

Supplementary information: Transcriptomic and Proteomic Analysis of Tentacles and Mucus of *Anthopleura dowii* Verrill, 1869.

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Alignments multiple of amino acid sequences corresponding to precursors from putatives venom components inferred from the transcripts obtained from the tentacles of *A. dowii*.

In all the alignments, the region corresponding to the signal peptide is highlighted in orange, in green is highlighted the region of propeptide and in blue is highlighted the region of mature protein. In some cases, the conserved Cys residues are highlighted in bold blue and in bold letters. The number of amino acids (aa) and the percentages of identity (I%) are calculated considering only the regions of the mature protein, this last value is calculated with the program LALIGN version 2.1.30 and with respect to the sequence indicated with 100% identity in the alignment. In some cases, the percentage of similitude (%S) also is showed, this value also calculated with the program LALIGN version 2.1.30 and considering only the regions of the mature protein and with respect to the sequence indicated with 100% similarity in the alignments. All alignments were made with ClustalX 2.1 and the characters (*), (:), and (.) are shown in the low region along the alignments to indicate positions with fully conserved residues, positions with conservative substitutions and positions with less conservative substitutions, respectively.

A) Sea anemone type 1 potassium channel toxin family. Type 1b subfamily.

		aa	%I	PSI-BLAST E-value
c23125_g1_i1	MNSKLVIVFLLCAILVSVTSRRVRTWDDFERDQDYEEEPAPYG--KRA CK DNYSAA TCK DVKKNN CG SEKYAT NC AK TCGKC	36	100	
Kappa-AITX-Aeq4a	-----G CK DNFSAN TCK HVKANN CG SQKYAT NC AK TCGKC	36	83.3	4e-14
Kappa-AITX-Avd6a	-----A CK DNFAAAT CK HVKENK CG SQKYAT NC AK TCGKC	36	83.3	2e-14
U-AITX-Avd11a	-----LVVSVTSRRVRFWDDFERDENFEEERP YLR NVKRA C NDYKSS YCR SVGS RNEC GIHKYR MYCR K TCGSC	36	47.2	8e-20
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B) Venom Kunitz-type family, Sea anemone type 2 potassium channel toxin subfamily.

B.1)

										PSI-BLAST				
										E-value	E-value	E-value	E-value	E-value
c17454_g1_i1	---MMKTLFLMSLAMLAVTMAPDSD---FCFLAPEVGKCRGHIRRYYYSTETGKQQFFYGGCGGNRNNFQSEDECRATCYPREK-----	aa	%I	%I	%I	%I	%I							
KappaPI-SHTX-Shd2a	---MAKLYFLCLALVACLTMATEEMPA---LCHLQPDVPGKRGYFPRYYNPEVVGKCEQFIYGGCGGNKNNFVSFEACRATCIIPL-----	61	100	42.9	44.3	37.5	50.8							
c27319_g1_i5	---MSLQKLLFATVVITACLFMRITVDGKPSRKKLCTLEPDSDGNCYGYFPSYYNPNSSGRCENFYGGCGGNANNFSTLKSACAVCRACK-----	62	54.0	51.6	48.4	35.1	41.9	3e-21	6e-20	1e-17	5e-12	1e-12		
c14257_g1_i1	---MKMRSVTLISIVVFSGAFAPARPEY---CNLPYETGKCMAYIPSYFYDPSTGTCTDQFIYGGCGGNKNNFDTLAAEKTCTMV-----	62	42.9	100	46.8	43.2	50.0	-----	-----	-----	-----	-----	-----	-----
c14874_g1_i1	---MAKSATLMVFLLCFFLVADVSYGINS---ICLLPKKQGFCCRARFPFRYYNLSRRCEKFIYGGCGGNANNFHTLEECEKVCVGR-----S-----	58	44.3	46.8	100	36.1	48.3	-----	-----	-----	-----	-----	-----	-----
KappaPI-AITX-Ael3a	-----INS-----ICLLPKKQGFCCRARFPFRYYNLSRRCEKFIYGGCGGNANNFHTLEECEKVCVGR-----GEAWKAP-----	71	37.5	43.2	36.1	100	52.1	-----	-----	-----	-----	-----	-----	-----
KappaPI-AITX-Avd3d	-----ING-----DCELPKVVGRCRARFPFRYYNLSRRCEKFIYGGCGGNANNFHTLEECEKVCVGR-----S-----	65	37.9	48.5	42.4	80.3	55.4	1e-12	2e-14	2e-14	4e-36	4e-21		
c10_g1_i1	---MKDIPLTCVILFGLSLTSARED---ICLLPKKVGFCRALIPRFYFNSKTRCEGFIYGGCGGNKNNFISIKDCQKACM-----	59	42.6	51.6	50.0	59.2	50.8	4e-12	2e-15	2e-16	5e-23	4e-16		
KIn-II	---MSSGCLLLLGLLTLWAEITPVSG---RPRICELPAESGLCNAYIPSFYYNPHSHKCKQKFIYGGCGGNANNFHTLEECEKVCVGR-----	56	42.6	38.7	48.3	52.1	100	-----	-----	-----	-----	-----	-----	-----
Kunitz inhibitor IV	---MSSGGLLLLGLLTLWAEITPISGQDRPKFCHLPVDSGICRAHIPRFYYNPNASNOCKQFIYGGCGGNANNFHTLEECEKVCVGR-----	57	47.5	50.0	53.4	40.8	45.6	1e-13	9e-17	2e-19	6e-17	4e-16		
	*****	60	50.8	50.0	48.3	41.1	46.7	4e-17	1e-14	1e-16	9e-13	2e-11		

B.2)

										PSI-BLAST									
										aa	%I	%I	E-value	E-value	E-value				
PI-AITX-Axm2a	-----APVNEDCLLPKKVGP---CRAAVPRFYNSDSGKCEGFTYGGCHANANNFKTKDECKNACH--									58	100	72.4	5e-31	8e-26	1e-20				
PI-AITX-Aeq3c	-----YPANEGCLLPMKVGP---CRAAWPSYYNSKSEKCEEFTYGGCDANANNFQTEEECKKAC---									57	72.4	100	3e-27	5e-27	4e-19				
c27319_g1_i1	MQKSNGINVKTVLLAALFCAFILILGLSLSKTAGAPANKDCLLPRMVGP---CRAAIPRFYNSKSGKCEGFTYGGCDANANNFKTEEECKNACHAA									60	78.3	75.0	-----	-----	-----				
c27319_g1_i4	-----MSLQKLLFATVVITACLFLSKISGAAANDDCHLPMKVGLCRASIPRFYFNSKSEKCEFTYGGCDANANNFKTEEECKEACHAT									57	68.3	70.0	-----	-----	-----				
c27319_g1_i3	-----MSLQKLLFATVVITACLFLSNISGAAAN-VCLLPKVVGHCQAVIPRFYFNSKSEKCEFTYGGCGGNGNNFQTKDQCTNACTT-									55	59.3	54.2	-----	-----	-----				
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B.3)

										PSI-BLAST					
										aa	%I	%I	E-value	E-value	E-value
cVamTi	MSSGGLLLLGLLTLWAEITPVSGQDHPKFCYLPADPGRCKAHIPIRFYIDSASNCKNFKIYGGCPGNANNFKTWDECRQTCGASAMGRPT	61	100	57.4	1e-19	8e-17	2e-18								
DrKin-II	MSSGGLLLLGLLTLWAEITPISGHRDPTFCNLAPESGRCAHLRRIYYNLESNCKEVFFYGGCGGNDNNFSTWDECRHTC---VGK--	60	57.4	100	8e-12	9e-18	2e-15								
c10125_g1_i1	MVKQMIFVLF--LAMVVGLS---MARPEFCLLPAPKPGRCKAFAKRYFYDKSIGACRQFIYGGCKGNRNNFNSKSEKCDRICGARR-----	59	52.5	39.3	-----	-----	-----								
c10208_g1_i1	-----MARPKYCLLPKVGGLCMASMRYYYEKSIAKCSQFFYGGCGGNKNNFKTMDECVKTCALL-----	58	50.8	53.3	-----	-----	-----								
c10208_g1_i2	-----MARPKYCLLPKIGRCRARILRYYDKSNAKCSQFYGGCGGNRNNFETRHECVKTCALL-----	58	54.1	50.0	-----	-----	-----								
* : *															

C) Sea anemone type 3 (BDS) potassium channel toxin family.

