLFVVM TDALCWLPIAI

■ TM5 ■ TM6 ■

Ptychodera ITAMVFTDIGVP GQVYAWTTVFVVPINSASD P L L Y T L T T V P C K Q G C L G M L D K K L K R Q K
 Periplaneta LKLVALGRVHIPADLYAWVVVFILP VNSAVNPLLYTF TTPKYRGQLCQLG----CPPQ
 Anneissia LKVISLNCNIP IGDNLYAWIVIFVLP LNSALNPILYTLSTTTF SOWFLKLL----KIHK
 Apostichopus VKVLAVADMPVSESIYAWVVIFILPINSALNPILYTLSTTGPFRRVLLQKI----KNRG
 Strongylocentrotus LKVM S L C N F I I S E T L Y G W I I V F V L P I N S A L N P I L Y T L S T T S F A M W F M R Q L ----KRGK
 Patiria LKILSLCSYEIPATLYGWIVIFVLPINSALNPILYTLSTTSFTQWFQKHL----KRRK

■ TM7 ■

Ptychodera ESGTRKMLVSSTTGSRSSRDSSGTTRLTSSGS-----SGSPSODT-----
 Periplaneta TLATKRHSSADTELSRSSSTNRNAVDRRADN---GLYAMLPA RDP AHT-----
 Anneissia QVS---HNYVTYSPQRTARRKSGIAEENGSTDGMMSYANRPSLQTNCS-----
 Apostichopus KHT---ETGAIPKNERFSNGTN---DTAGETLRLO--SNLTM-----MGGNKHEANK-
 Strongylocentrotus FKT---SGCYIGSNVDMSELRG---RIEESGA-FTSYTNMFKRASFFLPTRKHHVSSK
 Patiria GKS---SNGSLGSKNEFSTTRG---RIGSTTDQPT EYSSIPKRSYDSNNS-----

Ptychodera ---KPCIE M---DTAQPLVQN-----SSVGQIQSGQS-----C
 Periplaneta -----
 Anneissia ----DLLSTAI SEDAAEDVRNNTQYKAQHSD-----NEQPAST-YFVTC
 Apostichopus -----T-----MAENTC-----
 Strongylocentrotus VEAIPAVSSSVPSRSATTTAMTNNIRPLHTINEGEIVDNHSQSOGNHQLR RTPIVRLC
 Patiria ---SPVLEEE---QCSTV-----

Ptychodera A---
 Periplaneta ---
 Anneissia V---
 Apostichopus ---
 Strongylocentrotus DLME
 Patiria ----

Melibe MEESITPREGSGSEAEESGSTTTATAKLWQHTRARHYLVFLGVMICVALIVVLVCVT
Drosophila MSIAI-----MPHLPITFTLAAILLAIASNEGAQG
Periplaneta -----
Anneissia MEY-S-----DKCRPF TKVLFHCLLVLQLFFSFHL
Lytechinus -----MNLALLMVVVTSFFDTSLA
Strongylocentrotus -----MNWAVLMVVVSSFFGTPQV
Apostichopus ---M-----KTMALICHKILQVLI AALFLGV--
Holothuria -----MMTNILVFLIISMVTRD--
Acanthaster -----MRKLRNALRMLFVLHLCA--
Patiria -----MHKLRNALRMLLILHVCA--
Saccoglossus -----MNLIGDVRKLYLNTALR-A--
Ptychodera -----MKKSLRFLILSL-V--
Shizocardium -----

Melibe ST-----TEK-----AEALTNALGAS
Drosophila VESATRTAIEAIRTGIGTKPETE IADATEAEAPVREVISLLGIIDGAESDILVPAADD
Periplaneta -----MFLLOQLF-AVITVTETVGTFF
Anneissia VL--TC-----RVI-----INTCPDVQEVTSKSPHG
Lytechinus SH-NTK-----DDHLDDA-----P-VIRHRQAPMSTDPHA
Strongylocentrotus SN-ATK-----GDDLDDA-----PSLIRYRQSPMTSDPHA
Apostichopus ---TFA-----GKEVDQS-----VELHRVRRQ---SSSDVHG
Holothuria ---AVA-----TQGDLDV-----YGARRVRRQ---SNSDNHG
Acanthaster ---SR-----RAEQDGA-----IIRHIQR---RAVDAHK
Patiria ---AR-----RVKQDSA-----LRHLQR---RTVDAHK
Saccoglossus ---VH-----GYSQRQR-----MGRVHQR---IV--RGT
Ptychodera ---SS-----SVSKRGR-----LGHSPHR---RLPRSFF
Shizocardium -----

Melibe RCPNTERCPSDGR CINRTLVC DGRKQCTDGADEGTVCD--KDKMD-----LWSDM
Drosophila KCPGGYFHCNTTAQCVPORAN CDGSVDDASDEVN---CVNEVD--AKYWDHLYRKQ
Periplaneta LCKEQEKCNKSRLCVPQDRN CDGIPDCPKSDEWD---CSDKLG--SQFWDHLYRKN
Anneissia DCPGFREP CQNSSQCVPGNFI CNGISDCDNGSDELP--EECATNNPLYTNIWTHIYGSE
Lytechinus HCGE-WEP CINSTQCIPQEAIC DGNIDCDNESDES--EEDIDDKN--RRVYTFMDQGK
Strongylocentrotus HCGE-WEP CINSTQCVPQEAIC NGI FDCDNKMDSD--EEDIDDIN--RRIYTFKDQGK
Apostichopus HCQVTEEP CGNSTECVLOSKH CDSVVD CANGADEDE--EDDDMDN--TNNFDFLFGKK
Holothuria HCGL-DEP CGDSMCVVTOSQQ CDGVADCDNGADEEE--EEDTEDD--YRHFDEIIGRK
Acanthaster HCGK-DEP CLNSTQCVPQDSI CDGTPDCDNGSDEWEVEE CRDWNL--AKMWNFFGTK
Patiria HCGV-DEP CLNSTQCVPQDAI CDGTPDCDNGSDEWEMEE CRDLNL--AKMWDFFGTK
Saccoglossus CSGI-QVK CTNSTQCIFRDQL CDDHVD CDNGSDEWS--SECTEDD--NTNWDILIGOK
Ptychodera CLDN-SFK CLNSTDCIFREYL CDGIED CDNGSDEWD--EECTDYND--GENWDIKIGDK
Shizocardium -----

LDLa

Melibe FNKRLDADR-----
Drosophila PFGRHDNLR-----
Periplaneta PSAELDEED-----
Anneissia RRGGDGDSDEED-----
Lytechinus TDSSEEDD-----
Strongylocentrotus QDSSEED-----
Apostichopus ED-S--EER-----
Holothuria EE-L--DEL-----
Acanthaster NDDSGEEDDLDQGLRPQ---QTVFDAHGHCGEEFP CMNSTQCVPREAI CNGKPCD
Patiria D-ESGEEDDQGLSPDPLPQRSFDAHGHCGEDFP CINSTQCVPQEAICNGEPD
Saccoglossus SDSEEEED-----
Ptychodera DDESSEEGEDD-----
Shizocardium -----

