

**Supplemental Table 1** Parameters for phylogenetic tree reconstruction. N = total number of sequences, L = Length of sequence alignment, l = Length of mature sequence alignment, Model = best DNA/Protein model of evolution determined by MEGA, AICc = Akaike Information Criterion, corrected value, # = number of sites used in analysis, log(LN) = log likelihood values of maximum likelihood trees, G/I = Gamma/I value for each tree. Dashes indicate incomplete data as no gene network was reconstructed.

Toxin	<i>N</i>	<i>L</i>	<i>l</i>	Model	AICc	#	log(LN)	G/I
<b><i>Nucleotide</i></b>								
<b>PLA2</b>	20	696	417	Kimura 2 (G+I)	93891.62	270	-4781.1428	1.5149/18%
<b>Cyto-II</b>	14	709	540	Kimura 2 (G)	8155.884	485	-3958.8144	0.8889/-
<b>VKSC</b>	24	327	201	Kimura 2 (G+I)	2743.201	139	-1502.9669	2.3786/15%
<b><i>Protein</i></b>								
<b>PLA2†</b>	83	189	168	WAG (G+I)	6611.927	32	-3205.730	1.5760/12%
<b>Cyto-II</b>	13	223	173	LG (G)	4143.187	161	-2038.9973	0.9244/-
<b>Cyto-IV</b>	4	467	-	-	-	-	-	-
<b>VGSC</b>	24	109	66	Dayhoff (+G)	1600.385	46	-879.1404	2.8514/-
<b>VGPC-II/KPI</b>	36	107	72	WAG (+G)	3804.086	50	-1823.0990	1.7589/-
<b>VGPC-III</b>	41	110	70	WAG (+G)	3096.826	31	-1258.6265	1.6220/-
<b>VGPC-IV</b>	4	41	-	-	-	-	-	-
<b>VGPC-V</b>	6	88	-	-	-	-	-	-
<b>VGPC-I</b>	37	100	53	WAG (+G)	1794.406	26	-817.9125	2.7421/-
<b>Acrorhagins-I</b>	4	93	-	-	-	-	-	-
<b>Acrorhagins-II</b>	5	64	-	-	-	-	-	-

**Supplemental Table 2** Taxa included in this study, with GenBank accession numbers. Taxa are organized alphabetically for each toxin gene type. Bold GenBank accession numbers were used as query sequences.

<b>Phospholipase A2s</b>	<b>Genbank ID</b>
<i>Adamsia carciniopados</i>	<b>18033525</b>
<i>Aedes aegypti</i>	157137214
<i>Aipysurus eydouxii</i>	49472980, AAT66310
<i>Alligator sinensis</i>	XP_006019144
<i>Bitis caudalis</i>	P00622
<i>Bos taurus</i>	291575120
<i>Bothrops asper</i>	P24605.3
<i>Branchiostoma floridae</i>	260800263
<i>Bungarus multicinctus</i>	CAD24463
<i>Caenorhabditis elegans</i>	3874090
<i>Callorhinchus milii</i>	XP_007906926
<i>Canis lupus familiaris</i>	50979154
<i>Ciona intestinalis</i>	198415032
<i>Condylactis gigantea</i>	<b>283140837</b>
<i>Cryptophis nigrescens</i>	ABK63571
<i>Culex quinquefasciatus</i>	170048777
<i>Demansia vestigiata</i>	118151758, ABK63569
<i>Dicentrarchus labrax</i>	4454121
<i>Equus caballus</i>	149720537
<i>Gallus gallus</i>	363740066
<i>Heterocephalus glaber</i>	XP_004843730
<i>Homo sapiens</i>	4505847
<i>Hoplocephalus stephensii</i>	124020979
<i>Mus musculus</i>	12842453
<i>Nasonia vitripennis</i>	156540704
<i>Nematostella vectensis</i>	156339845, 156391018, 156391017, 156391019, 156391020, 156365766, 156365765, 156383321, 156378642, 156383865, 156383365
<i>Notechis scutatus</i>	71066758, 71066760
<i>Oxyuranus scutellatus</i>	71066728, AAZ22637, AAB33760, AAZ22635, Q45Z47.2
<i>Oxyuranus scutellatus scutellatus</i>	AAY47071, AAY47070
<i>Pagrus major</i>	2662295, 13928533, BAB20041
<i>Patiria pectinifera</i>	5902462
<i>Pseudechis australis</i>	71066788
<i>Pseudechis porphyriacus</i>	AAZ22670
<i>Rattus norvegicus</i>	13928792
<i>Strongylocentrotus purpuratus</i>	390366769
<i>Sus scrofa</i>	51592123
<i>Sycon raphanus</i>	AM765083
<i>Taeniopygia guttata</i>	XP_004175830
<i>Trichoplax adhaerens</i>	196012902, 196012904, 196012906
<i>Urticina crassicornis</i>	<b>152003427</b>
<i>Xiphophorus maculatus</i>	XP_005811202
<b>Cytolysins</b>	
<i>Actinia equina</i>	<b>FM958450, U41661, U51900, AF057028</b>
<i>Anthopleura asiatica</i>	<b>AB479475</b>
<i>Heteractis crispa</i>	<b>AY855350</b>
<i>Oulactis orientalis</i>	<b>AY861662</b>
<i>Sagartia rosea</i>	<b>AY247033</b>
<i>Stichodactyla gigantea</i>	<b>JQ353486</b>
<i>Stichodactyla helianthus</i>	<b>AJ005038, AJ009931</b>
<i>Urticina crassicornis</i>	<b>GQ848199</b>
<b>VGPC type I Toxins</b>	
<i>Actinia equina</i>	<b>P81897</b>
<i>Anemonia erythraea</i>	<b>Q0EAE5</b>
<i>Anemonia sulcata</i>	<b>Q9TWG1</b>
<i>Cryptodendrum adhaesivum</i>	<b>BAJ23161</b>
<i>Heteractis magnifica</i>	<b>AAD09480</b>