C.1)

PSI-BLAST										
		aa	%I	%I	%I	E-value	E-value	E-value	E-value	E-value
DeltaKappa-AITX-Avd4b	-----AAPCFC--PGKPDGRDLWILRGTCPPGGYGYTSNCKYKWP-NICCYPH--	43	100	95.3	47.8	8e-06	2e-08	9e-07	7e-06	2e-08
DeltaKappa-AITX-Avd4a	-----AAPCFC--SGKPGRDLWILRGTCPPGGYGYTSNCKYKWP-NICCYPH--	43	95.3	100	47.8	1e-05	2e-08	1e-06	2e-05	5e-08
PhcrTx2	-----ALPCRC--EGKTEYGDKWIFHGGCPNDYGYNDRCFMKPGSVCCYPKYE	46	47.8	47.8	100	2e-05	5e-08	5e-10	1e-04	2e-03
c30503_g2_i2	MAAKSVLMMLAIFMALAFLANGEE---EVRVNVRAIRCNCIGKDGQPGYDWWFWRGSCPDGYGYKTSICMLGID-ICCFPRA-	43	43.5	45.7	39.6	----	----	----	----	----
c30503_g2_i4	MAAKSVLMMLAIFMALLLLANGEEAQGEVRIKARALLCNC--EGKASS--GDWWFWRGSCPDGYGYKTSICMLGID-ICCFPRA-	44	47.7	47.7	43.5	----	----	----	----	----
c30503_g2_i3	MAAKSVLMMLAIFMALLLLANGEEAQGEVRIKARALLCNC--EGKASSGDWFWWRGSCPDGHGYTSSCSAGLGSICCLPKT-	45	48.9	48.9	47.8	----	----	----	----	----
c30503_g2_i5	MAAKSVLMMLAIFMALLLLANGEEAQGEVRIKARALLCNCCKEDNAPSGDWLWRRSSCPGGYGYTSSCNAGFGNICCLPRG-	47	52.1	46.8	37.5	----	----	----	----	----
c22963_g1	MAAKSVLMMLAICMALVFLTSGEEAQEDARVKPRAVSYCYGRYDKAPYGDWWFMRGSCPPGGYGYTSCQTGMN-VCCFPKA-	50	45.1	47.8	41.7	----	----	----	----	----
	* *									

C.2)

		aa	%I	%I	%I	E-value	E-value	E-value	E-value	E-value	E-value
Kappa-AITX-Ael2a	-----GTTTCYCGKTIGIYWFGTK-TCPNSRNGYTGS	42	100	64.3	50.0	3e-10	2e-15	0.020	0.079	5e-03	0.58
Pi-AITX-Ael2b	-----GTATCSGNSKGIYWFYR-SCPTDRGYTGSCRYFLGTCTPAD-	42	64.3	100	45.2	1e-17	3e-15	1e-03	0.075	8e-06	0.031
Pi-SHTX-Hcr5d	-----GTPCDYGYTGVYWFMLS-RCPSGYGYNLSCHYFMGICCVKR--	41	50.0	45.2	100	1e-08	9e-09	1e-05	2e-05	3e-07	8e-05
c29930_g1_i1	MSYQRFLFLVVVASLIATSLAVPKDLE-----ERGTTCSCGN	42	81.0	71.4	52.4	-----	-----	-----	-----	-----	-----
c29930_g1_i2	MSYQRFLFLVVVASLIATSLAVPKDLE-----ERGTSCRCGS	42	66.7	66.7	52.4	-----	-----	-----	-----	-----	-----
c13634_g1_i1	MSYERLFLCLVMVAALVATSAVHSQVEVEK-DDKLQERAVSCL	43	37.2	37.2	44.2	-----	-----	-----	-----	-----	-----
c13634_g1_i2	MSYERLFLCLVMVAALVATSAVHSQVEVEK-DDKLQERAI	42	35.7	33.3	47.6	-----	-----	-----	-----	-----	-----
c5043_g1	MSYQRVLCVVAVGLIAFAVAFPKDAALMEDDMLMKRVSC	41	41.9	44.2	48.8	-----	-----	-----	-----	-----	-----
c50300_g1	MS-SRFLFLVVLTVLIAASMALDYDE---EKGFMVKRVG	40	37.2	34.9	42.9	-----	-----	-----	-----	-----	-----
	* * * * *										

[illegible][illegible][illegible]

[illegible]

C) Nonclassical Kazal-type elastase inhibitor

D) Turriptide LoI9.1

E) Metalloprotease Inhibitor

E.1)TIMP1

c28108_g1
TIMP_DROME

-----MALLETAMVFLSVITMTSACSMPSPHQEHFCQAQFVVRGKVISGPGVQLPDKSLSSNVFGRFLAERVYTFRITKTYKGTAAIKKTGSLKVYGSRGRSFITKIHTPSK
MDLRKHLGLLTLVLAVFAFYGRPADACSMPSPHQTHFAQADYVVQLRLVLRKSDTIEPGR-----TTYKVHIKRTYKATSEARR-----MLRDGR-----LSTPQD
: * . ** :.***** *.**::*: :*: . :*: :.*****.***.:: ** : **..

c28108_g1
TIMP_DROME

LNSCRVDLNVGKVVIYIAGYFGRKKLFVSGCNFRMEWKISKQKRSFGFARKYGRSCCNHQKCYEDCGKESQAMACNFDISTNPANECRDRYQYQLSSDG-----RRCSWTKNAL
DAMCGINLDLGKVYIVAGRMP-----LNICSYKEYTRMTITERHGFSGGYAKATNCTVTPCFGERCFKGRNYADTCKWS--PFGKCETNYSACMPHKVQTVNGVISRCRWRRTQL
* ::::*:::** : :. *: *:::: .* **: *:: :*. *: : :.: * . . * * .*. *. * . ** * :.

PSI-BLAST

	aa	%I	%S	E-value
c28108_g1	YRKCMNKIP	208	100	100
TIMP_DROME	YRKCMSNP-	184	29.5	56.2
	*****:			2e-20

E.2)TIMP4

[illegible][illegible]

		aa	%I	%S	PSI-BLAST E-value
TIMP4_HUMAN	HLPLRKEFVDIVQP----	195	26.2	52.4	6e-13
c29197_g1_i1	GRGYRE C IKDATILGFYK	206	100	100	
	*: * *				

E.3)TIMP-LIKE

[illegible]

		aa	%I	PSI-BLAST E-value
XP_020895880.1	--SNKDY LISGHFWN----NKIRNSL CNSWNVEWSSVKQSFKDFTPKLKT C P C G V G C L L P L Q A L V A L A I I T C I I N Y F	155	100	
c26215_g1	RLHQQS FVLSGVS VDRREGONRMESES C QDWHSSSEEVTT SYKDI F P M L N T C K C A A N T N Y V G R F F L L S M L L T A W N M N	161	30.4	7e-24
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F) Serpin

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ILEU_XENTR-----MENLSSACTHFSFDLFRKI---NENNTAGNVFFSPISISTALAMVLLGARGNTAQQISRIHLHFDPAVK--DLHSNFQTLNABEINKKNVSSYALNLNANLRFGEKSKFPLPDFLSSVKKQYNADLGTVDIFSA
ILEU_XENLA-----MENLSSACTHFCFDLFPKKI---NENNSTGNLFFSPISLSTALAMVFLGTGKTAEQMSKTLHFDPAVK--DLHSNFQTLNABEINKKDVSTYALNLNANLRFGEKTFNPLPNFLSSVKKQYSADLGTVDIFSA
c25417_g1      MKLIITALKIAVVLLESEAFLCQGDEHDPESKTIKELVHSSNEFAFRLNLFGLTQNEKSKNENLFFSPSTISIALAMVFLGSRGNTAQISDALGVMYENGBEILHTAFKTLHEAHINSEDEVFLKLANRIGHWSDLHFLFVSSAMKEFTTLVDVFGK
c26903_g1      -----MSAVATAVNQFADVLHVLKLS--QEKFLGDNLFYSPTSLSIALGMVYSGARGSTAEQIANGFHWKSLEVEKLNESMSKFSDALTSSTASNELNANRLFLQQGFVEIQEFTDCCKKFYDAETALVDYKDK
c27265_g1      MYIIVLNTFRSRSLILTVSLVVVASISPSTMAQADIKASSNKFSKLKHQVLRG--QAS--SAENLFIYSPSSIILVALMTHLIGARGNTAKQMSKSFHLEEIPEKQLNEEFQKFLQSLNQSNARGNEIAMANRLFVQMGEFVSKQFQEESEKFFNAEALVDYQKN