LDLa

Melibe -----EKEAKNCVWDKIESRCVCR-----
Drosophila -----IGEC LWPNEFSCPC-----
Periplaneta -----L-VCELMINSSECAC-----
Anneissia -----FNPDNVCENGTYPPNCTCYLKCISRH
Lytechinus -----FIPPACDIGTYPEECRCVLLYEDPM
Strongylocentrotus -----FIPPACDAGTYPDVCRVLLHEDPM
Apostichopus -----PPPVTCTDTIFPDECECFVVFDEES
Holothuria -----PPREPCNGTVHPPECKCFVVAEE--
Acanthaster NGSDEEEIV-CRNKKM-----RDNIEDIRQEIPEEGTFPES CDFVEIEQTR
Patiria NGSDEWELEE CRDWNLAKMWDFFGDKAEDEDVRRREIPCEKGTFPES CDFVEIEETR
Saccoglossus -----NESETIECDNGSYPEECNCTHIFILREN
Ptychodera -----LGGSRIPC AKDTPNVNCTYIEFENG
Shizocardium -----

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Melibe -----EKGKLYC---RD
Drosophila -----RQDEILC---RF
Periplaneta -----VERSVLC---NN
Anneissia GGN-----A-----DDGCESEVFCYTTENT
Lytechinus AHF-----DYYES---MLQDA--YP----SVFAEPPIGATSEPLGLEIAC---TS
Strongylocentrotus VNF-----DYYES---LQDV--YP----SAFADPLFGESGEPMGLEIAC---TS
Apostichopus -----GLENDEPIGLQLDC---QL
Holothuria -----GEIIGLELLC---PQ
Acanthaster TAEPLSLASPYNTTGDASTYRDA--YDIDSNSTDGVRYGSEVRGVVIGIRLDC---RA
Patiria -KDLPSLASPFNATGDASMGAGVDDVGTETNVTDGIPYGLGVQGVVGVRLDC---SA
Saccoglossus GFM-----TSE-----N-----QFYTIIDTRLDC---SH
Ptychodera HNA-----TSR-----SDE---HPNDNSPYAIHIDC---SD
Shizocardium -----

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Melibe QDLSATAHPLPQYT-SVLELSGN-ITSTSRLSIGRLPSLHTIIVIHRSRVEKIGALTEFD
Drosophila QQLTDIPEERLPQHDLATLDLTGNFETIHETFFSELPDVDSLVLKKFCSIREIASHAEFD
Periplaneta MGLTLPPLLPARGIELDLTGSSFPVLNATIMDTLPDLEILVLSHAGIKEIQQEAFS
Anneissia TGFTTVPRDLPTNT-VLIDLSDNYTSVVRKGDLDHLPYLRTLYFSRNRNLRFESDAL
Lytechinus KRLERVPEGLPPGT-LYMDLSDNRITHLHGDSFQNLTRLRELVIITHNQMQSMDEDVVEY
Strongylocentrotus KQLDRVPEALPADT-LYLDLSDNRITHLHDDSFKNLTMLRELVIITHNQMQTMDEDVVEY
Apostichopus SELESVPDNLPRDT-VYINLAGNSLSNITVETFKTLTKLRRDLQSNRIGSLHPDSEF
Holothuria SGLTSVPRGLPRET-IYINLAANEITTDKDSFDEVTSLKKRLLYQSNKISILHPQSLN
Acanthaster KQLTNVPRNLPNNT-ISLDLSDNKITHLTKKDLTNLPQLRQLLSRNKLRMEEGAFK
Patiria RQLTEFPRLPNKT-ISLDLSDNKITSLTKKMEHLTHLRQLLSRNKLRNVEEGTEF
Saccoglossus RNLTSTPGGIPPNI-TKINLRYNSIQEVKAGDLYGLYDLTELLSRNIINDIAERALD
Ptychodera RNLTAVEQNIPDNT-TEIDLSONSIETIRKADFAGLFMVKNLLSKNSIREIEEGSEFD
Shizocardium -----MIQIEIGSEDLGGLVMLRELLLKKNNLTKLNSSSLS

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LRR

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Melibe EC-----
Drosophila RQAD-----
Periplaneta KA-----
Anneissia -----
Lytechinus DTR-----SLEMLDL
Strongylocentrotus DTT-----SLEMLDL
Apostichopus QLR-----SLEMLDL
Holothuria KLL-----KLEILDF
Acanthaster PLT-----
Patiria SLT-----
Saccoglossus HLANLMVLDLEANKLKTLPESVFSFLNNLVDLDLSKNDLGTLPYIYFKNLNKLQKMDL
Ptychodera DLRDLLILSLDRNKLTSLPASVFQVTNLRLELSLELNDISNIPDTVFQNLGHLLEEDL
Shizocardium DLVNLEKLAIESNKLTTIPVDIFSKMKNVQILTLAKNDLQHLFVGVFASLRRLEEDL

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LRR

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Melibe -----PSTANVHFTFNKLSRFS
Drosophila -----NPLRRLYMDDNKLPHP
Periplaneta -----PSLHTLYLDNNQLRTP
Anneissia -----NNLTISELNLVGCQMGTI
Lytechinus SDNRIERTITSAHFDSLRRSLRLSRNH-FRCEGDGCFRNLSVSLRELELVACGITELT
Strongylocentrotus SDNLIETIITAAHFDNLQKLTLLRLSRNH-FRCEGGDCEFRNLSVSLRELELVACGITELT
Apostichopus SNNRISSLSKEYFLFNGILKELLKHNPIQRLEDAELFINLQMLETLDFFGAQISELR
Holothuria TNNKISWLGSQLQQLFSLKELTLKHNPIRRLNDSDMFRHMYSLQTLNFLGAQISELR
Acanthaster -----DLETLRMIACDLEDVQ
Patiria -----DLQTLRMIACDLEDVQ
Saccoglossus SGNEIRLI-QSEFLFGQGSLDVLHLGWNRPLEISEHAFSALRNLTRMRLLDNGLSHLR
Ptychodera SGNEIRLL-GKNLLRNQVTLKKLQINWNRPMIEFGAEDNTVNLNTRLRIDNGISHIR
Shizocardium SGNELRRL-DKDLFENQSGLKTLLQLNWNKPLELEFGVFDRLKDLQIETGLLDTGLSHIR

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LRR

Melibe SSVFAKRNSIYYLNLMGNAIKE L TSGDFRRMKS LKKLDLRDNKITS TDEGVFEDTPHL
Drosophila EHFPEGNQLSILILARNH LHH LKRSDFLN LQKLQE LDRGNRIGNFEAEVEARLPNL
Periplaneta EPALQPGNILLDTLILRNNE LSKLPKN AFLN LQYLRE LDRHNHLADVDGDVEQPLVRL
Anneissia DGLFSGM SHLMTLHLQYNN LVT INKDTLKG L D W L M E L N L N H N E T S D L N P M A E N H T P N L
Lytechinus PDMFRNLHSLSVLQLSYNAITE I T P S H M N G L E G L Q D L Y L S S N H I S H T E N G S F D G M D R L
Strongylocentrotus PDLFSNLHSLSVLQLSYNAITE I T P S H M N G L E R L Q D L Y L S S N H I S N T E H G T E D G M D N L
Apostichopus TGVFSPLENLRKLVLAHNEIEAL T Q G N M E G L R N L L E L D L Q N N E V S F T E D G T E K E M P M L
Holothuria TGI F E P L T K L T R L V L S H N Q I E A L T Q G N M A G L S S L Q T L D V Q S N D I S F T E D G A F I E L S L
Acanthaster QRMFAAQKRLVTL D L R Y N K I T R L V K N S L F G L R N V K Y F D I R G N Q L S E T E T G V E D T P K L
Patiria PRMFATQNRLLVTL D L S Y N I L T R L V R G S L F G L H N L E Y L D I R G N R L A E T E T G V E K D S S R I
Saccoglossus SGMFRNLNRLKEL D L E R N Q I L S T K K Y D L Q G L T D L S H L K L K N N T I R R I E D G A F D H T P S I
Ptychodera SGI F R N L N K L T K L D L E R N F I L S T K K Y D L Q G L H N L S S L Q L R N N S L T R I E A G A F D H T V K L
Shizocardium SGI F C N L G K L T K L D L E R N K L L S T K K Y D L E G L D N L K D L L L T N N T I Q R T E S G A F D H V G K L