**Supplemental Table 2***(Continued)***VGPC type I Toxins***(Continued)***Genbank ID**

<i>Heterodactyla hemprichii</i>	<b>BAJ23162</b>
<i>Metridium senile</i>	<b>P11495</b>
<i>Stichodactyla mertensii</i>	<b>BAJ23160</b>
<i>Stichodactyla haddoni</i>	<b>BAJ23159</b>
<i>Stichodactyla gigantea</i>	<b>BAJ23158</b>
<i>Thalassianthus aster</i>	<b>BAJ23163</b>

**VGPC type II Toxins**

<i>Anemonia sulcata</i>	<b>Q9TWF8, Q9TWG0, Q9TWF9</b>
<i>Stichodactyla helianthus</i>	<b>B1B5I8</b>

**Kunitz-Type Protease Inhibitors**

<i>Actinia equina</i>	<b>P0DMJ2</b>
<i>Anemonnia sulcata</i>	<b>P10280</b>
<i>Anthopleura elegantissima</i>	<b>P86862</b>
<i>Anthopleura fuscoviridis</i>	<b>P0DMJ3, P0DMJ4</b>
<i>Anthopleura xanthogrammica</i>	<b>P81548, P81547</b>
<i>Heteractis crispa</i>	<b>P16344</b>
<i>Stichodactyla helianthus</i>	<b>13M7Q_B, P81129</b>

**VGPC type III Toxins**

<i>Anemonia sulcata</i>	<b>P11494, P59084</b>
<i>Anemonia viridis</i>	FK744472, FK722457, FK736010, FK723172, FK745823, FK754940, FK721972, FK740326, FK725608, FK752236, FK720902, FK736435
<i>Antheopsis maculata</i>	<b>P69930</b>
<i>Anthopleura elegantissima</i>	<b>P61542, P61541, B3EWF9</b>
<i>Bunodosoma cangicum</i>	P86461, P84919
<i>Bunodosoma granuliferum</i>	CCC86602, CCC86603, CCC86604, CCC86606

**VGPC type IV Toxins**

<i>Stichodactyla haddoni</i>	<b>P0C7W7</b>
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**VGPC type V Toxins**