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ILEU_XENTR      AEDARKEINTWVSEQTKGKIPEVLSAGAVNSF1KLVLVNAIYFKGDWAKKFKAETHTKDMPFQL---NKKEQKTVMKMYQMEKLFPNYIPEINCRVLLELPYVDYELSMVIVLDPNINDDTTGLQOLEKELSLEKIH---EWTENMMPIDVHVHLPKFKLEDYSK
ILEU_XENLA      LEDARKEINKVWSQETKGKIPLEVSTGTVDSTRKTLVNAIYFKGDWAKFNETHHTDMPFQL---NKKEQKTVMKMYQMEKLFPNYIPDINCRIELPVPDYVELSMI1ILPDNINDTTGLQOLEKELSLEKIH---EWTENMMPIDVHIIHLPKFKLEDYSK
c25417_g1       SDEVKRDNQNVHQQTQNGKIRDFPLHGVLNSATKLALINAIFYGWAKNFDEKETHTHAPFYASGNREYKMEVNMMQTKSKNKYIFDQEHSCHVLELPYSGNELSMVLVLPBEELD---GISLKESLDLENLD---RWMTLMVNTVSVSLSPRFKLNQQVDY
c26903_g1       FEGARKLINTWVEEKTDKDIKELLPSSGSLNSLTRATLVNAIYFKGIWEKQFEKAHYDSFTFFT---SLNKEMKIMMFQKSFKFL EARNLDCQLLEMPYTGGDLMSVILLPNEIE---GLSKLEEKLTYDALQGALTSVTKARPLEVEVSI PKFSMTRQFE
c27265_g1       SKGAREENVKNVVEEKTNNKIKDLPIEGMGFDPTRLITLVNAIYFKGSWMSGFDPNATQGTGFQL---TSSQSIEVPMMYQSKFKFYFENQDLCKCMLELPYAGEKMSMI1LLPDVE---GLSKLEESLSYKSLDDGINHLRMAREEEVEVTLPKFKLSEKFS

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			PSI-BLAST					
			aa	%I	%I	E-value	E-value	E-value
ILEU_XENTR	LKSQLAGMGMDLFEAGSADLSGMSG--NDLYLSEVIHKSFVEVNEEGTEAAAAA--AGIAMMCLMRE--EefnanHPFLFFIRHNATKSILFFGRYSSP-----	377	100	88.3	5e-95	2e-91	1e-90	
ILEU_XENLA	LKSQVLGAMGMVDLFNSGSADLSGMSG--NNLFLSEVIHKSFVEVNEEGTEAAAAA--AGIAMMCMRE--EefnadHPFLFLIRHNATKSILFFGRYSSP-----	377	88.3	100	8e-91	2e-88	7e-93	
c25417_g1	LKNVLPLQLGIQIDFDASKADLSGITES--SGLFVSNVIHKAHVDVNERGTEAAAAAT--GVTMMKRSLDLNEVFHADHPFIFFIRHHFSGSILFVGKVMQPSGLTEESDLPQRTVADEL	409	41.3	38.4	-----	-----	-----	
c26903_g1	LKEILQRMGMDGMDFDQVESNFTGLIKGPGKLYVSEVFHKAFVDVNEEGTEAAAAATAAVMMTRMMVRPPPSFTADHPFLFLIRHCKSDAILFLGRVAKPESKE-----	387	40.9	39.9	-----	-----	-----	
c27265_g1	LKEVLKMGASDLFNPSKADLTGINKD--GQLFVSEVVKAFVDVNEEGTEAAAAAT--AVGVALCMCPMNPFIFFADHPFLFLIRHNESGVILFLGLRANPN-----	381	41.0	42.1	-----	-----	-----	
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G) Reversion-inducing cysteine-rich protein with Kazal motifs

[illegible]

H) A.superbus venom factor 1

[illegible]

C) Venom metalloproteinase (M12B) family

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VM3E2_ECHOC --MMQVLLVTICLAVFFPYQGSSI ILESGNVNDYEVYPQKVLTALPIEAILOPE--QKYEDAMQYEFVNGEPVVLHLEKNKLNFTKDYSETHYSPDGREITT-KPLIED
VM3_BUNMU    --MIQALLVTICLAVFPYQGSSII ILESGNVNDYEVVYPQKVPLLPKGGVQNPPKTKYEEDTVQYEFVNGEPVVLHLERNKGLFSEDYTEAHYAPDGREITT-RPPVQD
c29916_g1    MFSLTLCVVLWCCVLTITNGETHRPLSEYIKIYETLS-YTSALTQKHDRHRSLNPKSSPILLNFIEAHRKFIRLRRHASIFSDDFVADNTFEFDTSKVVGEVEVLGHK
              : * : . : * :      : * : * :      : * :      : * : * :      : * : * :      : * : * :      : * : * :
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VM3E2_ECHOC HCYYHGRIGN---DAHSTASISACNLGKGHFKLQGETYLIEPLKIPDSEAHAVYKYENIEKEDEALKMCGVKHTNWESEDIPEAKSOLFATSEQHRFR-----E
VM3_BUNMU HCYYHYGIQN---EADSSAITSACDLGKGFKHQGETYFIEPLKLSDSAHAIIYKDENVEEENETPKICGLTETTWESEDIPIRNASLLIYTPEQNRYLKV-----K
c29916_g1 KSLVHGFIISDGIFEGEKIHAGNDEFHVHEPSHKIFYQGKQLFHSVIFKSDEDVQYPHEHGSGCGMRDKTKRWMEKVHAS-EIKEPKMQFOHSNYEPVLHRYRRAASQDPDPDK
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VM3E2_ECHOC      RYIEFFIVVDQRMYNKHHN--DSAAIRTWIFEMLNTVNEIYLPWNIH-----VPLVGLFWTQGDLINNVSSADKTLDSFGGEWRRRDLLNRKAHDN----AHLITAMH
VM3_BUNMU        KYIEFVAVDNRMYRHYKR--NKPIIKRRVVELVNILNTILRRLNPH-----TALIGLEIWSRKDKINVQSDVKATLKSFGKWREKKLLPRKRNDN----AQLLTRID
c29916_g1        KSCRLLMQADHLFTEHVGQGNKERALLKMTHEHVQAINTIYPGIKFFGKAESDKIEFVIARMLANGSAEQSEASNPFSSANIGVEKLELLNSQQGRNKGICYLGYIFTYRD
:  . . . . . * . . . . . :      :      :      * *      :      :      :      :      :      :      :      :      :      :

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VM3E2_ECHOC   FDAQTLGLAYTGSMLCPFKYSTGVFQDSSEINIFVAI-----TLAHELGHNLGISHDVP-SCT-CQTKA----CIMSPYLDQPTKLFNSNCSEIQK
VM3_BUNMU     FNGNTVGLAALGSLCSVKYSVAVIQDYSKRTSMVAS-----TMAHEMGHNLGINHDRA-SCTSCGSNK----CIMATKRT-KPASRFSSCSVREK
c29916_g1     FNDGVLGLAWGVSPTDAGGICEKERTYSDGTKILNTGVVTFINYGKAVPQRVSEITFAHEVGHNFGSPHDTSGECPTGGSDGNYIMFARATEGSKPNNRKFFSPCSIKKA
*:  . . . . . **          * : . . . : :          * : . . . : :          * : . . . : :          * : . . . : :          * : . . . : :