LRR

Melibe ISLDMRGNL L T E L V P G M F - D G L Q D L R K L Y L G N N A I A E I A P C A F A S L S K L R A I N L A R N R
Drosophila EVLYLNENH L K R L D P D R E P R T L L N L H T L S L A Y N Q I E D I A A N T F - P F P R L R Y L F L A G N R
Periplaneta EILYLNENRL D S V P L - - - S L P L P S L Q L L S L T H N H I A W I E P G A F S Q L P R L K H I Y L S W N Q
Anneissia VILNIQYNK L Q V L S P P L L - E P L T Q L K T L G M S F N Q I S E I K N G F F E S Q T H L Q D L L M G N K
Lytechinus LKILLHDNK L K N I S V G V F - P F M P E L V I L K L D E N E I D M I E P G S F S L V M N L Q H F T L M E N K
Strongylocentrotus LKILLHDNK L T N I S V G I F - P V M P E L Q I L K L D E N E I A I E P G S F A L I E N V Q H F T L M K N R
Apostichopus NELRLHGNK I H E V K Q G M F - E D L A N L T I L L L D Q N L I H T I E P G S F S K L F K L Q H I T M S N N M
Holothuria EE L R L H G N K L T K V K R G M F - T N L A Q L R T L L L D Q N E I E S I E P G T F A E L T N L Q H F T I S D N L
Acanthaster YFMLVSONK L S S I P A N L L - R P L R E L R T L D V H R N D I S V I E T G A F S T N T K L I E I N L R D N K
Patiria YFMHISQNR L S S I P A E L F - R P L R D L R S L N I H R N D I S S I E C G S F S T N T K L R D L N L G D N K
Saccoglossus SE L W L S M N D L T E V K R S V F - L P L K N L K T L D L S F N K I E F E D G A L S N S V I L A I L L L A G N R
Ptychodera Q L R L S L N T L P A I K K D V F - E P L Q E L K I L D L S H N K T E D I E S G L S N S T R L S H L L L A S N K
Shizocardium E T I G L S F N D L V E I K K D V F - S P L K E I R S L D F S F N K I Q R I E T G A F A N S R L M T H L F I S D N N

LRR

Melibe I R S L R D C G L D G L G N I T T L D L H Y N G M H T I E S H A F K S L V S A R S V D L R S N H L I S I G N C T E S
Drosophila L S H I R D E T F C N L S N L Q G L H L N E N R I E G F D L E A F A C L K N L S S L L T G N R F Q T L D S R V L K
Periplaneta L W L R N D T F D N I P E L L S L S L N G N K I R L L E V N T F K E V P L L T S L Y L Q D N Q L K L L D S R V L R
Anneissia L T V I K V G M F Q N L Y G L L S M T L R E N N I R E V Q A N S L D H I E S L Q S L S L A K N P F E S L P D H V F C
Lytechinus L S R I E L G M F D G L E N V T D M S L R Q N E I K A I E E N A F D N L I R L D H Y - L R E N K L T E V P R E L F T
Strongylocentrotus L S R I E V G M F D G L G N V T D M S L L E N E I K V I E E N A F D N L I K L E S L D L Q K N K L T E V P R E L F T
Apostichopus L T H L T V G M F D G L S V S S L S Y A N K I T E M E N G T F E P L I K V S S L N L K D N L F R V P R G I F D
Holothuria L T H L P V G M F E G L S R V S L G L F D N H I E T M E N G T F A P L N N V E S M L R E N P F R I V P R G V F D
Acanthaster L T E I R R G I F H S L T S T I T L S L S N N S I R H L E Q D A F A G M N L Q T L K L T K N P F T S L P V G T F D
Patiria L T E I K R G L F H N L T S V I T L S L R N N S I R H F E E D A F A G M N L Q T L K L N Q N P F T S V P I G I F D
Saccoglossus L P F V R T G M F A N L T K V S N L P L F D N E I A W F D A D S L Q D M E S L R T L D L Q H N P V O R L P M V I F D
Ptychodera L S I L R N G M F T S L S S V T N D L L D N E I R S L E P G C F D D M L S L Y T L D L R E N P F T L L P R G L F D
Shizocardium L H D I R I G M F S G L A T V T N M E L N N N D I E V V E A G A F D D M T S L Y T L D F Q K N P F T R L P R G I F D

LRR

Melibe YMH-QLHYIYFDK F H M C L Y A Q H S Q Q C L P L G D G I S S K E N L L E S I V L R I C V W V V A L L S L G
Drosophila N L T - S L D Y I Y F S W F H L C S A A M N V R V C D P H G D G I S S K L H L L D N Q I L R G S V W V M A S I A V V
Periplaneta H L Q - N L E H I Y F D E F K L C S A A L H V R V C E P K G D G I S S L Q H L L D S I V L R A S V W V M A V L A C A
Anneissia A M T N T L D T I E F D S F S F C G F A P H A R H C Y P S T D G L S S R D H M L K S V I L R I S V W I V G S I A L F
Lytechinus P L E - N L N N I Y F D Y F F M C G Y A P N V R V C L P K G D G I S N V D D L L G N W L L R G A V L V A L L G S F
Strongylocentrotus R L K - N L N N I Y F D E F F M C G Y A P N V R V C L P K G D G I S N V D D L L G N W L L R G A V L V A L L G C F
Apostichopus V M P - M L G H I Y F D H F F L C G F A P H V K D C D P K S D G L S T S E D L L G S I V L R V A V W L V S I L A S F
Holothuria V M P - K L S H I Y F D H F I L C G F A P H V K D C N P K G D G V S N S E N L L G S I V L R V S V W M V S I L A T F
Acanthaster Q L I - S L K A I Y F D H F S L C G Y A P H V R L C M P K S D G I S T A E N L L G N I L L R F A V W F V A L L A S L
Patiria K L R - S L K A I Y F D H F S L C G Y A P H V R L C M P K S D G I S T A E N L L A N N L L R F A V W F V A L L A S L
Saccoglossus D L P - S L E W V H F D H F W M C G Y A P T V R H C T P R G D G I S S E N L L D N V L R V M V W V V A M L A F V
Ptychodera N L L - S F E W I Y F D H F S L C G Y A P T V R H C S P R G D G I S S I E N L L D N M V L R I M V W V V A T L A F I
Shizocardium K L G E S L Q W I Y F D H F S M C G Y A P T I R H C E P R G N G I S S I E N L L D N M V L R I M V W V V A L L A F I