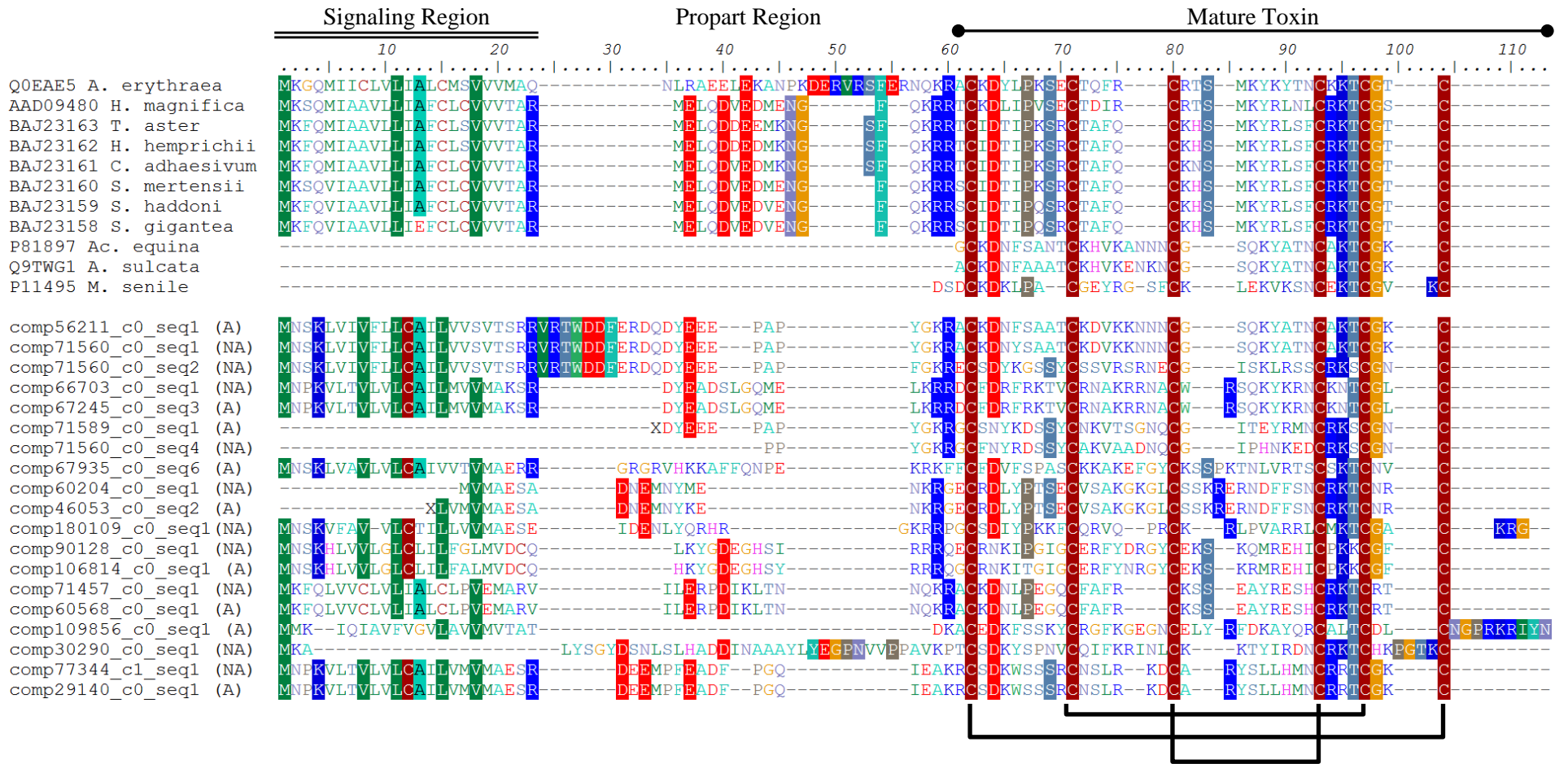
<i>Bunodosoma caissarum</i>	<b>C0HJC4</b>
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**VGSC type I,II,III Toxins**