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[illegible][illegible]

		aa	%I	%S	PSI-BLAST E-value
VM3E2_ECHOC	-----YKSGFDYISCLPCYRANEEDKGMVDEGTCGEGKVCNSNGYCVDLNVAY-----	419	19.1	43.7	1e-12
VM3_BUNMU	-----KRNSG---VCNCLILPDDPNYGMVETGTCKGDGMVCSDRCKVKLQTVY-----	426	22.9	43.2	5e-21
c29916_g1	LAWIKKYWVAVLMGVALILLMAAFIKLCSVHTPSSNPNNKKPARQLTLRRQHLQEEFNRRARQARDTEGYGPSYGDPPPPYPGRGMEMQGGRYHR	556	100	100	
	. * . . . : : : * : : : : :				

D) Endothelin-converting enzyme 2. Peptidase M13 family

```
c30734_g1_i2      -----MSNELPSETTHVPLLKYEDQDSLVG-----FS-GSREGMAD-SDSLEGHIIIVVKPSS-----DNYLVRIIKKPTFWL---AVLIFILLFTCIILGALL
ECE2_HUMAN        MNVALQELGAGSNMVEYKRATLRDEADPETPVGGASPDAMEVGKGASPFSPGPSPMGTPGTPRSSGLFWRVTCPHLRSISGLCSRTVMVGFGKQTROLLGSRTQLLEVLVLAGASLLLAALL
```

c30734_g1_i2 SRSKKEYKSLVLKE--DSVCLSEGLSDSAHYMLHAIDPKANPCEDFFQYSCGGWIKNHPDPSQAFWGTFTSSLWDNDNMKEMKRLLTDPAIKNSSSSTIKLAKTFYDSCMNMDEINKQGAQ
ECE2_HUMAN LGCLVALGVQYHRDPHSHTCLTETACIRVAGKILLESLDRGVSPCEDFYQFSCGGWIRRNPLPDGRSRWNTFSLWDQNQAILKHLEN--TTFNSSSEAEQKTRQRYFLSCLOVERIEELGAQ
* * * * *
* * * * *

[illegible]

c30734_g1_i2 MQIAKIFVPPNNRSQIDQMYSRKMSIKDLGNICPEIPWLDFFQETFKGSATIQDSENVVVMMATDYLVLSPIKKAGAKLLNDYVMVQIVRNSVGSLSRPFREAAHNLQKVLEGVSPQEE-
ECE2_HUMAN IQLANITVPQDQRDEEKIYHKMSISELQALAPSMDWLEFLSFLLS-PLELSDSEPVVVGYMDYLQQVSELINRTESPLNLYLIWNVLVQKTSSLDRRFESAQEKLLETLYGTTKSCVP
:.*:.* ** :.: :.:***** * :.* :***: **** ** :*** :* :*: *****:**** *: * * *

[illegible]

c30734_g1_i2 KGVNKNKWLMPQTVNAYYSPSRNQIVFPAGILQAPYYDKRYPKYCNYGSIGGAVGH^{ELVH}GFDNSGRMYDKNNGFVGQWWTNKSVEGFQVKADCLIKQYNQYSSYGKHEKGKFTLGENI
ECE2_HUMAN KPSPRDQWSMTPTQTVNAYYLPTKNEIVFPAGILQAPFYARNHPKALNFGGIGVVMGH^{ELTH}AFFDDQGREYDKEGNL-RPWQNESLAAFNRHTACMEEQYNQYQVNGERLNGRQTLENI
* .:::* ***** *:>::*****:* :::** *::** :.*****.*:.* ** **::: ** **:.*.:*: :.*****. *:>::*: *****

		aa	%I	PSI-BLAST E-value
c30734_g1_i2	ADNGGLKAAYLAYQHVVKQNGQEKLPVLGKTNEQLFFIAYGQSWCASIRPEKARAMLEIDPHSPNKFRLVLTLSNLKEFAKAFNCPLGSMNPNPKKCVI	781	100	
ECE2_HUMAN	ADNGGLKAAYNAYKAWLRKHGEEQLPAVGLTNHQLFFVGFAQVWCVSRTPESSHEGLVTDPHSPARFRLVLTLSNSRDLFRHFGCPVGSMPNPGQLCEVW	811	40.1	0.0
	***** *: :*:*:*: *: *: * *:***** :*: * *: *: * ***** :***** :*: *: * *: * *: * *: *			

E) Peptidase M14 family

E.1) Carboxypeptidase A2

CBPA2_HUMAN -MAMRLILFFGALFGHIYCLETFVGDQVLEIVPSNEEQIKNLLQLEAQEHLQLDFWKSPTTPGETAHVRVPFVNQAVKVFLESQGIAYSIMIEDVQVLLDKENEMLFNRRRERSGNFNFGA
c31568_g1 MTALKLAVAVVMTVVAIGYGKGYS GDKILRIIPTSRQH IKMLTKLEE QPMKLDFWKYPDNVGK PVDIHVSQDSDFANFTSIMQS IGMKF KILAADLQVLMDQQND--IVHYADEHSN--WYVH

*::: . . * .. **::*.**.:...:*** * **: : :***** * . *:.....: * :. . :*: *::: *::*:****:***: :. : *:* :

CBPA2_HUMAN YHTELEISQEMDNLVAEHPGLVSKVNIGSSFENRPMNVLFKS--TGGDKPAIWLDAIGHAREWVWTQATALWTANKIVSDYGDPSITSILDALDIFLLVTPNDPGYVFSQTKNRMWRKTRSKV
c31568_g1 YHPLDEIKAKINNLSVQAGDRAELIPIGKSFKEKRDQLAVKIKGAPQNNKPVLFINCGIHAREWVGVPATCVYMLDQLVNEYKNDTVKATLDKIDFIIPLVLPNDPGYVYSWTKDRMWRKNRKPT
.*:.:::***: . . . : **.*:** .*: . .*::::***** **::: :*:.*:** :*: ** :*:*** ***** * **:***.*. .

[illegible]

		aa	%I	PSI-BLAST E-value
CBPA2_HUMAN	SIDWSY-DYGIKYSFAFELRDTGRYGFLPARQILPTAEETWGLKAIMHEVRDHPY	305	100	5e-97
c31568_g1	TKDXYTGALHIKYSYVLELRDKDGKGFLLPQSQILPTAMETFAGIKAMVASMDLTQE	269	38.2	
	: *::* *****.:***** ***** ***** **:: *::*: : :			

E.2) Carboxypeptidase A4

CBPA4_HUMAN -----MRWILFIGALIGSSICGQEKFFGDQVLRINVRNGDEISKLS-QLVNSNNLKLNFWKSPSSFNRNRPVDVLVPVSLSLQAFKSFRLSQGLEAYVTI
c27510_g1 MARGIGHLIKTVVVLMISQSSVGRRKTYIGDRILRVTPKTEVDLKFNLGLVDDKNYELDFWTFPTFVARSDVHVSRSKCNQFERLLQLKNITFEVRL

: :: : **: ::::**::*: * : . : * : ** . * . * *** * . . : * : *: :: : * :

[illegible][illegible]

CBPA4_HUMAN SVVDFIQKHGN-FKGFIDLHSYSQLLMPYGYSVKKAPDAEELDKVARLAAKALASVSGTEYQVGPTCTTVYPASGSSIDWAYDN-GIKFAFTFELR--D
c27510_g1 NLAKFLFSRRKRIRGYVDFHSYGQLWMSPWGYKRFPPNYRKQALAMNKVKVKAIKHVGHTEFTYGPSSIMIYPTSGDATDWTFGVLGVTHSYGVELRPSL
...*: .: : ::*:***** * *:*. : .*: .: . . .** : * ***: **: .:*****: :*: .*: .***

		aa	%I	%S	PSI-BLAST E-value
CBPA4_HUMAN	TGTYGFLLPANQIIPTAEETWLGLKTIMEHVRDNL	308	100	100	8e-86
c27510_g1	MDLYGFLVPPSYITPVGKETFOGLKALAEVL----	343	29.7	58.3	
	. * * * * * . * * . : : * : * * : * :				

A) Retinoid-inducible serine carboxypeptidase, peptidase S10 family

[illegible]

B) PC3-like endoprotease variant B. Peptidase S8 family. Furin subfamily

[illegible]

Figure S5) Serine Peptidases. The sequences used in the alignment in A) and B) correspond to Retinoid-inducible serine carboxypeptidase (Uniprot: Q9HB40, RISC_HUMAN) from *Homo sapiens* and to PC3-like endoprotease variant B (Uniprot: P29145, NECB_HYDVU) from *Hydra vulgaris*, respectively.