TM1

Melibe G N M V V F L G R F - L L R E D N Q I H S F F I K N L S M A D L L M G L Y L L I I A I H D I K F R G O Y I L H D E S
Drosophila G N L L V L L G R Y F Y K S R S N V E H S L Y L R H L A A S D F L M G T Y L T L I A C A D I S F R G E Y I K Y E E T
Periplaneta G N T V V L L G R L V A R E - P N P V H S L Y I K T L A L A D L L M G I Y L M I I A S A D W H Y R D V Y V R H D F Q
Anneissia G N L F V L T T R L F V N E - T K R V H A F L I M N L A F A D L L M G I Y L Y L I A I H G A L F R D N Y I L Y D I V
Lytechinus G N L L V I L A R C F V S E - D N K V H S F F I M N L A V A D F L M G L Y L L I I G L H D V M F R G E Y I F K D L N
Strongylocentrotus G N L M V I F A R C F V S E - D N K V H S F F I M N L A V A D F L M G L Y L L I I G L H D V M F R G E Y I F K D L D
Apostichopus G N L I V L F A R C V S K E - D N K V H S F F I I N L A I S D F L M G A Y L F I V A H D V M Y R G V Y I L H D V D
Holothuria G N L V V L F A R C L S K D - D N K V H S F F I I N L A V A D F L M G A Y L F I V A H D V M Y R G V Y I L Y D L D
Acanthaster G N A F V L L A R C F V N E - D K K T H S F F I M N L A V A D L L M G L Y L L I I G I H D V I F R G S Y I L H D L T
Patiria G N A F V L L A R C F V K E - D K K T H S F F I M N L A V A D L L M G L Y L L I I G I H D V I F R G V Y I L H D L A
Saccoglossus G N L F V L V A R C I L K E - D N R I H S F F I M N L S L A D L L M G L Y L F I I A L H D V M Y R G E Y I K F D L E
Ptychodera G N I F V L I V R C V L K E - D N R V H S F F I V N L S F A D L L M G L Y L F I I A V H D V I Y R G E Y I K F D L S
Shizocardium G N I F V L I A R C I L K E - D N R V H A F F I M N L S F A D L L M G T Y L F V I A I H D V I Y R G E Y I K Y D L S

TM2

Figure S13-continued.

Melibe WRNSWECDFAGVLSSTLSEMSVLTLSVITLDRYISIMYPLSLRRRGLRVAYFVMAITW
Drosophila WRHSGVCAFAGFLSTFSCOSSTLTLTLVITWDRLMSVTRPLKPRDTEKVRIVLRLLLLLW
Periplaneta WRHSPVCNACGFLSTLSCASVLIILTLITRDRLVSVTRPLDRRQPSLRHATLLVAVLW
Anneissia WRSSDICTIAGCLSILSSMMSVFTLSVITLDRYVSVIVHPFSEYESKSLFRAAILMGVLW
Lytechinus WRSGWVCRMCGLLSLLSSEM SVLTTLTVITSDRFISIVHPFKFRQRHLAHAVILMVAFW
Strongylocentrotus WRSGWVCKMCGLLSLLSSEM SVLTTLTVITSDRFISIVHPFKFRQRHLAHAVILMVGFV
Apostichopus WRSSWVCQLCGAFSLLSSEM SVFTLTITADRYFCIVHPFRFRSRNLIPAAILMGCLW
Holothuria WRSGWVCQCGAFSLLSSEM SVFTLTVITADRYFCIVHPFRFRSRNLIPAAILMGVLW
Acanthaster WRNSSVCKLSGFLSLLSSEVSIMTTLTVITLDRFLSIVHPFRFKNRSLVHARLLMVFLW
Patiria WRTSSVCKLSGFLSLLSSEVSIMTTLTVITMDRFLSIVHPFRFKNRSLVHARLLMVLLW
Saccoglossus WRLGWVCQCGFLSLLVSEASVLTLLAIIITMDRFLSIVHPFKFKNRRNMKIAVFAMLLIW
Ptychodera WRTSWICKLGGFLSLLVSEASVLTTLTVITLDRFLSIVHPFKFKNRTIKLAFLLIMATMW
Shizocardium WRLSWVCQLCGFLSLLVSEASVLTTLTITLDRFLSIVHPFKFKNRRNLKLAFFWMLMVW

TM3

Melibe TVCIM-LVSLPVMG--LEYFGDSFYRDNVCTPLHLHHPRAK GWEYS SFLFLGINFCS
Drosophila GISFGL-AAAPLP--NPYFGSHEFYGNNGVCLSLHIDHPYAK GWEYS ALLFILLVNTLS
Periplaneta LVAADV-AAAPLCAETVEYFGEFFYGGNGVCLPLHVQDPFAD GWEYS AAMFIALNTVA
Anneissia LFGITL-VLIPIM--KQTFGELEFYGSNGVCLPQIRHPWATGWVFTTTLFVGLNSVF
Lytechinus LAAMLI-AILPVLH--RSYFGEFFYGGNGVCLPQFDRPFDHGWEFTLVVFFLNLIA
Strongylocentrotus LAAMLI-AILPVLH--RNYFGEFFYGGNGVCLPQFDRPFDHGWEFTLVVFFLNLFA
Apostichopus IIGITL-SILPLH--RSYFGDEFYGGNGVCLPQFDRPFDHGWEFTLVVFFVANLLS
Holothuria LLGITL-AMLPLVY--KTYFGDEFYGGNGVCLPQFDRPFDHGWEFTLVVFFVIANLLS
Acanthaster LLGIAL-ATIPLH--TAYFGEFFYGGNGVCLPQIDQPFADGWEFTLVVFFVFNLVA
Patiria LLGVAL-ATIPLH--TEYFGEFFYGGNGVCLPQIDQPFANGWQFSLVIFVFNLVA
Saccoglossus ISCVII-ATLPLID-AITYFGDEFYGGNGVCLPLHIDDPKADGWEYSLVIFVFNFMA
Ptychodera SICIFL-AVLPLID-HLEYFVFFYGGNGVCLPLHIDEPMTNGWEYSLFIFTFINLVA
Shizocardium IACVFL-AILPLIH-VITYFGAFFYGGNGVCLPLHIDEPKAN GWEYSLFIFVFNFVA

TM4

TM

Melibe EAFIAYAYVAMEYSIHMSALPLRSTRDSKERCLVQRFFIVLTDQVFCWVPIIILKILA
Drosophila LIFILFSYIRMLQAIRDSGGGMRSTHSGRENVVATRFIVITDCA CWLPIIIVKLA
Periplaneta LLFISFAYWRMLRVVRS SGLSLRSTQERODKAVAQRFVIVATDCLCWPIIIGVLA
Anneissia ELFVVYAYIAMEVMIRSD-DVRSTKKS QDSAILVRFTLLVFTDMLCWLPIICVIVLA
Lytechinus FIFILYAYARSKAIPRMNKMGRSTKES QDWNLLKRFTIIVATDFICWMPPIIVKIAS
Strongylocentrotus FIFILYAYAQMFAVRKKS LAMRSTKES QDWNLLKRFTIIVATDFICWMPPIIVKIAS
Apostichopus ETFIVWAYIRMEFTIRRSNLAARSTKVS ODYALLKRFTIIVATDFICWMPPIIVKFVT
Holothuria ETFIVWAYIRMEFTIRRSNLAARSTKVS ODYALLKRFTIIVATDFICWMPPIIVKFVT
Acanthaster ETFISYAYLMMEMTIRRSNLAARSTKKN QDWALVKRFTLIVATDFICWMPPIIVKFVA
Patiria EAFISYAYLMMEMTIRRSNLAARSTKKN QDWALVKRFTLIVATDFICWMPPIIVKFVA
Saccoglossus ELFIVFAYMAMETS IKKSRSNIRSTKEN QDLLLVKRFTLIVATDFICWMPPIIIFKFAA
Ptychodera ELFIAFAYAMENAIROSRTNIRSTTEN QDYMLAKRFTLIVATDFICWMPPIILKLVA
Shizocardium EVFISEFAYVAMESSIRKSRNIRSTKEN QDLVLVKRFTLIVATDFICWMPPIIVKFVA