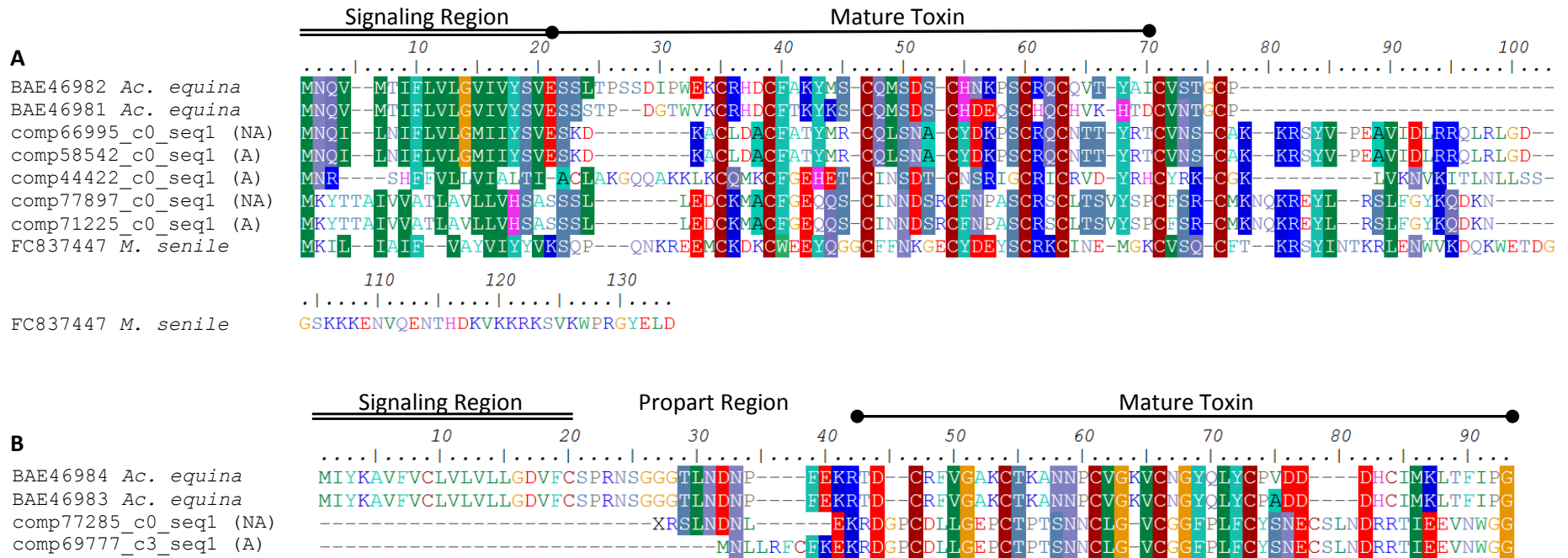
<i>Actinia equina</i>	<b>ABW97361, ABW97358, ABW97362, Q9NJQ2</b>
<i>Aiptasia diaphana</i>	<b>ACQ83467</b>
<i>Anemonia erythraea</i>	<b>P69943</b>
<i>Anemonia viridis</i>	<b>FK728784, FK754096, P01533, P0C7Q0, ABW97326, P01529</b>
<i>Antheopsis maculata</i>	<b>P69928</b>
<i>Anthopleura elegantissima</i>	<b>P0C1F0, P0C1F1, P01532, P0C1F3</b>
<i>Anthopleura fuscoviridis</i>	<b>P10453</b>
<i>Anthopleura sp.</i>	<b>P0C5F4, P0C5F5, P0C5F6, P0C5F7</b>
<i>Anthopleura xanthogrammica</i>	<b>P0C5F8, P0C5G1, P0C5G2, P0C5G3, P01530, AAA27737, P0C5F9, P0C5G0</b>
<i>Bunodosoma cangicum</i>	<b>P86460, P86459, P0C7P9, P82803, Q7M425</b>
<i>Bunodosoma granuliferum</i>	<b>P0C1F4, P0C1F5</b>
<i>Calliactis parasitica</i>	<b>P49127, P14531</b>
<i>Condylactis gigantea</i>	<b>P0C280</b>
<i>Condylactis passiflora</i>	<b>P0CH42</b>
<i>Cryptodendrum adhaesivum</i>	<b>D2KX90</b>
<i>Halcurias carlgreni</i>	<b>P0C5G6</b>
<i>Heteractis crispa</i>	<b>P30785, P30832, P30784, P30783, P30831, P0C5G5</b>
<i>Heterodactyla hemprichii</i>	<b>D2KX91</b>
<i>Nematostella vectensis</i>	<b>ABW97340, ABW97343, ABW97332, ACB 71119, ABW97348, ACB 71121</b>
<i>Radianthus paumotensis</i>	<b>P08380, P01534</b>
<i>Stichodactyla gigantea</i>	<b>Q76CA0</b>
<i>Stichodactyla gigantea</i>	<b>Q76CA3</b>
<i>Stichodactyla haddoni</i>	<b>B1B5I9</b>
<i>Thalassianthus aster</i>	<b>D2KX92</b>

**Acrorhagins**

<i>Actinia equina</i>	<b>BAE46981, BAE46982, BAE46983, BAE46984</b>
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**Supplemental Figure 1** Type I VGPC toxin sequence alignment of previously described toxins and candidate toxin genes. The identification of the signaling, propart, and mature regions is based on previously published sequences. The placement of the cysteine bonds forming the disulfide backbone is indicated in brackets. The transcriptome source is indicated (acrorthagi from A: aggressive or NA: non-aggressive polyps). For full species name refer to S. Table 2. Residues with >50% similarity have the color background shaded in.



**Supplemental Figure 2** Sequence alignments of Acrorhagin I (A) and Acrorhagin II (B). The signaling, propart, and mature toxin regions are based on previously published sequences. The transcriptome source is indicated (acrorhagi from A: aggressive or NA: non-aggressive polyps). Residues with >50% similarity are colored in.