A) Beta-hexosaminidase subunit beta

```
HEXB_HUMAN -MELCGLGLPRPPMLLALLLLAFLLAAMLALLTQVALVVQVAEAAARAPSVSAKPGPALWPLPLSVKMTPNLLHLAPENFYISHSPNSTAGPSCITLLEEAFFRRYHG YIFGFYKWHHPAEFQ  
c30952_g1 MAELCNTLL-----VIFGLFCFALPSSTTKPSLSDDLNLQRYGGKKQILAE DYVKGIWPKPQQQTPTGVKFSLLPKSFSFS-----IKGKTSDVLTDVAKRYMKLT-----PD SGVT
```

[illegible][illegible]

HEXB_HUMAN EFKWCWSPNKIQDFMRQKGFQIDFKKLESFYIQKVLDIATINKGSIVWQEVFDDKAKLAPGTIVEVWKDSAYPEELSRVTASGFPVILSAPWYLDLISYQDWRKYYKVEPLDFGGTQK
c30952_g1 SDFCDKSNPNITAWMKQKHGMGSNYSLLEQYYEQKLLNIIVGGLKKQYIIWQEVVDNNVVLPLPTVVNVWKG-GWQAEALAKVTKLGLTKLSSCWYLDGSIYGLDWNKYYQCEPNTFTGSDA
* * * * *
* * * * *

		PSI-BLAST		
		aa	%I	E-value
HEXB_HUMAN	QKQLFIGGEACLWGEYVDATNLTPRLWPRAVGERLWSSKDVRDMDDAYDRLTRHRCRMVERGIAAQ-PLYAGYCNHENM----	435	100	1e-167
c30952_g1	<u>QKELVMGGTGCMWGEWVDGNTILPRTWPRALAIARLWSSKATTDLGDATNRIWEQRCRYLRGIPAEHAVQSKYCRHEWPAD</u> ***. ** .*****. ** ** ** ** ** ** ** ** . ** .*****. - .*. ** .*. .****. . ****. . . . ** **	441	51.7	

B) Beta-hexosaminidase

[illegible][illegible][illegible]

c30078_g1_i1 LDVGRNFMPKSAVLRLLDVMATYKMNKFHFLHTDDEGWRLEIPDLPELTQIGSKRCYDPDTGLKCIQTDLGSGPDEPTSR-T-YTVNEYKEILQYANDRHIQVIPFDFMPGHGYAAVKSM
HEX_VIBVL MDVSRNFHSKELVFRLFDDMAAYKMKNKFHFLADDEGWRLEINGLPFLTQVGARCHDHVEQNCKMMPQLGSGAELPNNGSGYYTREDYEILAYSARNIQVIPSMDFPHSLAIAVKSM

..*.*.* * .*.*** **.....***** *****:*.*.* * *.**.:**** *: :*:* ..*

[illegible][illegible][illegible]

		aa	%I	PSI-BLAST E-value
c30078_g1_i1	KSSGDKILTKTAIPGLTVQYSDDNGQTRDIPDKVHGKVKLATRSADGRRISRSVEYQGSTIKSSSSIPSAIQCLVFISVISYLFISKVDF	862	100	
HEX_VIBVL	VIKNNILDVVTEFHGVAIQYSLD-GKTWHKYDDTKK-----PQVSTKALVRSVSTNGRTGRAVEVLAK-----	847	37.4	2e-178

Figure S6) Glycoside Hydrolase Family 20. The sequences used in the alignment in A) and B) correspond to Beta-hexosaminidase subunit beta (Uniprot: P07686, HEXB_HUMAN) from *Homo sapiens* and to Beta-hexosaminidase (Uniprot: Q04786, HEX_VIBVL) from *Vibrio vulnificus*, respectively.

A) PLA₂

A2-AITX-Ucs2a	---MKNN--IILVILLGI-----SVFVDCPLPN-DQEEDKSLNAQSEVSAVQKRDIQFSGMIRCATGRSAWKYFNNGWCGWGGSGTAVDGVDSCCRSHDWCYKRHDS	CYPKIIPYIASTSGS----	HPSCSITC--
c54261_g1_i1	MMMKKKSTTTLIVLLGM-----AFLVEGLSLN-NLEDDKRMNVKTGDGRAE-KRNLWQFGNMIKCATGRDAGDNGYGNVCGWGGSGVPVDGVDRCCQAHDRCYDNHDS	CNPKTNYYSYKSGK----	HPSCTISC
c18858_g1_i1	---MFFK--TILLVIVAA-----FLLTEIQGKRRNIKADESTKAVR---PAVMKRNLVQFGIMVYCMTGRFALDYNNGYCNVGGSGTPVDGLDRCCKVHDDCYGRYEN	CSPYYISYVYRTGW----	HPTCSLT
c28522_g1	---MKGAAALLWMLVFAAASLQFVFSMEEEDESIDQLHKVESDSDLQDEQSPVQKRNLIQFADMVRCATRRNPFYDNDYGNWCGVGGRGIPKDGVDRCRAHDKCYERYHGC	CNPKWRTFRYRAKKRRRRFRSR	CRITCK-
	* : : : : . . : . : : . . * : : * : * * . . * . * : * : * : * : * : * : * : * : * : * : *		

		aa	%I	E-value	E-value	E-value
A2-AITX-Ucs2a	HSANNRCQRDVCNCDKVAACEFARNTYHPNNKH-----	111	100	1.1e-57	3.4e-39	1e-35
c54261_g1_i1	STQNDQCERNVCSCKVAACEFARNNNYNNANKH-----	117	59.0	-----	-----	-----
c18858_g1_i1	--DTDACKKAVCTCDKEAAECFARHKYNSKNNNSWFLWFRK	139	40.7	-----	-----	-----
c28522_g1	-NKWGSCEGRAVCECDRVCLALCFARNRYHRKYKKK--SWWR-	204	40.1	-----	-----	-----
	. * : * * * : . * * : * : * : *					

B) PLA₂ / Group I

c25131_g1_i1	-MTVKRLVKTVILLCFVLLAVAG-----HTDSRRSKRSIAQLTTMIACATKN-NWVYYSNYG	CYCGPGGKGPVDEIDRCQKHDMCYGRIMSSWK	CMLS-LEVYFLSYEVTGCYNCKPS-N
c3686_g1_i1	MGALKLLVLLAVVACVACTSLDLGKLKKKSLKALKTQVHTRARRSLYEFYKMITCETGR-SWQDYNLYG	CFCKGKGTTGTPVDALDQCCFDDHDECYSQAAAS-VCPWP-LQIYLDYWHKN	CSECDAKSN
PA2AD_NAJSP	-----MNPALLLILAAVCVSPLG-----ASSNRPMPLNLYQFKNMIQCTVPNRSWWDFADYGC	CYCGRGGSGTPVDLDLRCQVHDNCYGEAEKISR	CWPY-FKTSYSECQSG-TLTCCKGG-N
A2-HRTX-Apt1a	-MQLYTY-FFTFSLVLILALADQENKSLDFTQEGGIA-----KRGAFQFSYLKIKYTGR-NPLDYWGYG	CGGLGGKGTTPVDGVDWCCYHDMCFNSITQGP	RPTCSKNAPYHKNYFSGLK
c513_g1_i1	-MGFLKLCFLVVLNLSLSQAAFISAADYEQDSGLSRGSYRSKRNLIQFARMITCATGR-DWSDYNEYG	CWCGYGGSGRPVDGTDRCQIHDRCYDSVVASNV	CTIGQLQIYETIYTRVNC
	. . : : * . . . : * : * : * * * * * * * * * * * : . *		

		aa	%I	%I	E-value	E-value	E-value
c25131_g1_i1	SPCALAICCKDSSLSKCLKNKPLHK-RYKLYDQTKCSHNFLGS	124	37.0	33.1	-----	-----	-----
c3686_g1_i1	SACEQALCECDKAARCFKNNKWDP-QYDDYPQEKCA-----	118	41.9	34.7	-----	-----	-----
PA2AD_NAJSP	DACAAAVCDCLRLAICFAGAPYDNNYNIIDLKARCQ-----	119	100	37.8	1e-23	3e-20	5e-19
A2-HRTX-Apt1a	SKCGRAICACDIAAVKCFMRNHFNKYNKYKN-IC-----	119	37.8	100	2e-15	1e-19	2e-27
c513_g1_i1	NRCEQAICSCD SHAVRCFRNRNYSRYANYNKQRLCNYN----	116	35.2	37.4	-----	-----	-----
	. * * : * * * * : * . . : *						