M5

TM6

Melibe LSGVALTVDLYAWVIVFVILPVNSALNPILYTLTTOYFKKKLFSKFSAVVFRPVLRS D-
Drosophila LSGCEISPDLYAWLAVLVLPVNSALNPVLYTLTAAAFKQQLRRYCHTLPSCSLVNNET
Periplaneta LAGARVDQQLCAWLAVLILPVNSALNPVLYTLTTSF FKSQMSRLLHAWKSRDTGPHSD
Anneissia ISGYPVSGDVYSWLAFLVLPVNAALNPILYTLTTSKLFROQLR---IILHKRRATGY
Lytechinus YAGIVIPQSVHAWFAIFVLPVNSALNPILYTLTTOYFRQKFLRPIRRICGRQKQKAY
Strongylocentrotus YSGIALIPQSVHAWFAIFVLPVNSALNPILYTLTTOYFRQKFLRPIRRICGRRQKQKTY
Apostichopus YGGVALPPAAHAWFAIFILPVNSALNPILYTLTTOYFRKRMIFHPSRTFMGKQKSTAGH
Holothuria YGGVILPPTAHAWFAIFILPVNSALNPILYTLTTOYFRKRMIFHPSRALMGMSKSAGGN
Acanthaster LGGVSVSOSVYAWFAIFVLPVNSALNPILYTLTTLVLFROKILAPLGIKAKRK--KGY
Patiria LGGVSVSOSVYAWFAIFVLPVNSALNPILYTLTTLVLFROKILAPLGIKAKRK--KGY
Saccoglossus LAGAQLISGGVYAWVAVFVLPVNSALNPILYTLTTLKMFQKQFMKLLGISNKKKN--AG-
Ptychodera LAGVKVNGDIYAWMAVFPVNSALNPILYTLTTLKMFQKQMLRALGVHLRD----KA-
Shizocardium FAGAKLNGDVYAWIAIFVLPVNSALNPILYTLTTLRMFKQKMLRAFGVATK----KE-

TM7

Melibe -----KDS-----N-----QSRSSMKNNNTLYSRHMHD
Drosophila RSQ-----TQTAYESGLSVSLAHLGGGVGGGSGRKRMSHRQMSYL-----
Periplaneta SAG-----SLSNIQLSTRKRHLGSPPTRSSTL-----RSHSSYKSIRGT-
Anneissia RRG---RRDDSDSFKRSGTRLSLI--PVRSKASLKS KSS--IDKTKSNS-----
Lytechinus QSG---SYDDSIITGTKITATKLSII--SHNGKPRAGSVNG--RLNSTKGS HGHHRP--
Strongylocentrotus QSG---SYDDSIITGTKISATKLSVI--SHNGKPRAGSVNG--RLISTKGS HVHHRP--
Apostichopus EMSQSMSRTRDREIGHTATSRLSVI--SHSNTMKNGT-----
Holothuria DMSQSVSRSRDREMGNATSRLSVI--SHSHQMKNGGGTA--TPG-----
Acanthaster ITG--VSVDETSTMSKNSGTRLSII--SNKS--RGGSLNG--R-----FNSQ
Patiria LTG--ISVDDTSTMSKNSGTRLSII--STKS--RGGSVNG--R-----FSSH
Saccoglossus -----DESYSAKTTGTRLSV--ASSR--NRISLNG--NIKIYYSIPFICSTI
Ptychodera -----DESLTASKTTGMRVSTF--GQR--SRSTTST--NGKARNGSFHDNVQDN
Shizocardium -----DDSFTASKTSGTRLSST--GSR--TRISISA--K--NSNGSIGTRATSL

Melibe LEMDLLRRYGNASRSGT----QTTTTTLSTSR---IPHNGKATSVRPRAQSDNALNIR
Drosophila -----AV-----
Periplaneta -----AV-----
Anneissia -----AV-----
Lytechinus ---SEVQPWLPDSSGRP SHLKRPSLRMEDMSCRKE-----PEVVV
Strongylocentrotus ---SEVQPWLTPDSSGHP SHPKRPSVRVEDTSCREE-----PEVVV
Apostichopus -----PTTPRNG--HMENLSHED-----
Holothuria -----GTPAAERNA--HMENMSNDD-----
Acanthaster KKLKNLSSLDSTDESVTCSAAQTT---SLKIKKHRA-----A-TAD
Patiria KKLKNFDSLDSSESVICTATKTT---T---KKRA-----V-TVE
Saccoglossus FRLKTI LFFIIKKS DTPAS--STT---LRDIKLAAA-----PKSLR
Ptychodera -QFDRDVAFDNQ GADMS-----GEPIALSVQ-----AEHLR
Shizocardium RTTSREQTYPVKDCNYV-----ELTTIYTP-----PE---

Melibe PNVGNA---SQPISNI-----
Drosophila -----
Periplaneta -----
Anneissia -----
Lytechinus VHSNSQN--RIECS DVAEPLIET-----
Strongylocentrotus VHSNSQN--RIESS DVVEPLIET-----
Apostichopus ---NTNN--EDRDQNMDSPE-----
Holothuria ---NKKE--RNEE--MAAL-----
Acanthaster YHELPTSDP-DCAPSGVND DME-----
Patiria YHQLPVSDS-DERPLASTVT-----
Saccoglossus RTLIEQGDGSSEVRSAAAIEIQRAWRGYWARWS
Ptychodera GTE-----
Shizocardium -----

Apostichopus ---MMRILOSVVFLAII LLM-----VVNISQSSPPD C-EETDIEF
 Anneissia ---MEH---RLVPMIIAIAWISLC-----VVSKSELHGSVS C-KSTDVK
 Strongylocentrotus ---MMMG-RQAFIFLVIGIA-----LVDIVAGVNLQV C-DVEVEFE
 Patiria ---MR-LT[S]ILLVVFII SLFLA-----SDARLRNKDETTSCENEADFE
 Ptychodera ---MGRYLGSCRFFLYVIWFS-----VTVAETQHQQV C-DIDTELE
 Periplaneta MLFQLLPNKASLVFVICIQIYYICSSSTNEPVLGSGVMHGAVPGGSVMP C-NSSEAVEFH
 Lymnaea ---MA-TMSGTTIVCL---IYLT-----TMLGNSQGVNLKIESPSPPTL C-SVEGTFH

LDLa

Apostichopus CDN---KCLNVTMQCNNVYDCVGGEDDESFLICGCRHDEFQSD-GCTPLHERCDLNC S
 Anneissia CGT--GE CVAANSS CNSISDCPDGSDSPAYCGCRHDEFQ CYN-S C ISLFGRC DGTCD
 Strongylocentrotus CEP--GV CIPRNLTCNGIFDCELGQDEEVAF CGCAKDEFPC SH-S C IPIELRC DNTNC D
 Patiria CEP--GV CIDASLANCSAYDCESMADETVML CGCPSGEFRCLN-S C IPLEKRC DRHCD
 Ptychodera CSP--GV CIDLQYRC DGI PDCENGHDESTLV CGCPSHEFR CNETT CIDLIRRC DWSMD
 Periplaneta CDA--VV CVPKSSLCNGIPDCQDGRDESVAQ CGCLPNEFRCSN-S CVDLVRRC DRQPD
 Lymnaea CDDGMLQCVLMGSKCDGVSDCENCMDESVEFCGLQSEFCNHTT CIDKILRC DRNDD

LDLa

Apostichopus CSS-CEDEDECEGYS C PPTHN-KCK-NHY CIPQINF CDFIDD CGDNSDEEN CNHPP C S
 Anneissia CDF-CEDEDCDLHQ C PSTHM-KCATSHI CIHLSLQ CNFVDD CGDGSDE-M CEHRE C Y
 Strongylocentrotus CEVDCADMDCGEAFP CPESTHME-KCTKNHY CIAKHLW CNFVDD CGDNSDEDL CYHPD C W
 Patiria CQDDCAEDHCDSFQ CLPGFQ-KCE-NHF C MPTYAW CDFVDD CGDMSDEAL CERLD C W
 Ptychodera CPD-GSDEDN CETFQ CLHTHS-KQNTHK CIPRDKT CDFIDD CGDKSDEED CYRRP C Y
 Periplaneta CAD-GEDEQDC EAYV CPT-THFKC-NNHF CIPGDSV CNFVDD CGDGSDENK CSHRK C W
 Lymnaea CSN-GLDERE CDIYI CPLGTHVKC-DNHFCVPRDKQ CDFLDD CGDNSDEKI CERRE C V

LDLa

Apostichopus SMFLFE CENHQCISNAYA CDGIED C FDGSDE R--H C EEN-FHI CEDGNKIHEGRK C N
 Anneissia T-HEFQ CANGE CLKPGYR CNGEVN CRGGDTSDEDN CIENYDYIM CR-SGRIFRNLFC D
 Strongylocentrotus K-GEFQ CSNKQCINTWFV CDGSQD CIDGSDE--ARC GEEH-FVL CENCKKVEHEW C D
 Patiria Y-GQFQ C INQCINSFFL CDGIQD CTDGTDEMEST CSPGN-FAD CGDGTVRVRAQQ C N
 Ptychodera AYGEFR CENEQCISYIV CDGIND CLDGSDEV--Q CQED-FVT CSDGTQTHRHW C D
 Periplaneta N-LEFK C NNGE C IRPGFV CDGTQD CKDGSDET--D C GPDQ-FAL CGDGSRVHRYW C D
 Lymnaea A-TEFK C NNSQC VAFGNL CDGLVD CVDGSDEDOVA C DSDK-YFQ CAEGSLIKKEFV C D

LDLa

Apostichopus MVRDCPSGS-DEHGCEC--QVYQTC PAEKS C FDNDIHCNSF CECAD-----C
 Anneissia FFIDCELTEDEKONCS DSADGEMCS-TGV CILRSKLC DGCDCDRDL-----C
 Strongylocentrotus RLVD CPDNEADETNCV C--TADEYRCP-NGK CLRPSVRCNGV C DCLS-----C
 Patiria GDAK CQLNKAVENCD C--SDDEFRCG-NGK CLPPAKQ C DRL C DCSN-----C
 Ptychodera GIPDCRESHDDEVNCY C--AEDDFRCG-NGR CISRAYL C DLS C D CAGT-----C
 Periplaneta GWPDCPDNHADLKCQNC SGVDEELCP-NGR CIRRANV C DSQ C D C VPPGSAAVNVT C
 Lymnaea GWVDC KLTFADELNCKL C D-EDDFRC S-DTR CIQKSNV C DGY C DCKT-----C

LDLa

Apostichopus SDETNCDEI-----CDV-SNGIY CPWMNYIIGSYRLSG CVKTERFC DGT PDC LG
 Anneissia EDENN CGDT-----VCSA-GSDYFCA-----HSFRCLNSEFV CNGYND C EN
 Strongylocentrotus DDEKE CAEDM-----CNYETNGIL CQ-----IANNKPSRCVVRKEYIC DGFDC PN
 Patiria EDEEG C DNKDD-----C DTD-T HIF C P-----PVDGKPPV C LQKQF ICDGRRDC PI
 Ptychodera EDEKN CSSG-----LCTL-ENHFWD-----EFSRCLHKDTIC DGFDC FD
 Periplaneta DDEVDCDLYYTNINGIHLCTQ-TETLNCIEP---NQNRDKDR CIHREFIC DRTNDC QN
 Lymnaea DDEEV CANN---TYG---CPM-DTKYMC-----RSIYGEPR CIDKDNV CNMIND C RD

LDLa

Apostichopus Y---QDEMF C SVPLHVP-----VRC C---PSTRDPRYIPES-EF C DN--SS
 Anneissia KDDE---L C ESRYKTD---VGYECKLNSDM CQL---DNNAFCYPT E-IF C ER---RP
 Strongylocentrotus K--AD- EFN CQL--PGNTTGHCDSEGNPPYMM C DIKDGDPRCLPTLKVQ C DRYRRP
 Patiria F--GWDEDD C QTLPDGESVASCNVP G---TVS C---GAGDPRCPPSKYVK C DK--RF
 Ptychodera ---WSDEYGC GDDVNCS---THEYENQMEFFRC G-GVESDDGRCIPER-AV C DY--QR
 Periplaneta GNYLSDEFGC PDDLVI-----GESIV C-----SDNRSLEKA-LE C DF--KW
 Lymnaea GNVGTDEYY C SNDSECK---N--FQAAMGFFY C-----PEERCLAKH-LY C DL--HP

LDLa

Apostichopus Y C FQGS EETNC THGERV C SVGQFQ CADS--S C VEE SLR C NGFWD C KDF SDEID C PNYI
 Anneissia Q C QGGS NGS HCL-VEAL C NSNEFK C TNG--M C IPDYLR C DNIAD C LDHSDELN C ESHP
 Strongylocentrotus H C MYGFDEETCNATRPC DPEVEYEC PYG--R C IDLTSR C DAQLD C DFD SDEAN C ESFE
 Patiria D C LTGVDEQNC TV-MPC PPGQH C RRGG--Y C VKEELW C DGYVD C DFD SDEDN C ELFE
 Ptychodera H C ILGTDESNDERC GHPAC MEDEFQ C NNNGHVK C IPIVOR C D TNPDC LDGSDERN C EDYL
 Periplaneta D C LEGNDEHG-CV-PDACAEGEYTC KNG--Q C VNSTQR C D LQFD C WDKSDELN C VNEK
 Lymnaea D C INGEDEQS-CLAPPK C SQDEFQ C HHG--K C IPISKRC DSVHD C VDWSDEMNC ENHQ

LDLa

Figure S14. Sequence alignment GRL101 receptors.

Apostichopus CPNENMFKCRGTGQCLASHQR CNGEVECTYINGT-KEDSDEEN CV--LRD CEENEFR C
 Anneissia CEE-GMWKCR-EGHCIEEMHR CDYVD CANFGQY-RDASDEEN CD--FES CKNEFC
 Strongylocentrotus CLP-GTWKCH-SGQCISEKMK CDYTPD CFYVNGT-VDSSDEDK DYKIFG CREGEFC
 Patiria CPP-GLRKA-AGQCISQRLF CDYHLD CFYYKNSTRDVSDEAH CT--RRQ CREDEFQC
 Ptychodera CDE-GQLQCNESGQCIHRDML CNFIKN C-----ADNSDEEN CGHVIRN CTEDEFQC
 Periplaneta CPS-GKKKCVHSGQCVSAAFW CDFIVDC-----PDGSDETD CGEKPPL CGPNQFC
 Lymnaea CAA-NMKSCL-SGH CIEEHKW CNFHREC-----PDGSDEKD CDPR-PV CEANQFC