C) PLA₂ / Group III

c26312_g1	MDSYVSKIFVILAVILHASLCQAMYDWKTKTFRKDNSKLVVPGTKWCGKGNNAASFDDLGEHRETDLCREHDCPTIYILFPORRFGILNLYPSHLSL	CCEMKLYNCLWNVTSHVAVAV
PA23_HELSEU	-----GAFIMPGLTWCGAGNAASDYSQLGTEKDTDMCCRDHDCENWISALEYKHGMRYNPSTISHCD	CNDNQFRSCLMKLKDGTADYV
PA2_XYLAI	MHALRSSVLALWLCLHVSRAWMTYRSANGLDEYEPEDRIIFVGTKWCGNGNVAEGPEDLGLSKETDACCREDHDCPDLEIAGQSKHGLTNTASYTRLN	CACDEKFYNCLKNSSETGSGAV
	. : : . * * * * * . : * : * : * : * * . : : * : .	* * : : . * * : . . : *

		aa	%I	%S	PSI-BLAST E-value
c26312_g1	GRMYFNVLVRVPCFHLVEKKVCCKERSFDWWKFKYVCKKYGVVEVKQTGFMPKRFHKQLQVQPSNWNATANGTMT	159	100	100	
PA23_HELSEU	GQTYFNVLKIPCFELEEGEGCVD-----WNFWLECTESKIMPVAKLVSAAPYQAQAEQSGEGR-----	143	34.4	61.9	1e-30
PA2_XYLAI	RFTYFTLLGTMCYRNEHPLICVK-----KGWFSCKSYELDQS-----QPKRYQWFDVSSNFAFPRMLT----	140	33.3	54.1	2e-21
	* : * : * : . * . : * : : . : : . : * * * * * . : : * * * * : * *				

D) PLA₂ / Group IX

c23289_g1	-----MR--DPMLRVYLLLLMI-----HHTTAHQCR--VQVNGCSIPGNLPFLYKKKFTPA	CNKHDVCYS	CGQYYHWSRKS	CDVSFQNDMYYL	CTL
X2G7F0_9CNID	-----MQTYKGAILVFVTLGCF-----IGGVLSTCPADVHVNGCSIPLNAPFPYKELFKPV	CNRHDVCYI	CGNRYGWTREI	CDVAFKRDMEQK	CTD
c38288_g1	-----MLPRMLLTRTISFTEFLIVLMFGFYSCSWCHTNSTROCAADGYSNGCSVPLGMEAPYKASFTPA	CNKHDICYG	CGHHYNWTRDL	CDDAFLADMKNT	CKN
A0A2B4RAB8_STYPI	-----MGNSVSLTIAWLLLSMS-----WQVISAGSDCTIQTNCGSVPLGLKAPYQITLTPA	CVKHDVCY	CGELYRWNQEQ	CDKAFKRDYKLC	ER
COMA_CONMA	-----XQPSTAECLKINSNACSVPFSSX-IPQKXFLAACDRHDTCHYCGKHFGFKQDD	CDAFFRDMTALC			
A7T072_NEMVE	MARVTSTKQYKNGMFSRYNGITPWNFEGIMSPVLVIFVIALPLSALASEGVTVDLQDQVCPFESNGCSVPGLPMLYKRLFTPA	CHMDHVCY	RCNKVHDWEKID	CDTKFWENMYFL	CEG
	* : * : * : : : . * * * * * . : : * * * * : * *				

		PSI-BLAST				
		aa	%I	%I	E-value	E-value
c23289_g1	PHN---KGFVFELKGVKKVLKTKEEA-----HCHTIAYLYYKAVDLLGGDRYDYISPEWCRDRCEVEKIGSPNRRIGYSKNI	136	100	33.1		-----
X2G7F0_9CNID	RYNNR---KRFFSSIWNGITGATKVATEIAKWPIRGDLNCHKHGAKIYYEAVKYFGKSYFVSSSPSEWCKEECAKNAGNPN---I-----	142	40.4	36.9	3.9e-31	
c38288_g1	LHGNVRRKRFLSALLEVWYFIQIGISKDK-----RRCNLFAEMYKYGVRTFGKSHFEIRDHDYCWNTCADKHGSPFEDVPREFF-	147	33.1	100		N.D
A0A2B4RAB8_STYPI	KGK---RWFIGDLLTKEKCKSLGADA-----YTTAVRIAGHLHWEKNSPPWCOKACAKDLGDPNILIRH-----	125	37.7	36.1	1.2e-26	6.1e-26
COMA_CONMA	-----AHGTDDE-----GX-----CPX-----	77	N/D	N/D	1.4e-08	2.9e-09
A7T072_NEMVE	QYGTPTDDHLDKRFLWNKQKMCNKVADG-----YHTAVQMFGEHSHWDTAKPDWCKKKCVKKIGDPRNHIQL----	138	36.1	31.2	2.2e-29	4.3e-18

A) BPI/LBP/Plunc superfamily. BPI/LBP family

BPI_HUMAN
LBP_BOVIN
c30974_g1
c24158_g1
c28966_g1
c25445_g1

MRENMARGPCNAPRWASLMVLVAIGTAVTAAVNPNGVVVRISQKGLDYASQQGTAALQKELKRIKIPDYSDFSFKIKHLGKGHYSFYSMDIRFQQLPSSQISMVNPVGLKFSISNANIKISG
----MVTSTGTLP--SLLLTGTLTFTSGALGANPLGVVRI TDQGLE YVAQEELLALQSKLHKVTLPDFNGDVRIKHFGSVDYRFHSLNIQSKCLLGSALKLLPNQGLHFSISDSFIQVTG
----MKS-----CLIFVMLVLVIGVSLAKNPGRIRLTNNGLAYAAKITKDLIHEKIKILHKIDINGRADTP-IGHISYSLSSIHVNSFSIPTLTTLTKPKGVGLELSVSGVNI DMGG
----MKN-----LLTLLVLVTLAVFSLATNPGIRLRLTDKGLSYAKIAVEVLNEKLTIKIPDIKGEDTP-VGHISYSLSSIKVSSLSIHTYSLTKADVGLELSVSSVSI SMSG
----MAKMLLFFC-VAVAVFSGVARSSLPSPSEANVRLFLT KKGMDYANEAMSSIVSEVRGLRIPPVS-ITKSIWNNRIDLSLNSKVNKNVNLGSSSLSFYGYG-HIKLSLQLSSAEIVG
----MYRMWLI FCLVFIGVCFDGGRSSPPPSKANVGLYLTKKGADYANVVMVNKT KSTMEGQKVPPVS-ISKSIWNTTIRLSLAKSKIRSVSLGDTSIKFQNG-FVKVLINIKSAEVAG
* : : : : : * : : : : *

BPI_HUMAN
LBP_BOVIN
c30974_g1
c24158_g1
c28966_g1
c25445_g1

KWKAQKR---FLKMSGNFDSLIEGMSISADLKLGSNPTSGKPTITCSCSSSHINSVHVHISKSKVGWLIQLFHKKIESALRNKMNSQVCEKVTNSVSSELQPYFQTL PVMTKIDSV--AG
DWKVRKR---ILRLDGSFDVKVKGITISVNL LLDSEP-SGRPKVAVSSCSSHIRDVEVHIS-GDLGWLLNL FHNQIESRFRVRVLESKICEI IEDSVTSELQPYLQTL PVTTEIDHL--AG
DWHYRKDHWPHISDSGFSFLKNGISFDALVKIGANP-QGHPTIAAAGC SSSVGGVDIHFS-GGASWLYNLFAGKVEHSIKKSLQSEMCKAANSAITDQGA KSFA RFPIKKKLDKW--TF
NWHYREDHWPHISDSG SFTLTASGISFDVSIKIGATA-DGHPTIAAAGCSASIGVSIHFS-GGASWLYNLFASKIEGVIKSSLNSELCKAATSAINDQAKAVAKFPVKKQLDKY--SL
DYKYAGG--FLGRGRGTYEVLKLRVSLTKYLSLEANT-KGKPYVNVNRECNTWIGDIDPTFR-GE SSIILNLLVQLVKRSVQRD VQKMICKSITDGINERGKKL PKLYQDKFPPIQVPSAK
EYNYNGG--ILGSGRGTYIVKLTNVWITKELSLGVNA-KRRPFLINGKCSNWIQDTSPEPT-GGSSFIILNLLVALVRSSVNNEVRKKICTSINEAVDKQ GKMLPTYYPENYNVSRVQCAQ
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BPI_HUMAN
LBP_BOVIN
c30974_g1
c24158_g1
c28966_g1
c25445_g1

INYGLVAPPATTAETLDVQMKGEFYSENHHNPPFPAP---PVMEFPAAHDRMVYLG LSDYFFNTAGLVYQ EAGVLKMTLRDDMI PKESKFRLT TTKFFGTFLPEVAKKFPNMKI QIHVSAS
LDYSLMGAPQATAQMLDMVFKEIFSRDDRFPVAF LA---PVMNLP EEHSRMVYFAISDYAFNTASLVYHKAGFLNFTITDDVIPP DSSIRQNTKSFRAFVPRIARLYPNTNLELQGA VI
IDYSLVSSPNSTVSFIDIFLKGEFESLAHPSEAPFSP---EPLPIDSESSSMVYGWITDYMFN TAGFAYMKAGFLNHTFVPDDFPKNSSYTPNTKT FKS LI PPLYDKYPNRPMTFKVIAT
IDYALVKSPNSTFSFLDIFVKGEFESVAHPTEAPFSP---ASLPIDS-----
IHFPIL ESPSIQ RGSVEFVIEGGIYSRTYTL DSSSRGQGISHIRYYP SHSKMLSIVLSDRMFNSLAELYFKAGVVQINEMQM DRVNPP-----MSIKVDLA
INIPILQOPLIMTSYIEFLMEGGVNSSCYQLNNSRLRGIRHIKIYPNLSKMISVVLSDRVINSMTDLYYKAGLMKLIETQSTDLLDP-----LWAALHLT
.: .: * .: . : * . * . :

BPI_HUMAN
LBP_BOVIN
c30974_g1
c24158_g1
c28966_g1
c25445_g1

TPPHLSVQPTGLTFYPADVQAFVLPNSSLASLFLIGMHTTGSMEVSAESNRLVGELKLDRL LLELKHSNIG--PFPVELLQDIMNYI VPI LVLP RVNEKLQKGFP LPTPARVQLYNVV
SAPCLNFSPGNLSTAAQMEIEAFVLLPNSVKEPVFRLSVATNVSAMLTFTNTSKITG FLEPGKIQVELKESKVG--RFNVELLEALLNYYLLNNFYPKVNDKLAEGFPLPLLRKIQLYDPI
KIPNVTSKTSGVSL LIECNIEMFVDLANGSSVFALSLGLTITADLHFNFKETNLTVNSTFVRLKASLVRSAIGDITKNIQGLQFYLDFFVNGMIIRKINDRGVKGFPLPVNDGLKLVNPR

RPPFTNTNTSGSFFTL YLNG-----TIKDRSS IYEVGLHVTGEFKIQEKKRILSGSVSNLRFELTHCAENTP--KDLKEI I VPSLFSERVQVAKEVSE S FMNDMAPLPIPTVKI INER
SSPQINTTVNSSLV VFKMNA NF TPTCSVNKESETFSVDLEIVGDFYLEENWEVSGKVKNLRIEP-FFTDDIP--EKIKSLVLPVLKTHDSQIINQLNE-FLDKI I PLPKYSYVHFTNNO

PSI-BLAST									
	aa	%I	%S	%I	%S	E-value	E-value	E-value	E-value
BPI_HUMAN	LQPHQNFLLF GADVYK-----	456	100	100	43.0	79.5	2e-39	2e-15	7e-04
LBP_BOVIN	LQIHKDFLFLGTNVRYLRV-----	456	43.0	79.5	100	100	3e-73	1e-37	2e-14
c30974_g1	IRSGKSFTLVSTDISYTPSEDPLEQEKLIFFGNRKIPIV-----	481	28.3	64.3	29.1	63.6	-----	-----	-----
c24158_g1	-----	248	N/D	N/D	N/D	N/D	-----	-----	-----
c28966_g1	VKYGGQYIVFECDLLEKE-----	434	20.4	58.6	19.1	54.1	-----	-----	-----
c25445_g1	FLRKEGYTVFESDIKV-----	436	19.3	53.7	16.9	53.2	-----	-----	-----

B) L-amino-acid oxidase

OXLA_BUNMU
OXLA_CALRH
c29905_g1
c10621_g1

MNVFSIFSLVFLAAFGSCADRRSPLEECFREADYEEFLEIARNGLKKT SNPKHV VVVGAGMAGLSAAY-VLEKAGHRVT LLEASDRVGG RANTYRDEKEGWYVNMGPMRLPERHRIVRTYIAK FGLK LNEFF
MNVFFMFSLFLAALGSCADDR-NPLAECFQENDYEEFLEIARNGLKATSNPKHVVI VGAGMAGLSAAY-VLAGAGHQVT VLEASERPGGRV RTYRNEEAGWYANLGPMRLPEKHRIVREYIRKFDLRLNEFS
-----MAEVDADVI I GAGISGLCGAKSLQDKHGLRVLVLEARDVGGRTLT SKDPL YGYLDGGTYIGATQTHIMN-LVKELGLDLYQTN
-----MVQSVVDVIVIGGSI GLCAAK-LLKEYGFDVLVLEARDVGGRTETLE DPLFKYIDLGGSYVGADKHRILR-IAEELGVKTYPVE
.. .: : *.: : *.: : *.: : * : * * : * : * : * : * . : : * . . : : : : : :

OXLA_BUNMU
OXLA_CALRH
c29905_g1
c10621_g1

QENENAWYFIRNIRKRVWEVKKDPGVFKYPVKPSEEGKSASQLYRESLKKIIEELKRTNCSYILDKYDSYSTKEYLIKEGNLSRGAVDMIG--DLLNEDSSYYLSFIESLKNDLDFSYEKRFD----EISGG
QENDNAWYFIK NIRKKVGEVKKDPGLLKYPVKPSEAGKSAGQLYEESLGKVVEELKRTNCSYILNKYDYTSTKEYLIKEGDLSPGAVDMIG--DLLNEDSGYYVSFIESLKHDDIFAYEKRFD----EIVDG
TEGCDIHLFLGIMKTI SHDIP LGTS-FLGALDINNFWQAIEKMSKDVP LQAPWLATKAK EWDKMTFKQFIDEKCVTRYGRAVASAFVNVNLSSEPSDISLFFFLWFLRSGGGVIRN-WEDSLGGAQ EYKIVGG
CKGKTTDHLY--AKVRQHDGSFSTWNPLAIDYWNVAYTLDKMC DTVPDQPWEASRAIEWDHITAE EFNKVCWTSYCKKRMVQNT HHALAVELWEISLLNLYLWNRKVGEGLKHSSADDVE--DEKQFIGG
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OXLA_BUNMU
OXLA_CALRH
c29905_g1
c10621_g1