LDLa

Apostichopus HSGHCIENWRRCYKAPDEHLYCCKDRSHLWD CGQWE CADESQFKCPRDHCISTMSRCN
 Anneissia NNGRCIDESKCKFRDY--SSEE CRDN SHLRE CEDFE CPA-GYKCKQKSHCIPDFRVC
 Strongylocentrotus HSGQCIPQDEVCFDST-MKKGCKDRSHLND CANRT CRE-NEFKCRNAHCVNMSDVCN
 Patiria RSGQCIPASRRCYRDQHDHVQGCADLSHLRN CSDFV CPA-GAFKCARSHCINGTMVCD
 Ptychodera RNGQCIDLRRCYFDELDDVYGCCKDKSHLIG CNDFE CSA-DTLKCRNGHCVSQSLVCN
 Periplaneta NNSQCIDASLR CFN-SGNPRYGCADGSHLIG CKNWT CPS-NAFKCRNGPCLNSMVCN
 Lymnaea KNGQCIDPLQVCV--KGDKYDGCADQSHLIN CSQHI CLE-GQFRCKKSF CINQTKVCD

LDLa

Apostichopus GLLDVNVNE-DEA-----NCLMYCHPA----KYPGCFCKGKIFNCSYTGLTQVNIHF
 Anneissia VHVDCILFYDDEV-----N CYGK GTDFEFYSIPDCI CNDKTVD CNDLKYGTLDKFEL
 Strongylocentrotus GAVDCIPYWTDED-----F CPHECGP-----A-LMCICNHTQMS CINAGLESFHNFYV
 Patiria KNVDCLESWDDAPRHGDT CIQECAS-----SGCGSQFDMT CTNIGLNESSFSLN
 Ptychodera GNIDCGLIWTDEE-----G CSHI CSN-----L--VCMQDDEMN CEDKNLHEIPYF-I
 Periplaneta HNIDCPGTWEDED-----G CLFACSN-----VEPRCE CRDIHVN CTNLGLVVRPPD-I
 Lymnaea GTVDCILQGMWDE N-----N CRYWCPH-----GQAI CQCEGVTMD CTGQKLEMPVQOM

LDLa

Apostichopus A--DDEVITWIFYFNHNLTV--SALTFGNSTVQNI VHLDLSHNNLQDLPAGLESMMIGL
 Anneissia ---KDMNIMKFSGT---ELVLESSTFSNVTAITF LDISRNNLMDIGDGYFKDMFFL
 Strongylocentrotus ---EEQISEINTSGNRIQ---ISNEVLSGLPGLLR LDLSNNSLNDIGNDTEKGLANL
 Patiria AKDTRLIHFSLPGNNLHH-LLQDPTALEGLTRTIL LDLSDNGVTFTINKAALLNVPNL
 Ptychodera ---EPGYIKLKLGHNYLGEDPNLSNYTFAKLGRITYLGLLEDNITDTKSFTESNLWRL
 Periplaneta ---EEETWFHMANNLINS--TFSEDYQLERLRLYLDIRNNSISSIPPLAERNLWRL
 Lymnaea ---EEDLSKLMIGDNLNLN--TSTTFSATYDKVTV LDISRNNHLETPIYSEQNMWKL

LRR

Apostichopus HYLNLYGNGINKLEAQVESGLTNLKQLVLTGNVIQIIEEGSFLGLTSLKVLDDLSHQRL
 Anneissia QTLILSENKITTLLKKAFAQGLSNLRYLNLTKNIENIEADAFDGLDSLTTLLDLSYQNT
 Strongylocentrotus RYLNLENNLRVIRKQTEGLEGLQTLRLRGNNIHAIEPHAFEGLRNITTLLDLSNQNL
 Patiria QTLILADNKITTKLGNQTFESSLQHLRTLILIRGNAMQT VAGQAFGLGLGELTTLLDLSQOKI
 Ptychodera LTLNLEDNF LTTLRRDTEFGLGNVRSLYLQGNSTIGEIEAHAFKGLSALPTLLDLHGQRL
 Periplaneta LTLNLQYNCIRILSNSSSEYGLTNL SNLHLQNGIQVIEAMAFYGLSSLILLDLSWQRT
 Lymnaea THLNADNNTITSLKNGSLLGLSNLKLHINGNK IETIEEDTFSSMIHLTVLDDL SNQRL

LRR

Apostichopus IHIGGNFVGLYH LTLNLSNNNLQTV EQGIFLKL DNVHTIDMSHNOINF IHENTFNG
 Anneissia QRIPINAFYGLRS LKYLTLRGNKLI FIVGGTFNGLPNLRSLDISENTINKIDGRAENG
 Strongylocentrotus TEIPNAAFVGLYR LHFLLDLSANHTVMVPDGA FYGLYQLKKLDISENAIEVVSRR-TFN
 Patiria QSINKGAFDGLNKLAFNL SHNRMTDIPRGTF FGLNELKELDISENNKLSQIHAFAFYG
 Ptychodera QWLHINAFAGLSRLLSNL SHNQIQYIDNGVFNGLSKLLVLVDISHNVVIEIDSKVFEY
 Periplaneta HNISQGAFAVGLRSLVGLDLSHNEITYLV DGSFNGMPLLSDLSLSSNTIKVISNVSERS
 Lymnaea THVYKNMFKGLKQITV LNTSRNQINSIDNGAFNNLANVRLIDL SGNV IKDIGQKVFEMG

LRR

Apostichopus LTNLEKTIISDELRFCCVAKH---VKECLPEADEFSSCEDLMRNTFLRFNLWVGLVAT
 Anneissia LPSLDYLYTDEFRCMSEG---VPNCYPEPDAFSSCDLMSNYVLRVSIWVLGVATF
 Strongylocentrotus LRLLEELITDEYRFCCMARH---VSKCLELPDEFSSCEDLMSNPILRMCIWIIGMIAL
 Patiria LPKLRVLHTDEFRCMVREMSVETCTPPDEFSSCEDLMANVFLRGSIVVIGIIAS
 Ptychodera LMELELYTDEYRFCCMAKF---VQKCHPPDPDEFSSCDLMSNVVLRGGIWLGLVIAS
 Periplaneta AASLTKLV TDEFRCCLARH---VKHCLPEPDEFSSCEDLMSNLVLRICVWVLGVLAT
 Lymnaea LPRLVELEKTD SYRFCCLAPE---GVKCSPEKQDEFSSCEDLMSNHVLRVSIWVLGVIAL

Hinge region

TM1

Apostichopus FCNAIVIVTRSGKRRDSRVQSFLLITNLAIGDMCMGTYLLIIAIAIDLNYRGRYAAYESL
 Anneissia LGNLLVVIWRVTHNRENKVSFLLITNLAAGDFCMGVYLLIIAIVDLTYRGEYIHDME
 Strongylocentrotus IGNLVVIMWRVNSKRDNKVHSFLLITNLAAGDFMLMGTYLLIIAGVDAYRGDYIVHDKT
 Patiria IGNLAVIMMRMNNKRDNRVHSFLLITNLAAGDFCMGVYLLIIASVDAFYRGYIYDAQ
 Ptychodera VGNLVVCFRRLRDRDNKVSFLLITNLAAGDFCMGVYLLIIAIVADTYRGNYIHDKV
 Periplaneta FGNILVIGWRMRFKHTNQVHSFLLITNLAAGDFMFGSYLLIIAGVDARYRGVYFIHDS
 Lymnaea VGNFVVVIFWRVRDFRGGKVSFLLITNLAAGDFMLMGVYLLIIATADTYRGVYISHDEN

TM2

Figure S14-continued.

Apostichopus WKRSLECFKFAFGLSTFSSSELSVLSLTFITLHRVSSIVFPFRTKDIGESRIVWIMTSTW
 Anneissia WRSSSWCRFAGFLSTFSSSELSVSLTIITLQRLTSILFPFRSKNMELGWAMKMMALTW
 Strongylocentrotus WRNSGLCKFAGFLSTFSSSELSVFSLTIIITLHRLSSIVFPFRKDMEEFTRAVVVMCVSW
 Patiria WRDSALCRFAGFLSTFSSSELSVFSLTIIITLHRLSSILFPFRKDMEEFSGAVRVMVVTW
 Ptychodera WRQSQFCKIAGFLSTFSSSELSVFTLTVITVDRLVCIVFPFRFNRLFEKGAARLMAALW
 Periplaneta WRSSELCHLAGFTSTFSSSELSVYTLTVITLDRFLVIIFPFRVRRLEMPKTRLLMALGW
 Lymnaea WKQSGLCQFAGEVSTFSSSELSVLTLSITLDRILICILFPPLRRLGLRQAIIVMSCIW



Apostichopus AIVFFFLAGIPLLCFSYFDNFYGRSGVCLALHITPDKPNGWEYAVFVFLALNFFSFTFI
 Anneissia LLAIFLAILPLCRVNYFGNFYGRSGVCLALHITGEKTSGWEYAVFIFLAINLFSFII
 Strongylocentrotus GLVAFLLAALPLCGVAYFGNFYGRSGVCLALHITPDKPSGWEYSVFIFLGLNEVFSITI
 Patiria LMVIFLSAFPFLGLSYFGNFYGRSGVCLALHITPDLKPGWEYSVFIFLALNFSFLTII
 Ptychodera LIVFFISAVPLFLSYFTDYGRSGVCLALHITNERPDGWEYSVFVFLIINLVNFLII
 Periplaneta LGAAFISGLPLLQIDYFRNFYGRSGVCLALHITPEKPSGWEYSVFVFLNLSFSII
 Lymnaea VLVFLLAVLPLLCFSYFENFYGRSGVCLALHVTPDRRPGWEYSVGVFILLNLSFVII



Apostichopus AVAYMVMFYVARRTQQAARSLRGNKGS DAMARKMTLIVETDFCCWPIIILGVASLCL
 Anneissia ILSYVIMFVARRTORAV--R-PQNRGDSMAMRMTVIVLTFDFCCWPIIFLGLIASLL
 Strongylocentrotus MVSYGVMFNVARKTOKAAMRSL-KSKGSDSMARRMSVIVETDFCCWPIIILLGLASLS
 Patiria AVSYSVMFVARRTQKAVNRSR-DTNTGDAMARRMTLIVMTDFVCWVPIILLGVASLGL
 Ptychodera LLSYIAMFIVASKTQOAV-RNR-DLKTESAMAKRITVIVMSDFFCWVPIILLGLASLGL
 Periplaneta ALGYLWMYVVARVTQOAV-KKE-QRPSDNAMARRMTLIVATDAACWPIIILLGVLSLGL
 Lymnaea ASSYLWMFVSAKKTSAV-RTA-ESKNDNAMARRMTLIVMTDFCCWVPIIVLGFVSLA



Apostichopus GANIHEPVAWVAVFVLPNSAVNPLLYTLWTAPYARKIINSARSTFGRS--TATTEY
 Anneissia GASVSEPKVYAWIAVFLVLPNSAANPILLYTLWTSPYVRRFLKKARPSMRSLST-YYTDT
 Strongylocentrotus GAYVPTS VYAWVAVFVMPVNSAVNPILYTLGSAITVRRAIQRF SINPSTT---VTSEY
 Patiria GAKIPPQVYAWVAVFVLPNSAANPMLYTLWTAPYVRRVMSRARTSLNLSLSTVTTDM
 Ptychodera GAVIPPQVYAWIAVFLVLPNSALNPVLYTLSTPTFVKRTKMKMADSIGESFRSRWRDTG
 Periplaneta GITVPPQVFAWVAVFVLPNSAANPVLYTLSTAPFLGPARRGLTTFKRSCKLSLTMDDQ
 Lymnaea GARADDQVYAWIAVFLVLPNSATNPVIYTLSTAPFLGNVRKRANRFRKSFIFHSFTGDT



Apostichopus KLSANLSTS-----EKVSSTANGRRRAQRGL-----ASTSN-----SK--
 Anneissia RHGSVREH-----HRSNGNN---FKMRISQ---RSK-----KTSCLKFIP
 Strongylocentrotus KTVMN-----NS-SDRKQGGYKGRP--M-RTMSNTANENCKPA----TTTTTK
 Patiria KQVNH-----GDRQGRMCNGRKGWQKGI-RLPKADANKNAIKLNTIISQSDTE
 Ptychodera RTNSFTVSESOA-----RSS-----FSYTGIDRLDRCASVA
 Periplaneta RRTYSSTLGSTFANNCSRCELDYNLYPRLEQTNGKLOEGAGGCHYDGEDLDSEQDMK
 Lymnaea KHSYVDDGTT--H---SYCEKK-SPYRQLELK-----RLRSLN

Apostichopus -LPPEKSTGSIRS---SDVINDPEEGIRLEHDVSHDKGNVYVNPNNDD-----RLGN
 Anneissia SSPPKNNNSTTNKRTDAGVITNDEQYNKLLSDQ-RNKDSYE-----RALTSAAGN
 Strongylocentrotus PKPPPAKEETIKM---IDLGK-----RRHDNGDDGK-----GKEAEGM
 Patiria PDEPATAQTRSEE---LNLLQ-----DHSPTQGAES-----GKEAEGM
 Ptychodera SSNSATVAIRLRS-----FS-----GGHGGADLTGCYDKRTGSDPSTRECRDSSGK
 Periplaneta NEAPLFS-----LT-----KREHOPHRWRSGSYHATNNVPPSSSVSTPG-
 Lymnaea SSPPMYY-----NT-----ELHSDS

Apostichopus HGNKDAYEKML-----SDKSMDIDGGHSSEE-----G-----
 Anneissia -----
 Strongylocentrotus NNEK-----
 Patiria HT-----
 Ptychodera SVTFASDSRTWLRRALQAPPKDIKIVEKLEVIIIEFKPEEQSVGAMIIGFLELFSEA
 Periplaneta -----ATILWQSSSCRHGSSSIDTAVSA-----HGEIIPLRRLHSDS
 Lymnaea -----

Apostichopus -----
 Anneissia -----
 Strongylocentrotus -----TSNNV-----
 Patiria -----GNV-----
 Ptychodera QEKHFTRLRDMCLKKLSNDTAHENIIRMLWSGSVSDLLSSQAITEQFPGEFKWCICVE
 Periplaneta -----RGNGNK-----
 Lymnaea -----

Figure S14-continued.

Apostichopus -----
Anneissia -----
Strongylocentrotus -----
Patiria -----
Ptychodera YIEGVTLKTFADKIDTRELSRIVIQIAKALDHLRKHKIVYNNLSTSSIIIQRVGQES
Periplaneta -----
Lymnaea -----

Apostichopus -----
Anneissia -----
Strongylocentrotus -----
Patiria -----
Ptychodera SRKVRPILFDFCKAVDLSVALSTDSEVDHMNDVMGIARMLNDLCTTVMVTTDSEDTD
Periplaneta -----
Lymnaea -----

Apostichopus -----
Anneissia -----
Strongylocentrotus -----
Patiria -----
Ptychodera YERTPLFPMSQSVKRNGLRADDEVLRMCITECATEPPSAFDILNQLTSLMSDPDIVYYV
Periplaneta -----
Lymnaea -----