FDQLPKSMHQDIA-EMVHLNAQVT KIQHDAEKVRVAYQTPAKTL SYVTADYVIVCATSRVRRISFEPP LPSKKAHALRSIHYKSATKIFLTCTQKFWEADGIHGKSTTDLPSRFIYYPNHNFTSG--VGVI
MDKLP TAMYRDIQ-DKVHFNAQVIKIQNDQKVTVVYETLSKETPSVTADYVIVCTTSRAVR LIKFNPPLLPKKAWHALRSVHYRSGT KIFLTCTTKFWEDDGIHGKSTTDLPSRFIYYPNHNFTNG--VGVI
AQCISKLAERIGSDNIFNSDVTHIDQTQSEYVTVR---CLDGSVYKACVISTAPPALLNRI RFTPFLPALKQAGLSHRIPVGS IIRTVSVYENSFWREKDLTG YFLTDDGFGGPVTEAVEYSARDGNYPAL
AQQISNKLKERLD-DKVI LNSPVQVQVKQ-ENDHVI VT---CKNRNSYQSKYVISAVPQALLSKISFEPP LPA LKNQLIQRFPMGSSIKTFAFYETA FWRSKGLNGAILSD--FG-PIHTSMDDTKPGSNLPVI
: : . : : : : : * : * : : : : . ** . : * * * * . * : : . * : . ** . . : * : . : : :

OXLA_BUNMU

VAYVLADSDSDFQALDIKTSADIVINDLSLIHQLPKNEIQALCYPSLIK KWSLDKYTMGALTSFTPY-QFQDYSETVAAPVGRIYFAGEY TARVHG-WLDSTIKSGLTAARDVNRASQKPSRIHLISDNQL-

C) Phospholipase B

PLB_CROAD MIRFGNPSSSDKRRQRCRSWYGGLLLLLWAVAETRA^{DI}HYATVYWLEAEKSFQIKD-VLDK-NGDAYGYND^{AI}QSTGWGILEIKAGYGNQ^{PIS}NEILMYAAGFLEG^{YL}TASHMSDH^{FAN}LFLPLMIK^N--
T1DLW3_CROHD MIRFGNPSSSDKRRQRCRSWYGGLLLLLWAVAETRA^{DI}HYATVYWLEAEKSFQIKD-VLDK-NGDAYGYND^{AI}QSTGWGILEIKAGYGNQ^{PIS}NEILMYAAGFLEG^{YL}TASHMSDH^{FAN}LFLPLMIK^N--
PLB_DRYCN MVRFGSAASSDNR^{RR}RCRSWYGGLLLLLWAVAETRA^{DL}HYATVYWLEAEKSFQV^{KD}-LLDK-NGDAYGYND^TQSTGWGILEIKAGYGSQ^{LV}SEILMYAAGFLEG^{YL}TASRMSDH^{FAN}LVHQ^{MI}K^N--
c31154_g1 MALFAVG-----YFFVVV^{VCY}CLGSRVQSASLNGT^{VY}VNPIDGSYDV^KFGVLDKMNGAAYGTFDDNV^{MT}SGWGELNIVAGK^{GK}-YQDHEIMYAAGFLEGAL^{TAR}QINDHYSNIYGIFFK^{NG}-
V9KKP6_CALMI ----MCVCVRGQGLGLGLPL^{LV}LAAVGSASARGHLLRSV^{LV}LDEHSGRLRVVGG^{LN}PH--SI^{AWAN}LTD^{RI}RATGWSFLE^{TG}T---NGKYNDSIQAYAAGVVEAA^VTQPL^IYMHWMNTMP^{NY}CGP^{FK}
c29069_g1 -----MASNALLFL^{AI}TASVCC^{FT}IKATTYVSV^{LL}PDGKTLK^{VS}TGK^VFP--NV^{AWAR}FTDEIQVGSY^{LV}EH^{VS}---NGSY^{PD}MLQAKAAGMAE^{GY}ITSEMI^SMAVYNQYK^{GY}CD---

[illegible][illegible][illegible]

		PSI-BLAST				
		aa	%I	%I	E-value	E-value
PLB_CROAD	-----AGCYDSKVADISMAAKFTAYAIINGPPVEKGLPVFSWVHFN-KTKHQGLPESYNFDFVTMKPVL-	518	52.3	33.2	1e-179	6e-85
T1DLW3_CROHD	-----AGCYDSKVADISMAAKFTAYAIINGPPVEKGLPVFSWVHFN-KTKHQGLPESYNFDFVTMKPVL-	518	52.5	33.0	5e-177	N.D
PLB_DRYCN	-----AGCYDSKVADINMAAKFTAYAIINGPPVEKGLPIFSWVHFN-ETTHQGLPESYNFDFVTMKPVL-	518	53.2	33.0	2e-176	N.D
c31154_g1	----DGCYDAKVTDFFMANSLVSSAISGPTAQD-QPPFHWISQYFPDPDTHNGMSDLFNFDVFKMKPKL-	522	100	34.2		-----
V9KKP6_CALMI	EHRSHGGMKMTVTSFEMYKTFEMIAISGPAWDQVPPFQWSKSSYSLIHMGHDPDLWKFPVPMVRWS--	540	36.2	47.8	3e-61	9e-124
c29069_g1	GHREHGTDCKITISLELFFKKFQCRAVSGPTHDDQVPVFQWSKTEWK--KPLGHPDKDFEPITVSWDKN	525	34.2	100	-----	
	* * * * * : : : : : * : * * : : : : : : : * : * * : : : : : : :					

D) Lysosomal acid lipase/cholesteryl ester hydrolase

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LICH_CROAD      -----MWRLLIIITAIL-FQGLVNSAMLERRKRGVD-----PETAMNISEIILFRGPYPSEEEYVVTTGDGYILCLNRPYGKI-SQKTKEP-KPAVFLQHGLLADGNSNWVTNLDYNLSGLFALADAGFD
LICH_MACFA      -----MKMFLVLGVVCL-VLWTLHEASGGKLTAVN-----PETNMNVSEIISYWGFPSEEEYLVETEDGYILCLNRPHPGRK-NHSDKGP-KPVVFLQHGLLADSSNWVTNLANSLSGLFILADAGFD
c2855_g1        -----MFTLVILALLGFASARQVNFVLVRQDQGVHVG-----ELPEVSMNVSQMI IYNGVPVENHEVTTDDGYILSLQHHPHGRQ-DKYKDVPSPKVVFLQHGLLASATNWVTNLQNSQFALADQGF
c28203_g1       MLCTNSASTATALLICMLLAFGPLQAVCRCINNTDLSKPGCIKVDPDVTRNVTQLIKSRGFPVSEYEVTTEDGFILGVQIRIPHGKKGVKTN-----GSKPVVFLQHGLLADATNWVTEWEDDSFGYILADQGF
c29969_g1       -----MSRALLVLVIFSITSHLVLGLPPLYKDKK-----VEARHPDIIDRNASQLIQNRGYPVEEYVTTKDGYVVLNQLRIPHGRNHQRTLAGCPKPAVFLQHGLLMDSTNWILNSANDSLGYILADBEGFD

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[illegible]

[illegible]

Figure S9) Other enzymes. The sequences used in the alignment in A) correspond to Acetylcholinesterase (Uniprot: Q92035, ACES_BUNFA) from *Bungarus fasciatus*; in B) correspond to Venom phosphodiesterase 1 (Uniprot: J3SEZ3, PDE1_CROAD) and 2 (Uniprot: J3SBP3, PDE2_CROAD) from *Crotalus adamanteus*; in C) correspond to Phospholipase B (Uniprot: F8S101, PLB_CROAD) from *Crotalus adamanteus*, Phospholipase B-like (Uniprot: T1DLW3, T1DLW3_CROHD) from *Crotalus horridus*, Phospholipase-B 81 (Uniprot: F8J2D3, PLB_DRYCN) from *Drysdalia coronoides* and Phospholipase B-like (Uniprot: V9KKP6, V9KKP6_CALMI) from *Callorhinchus milii*; in D) correspond to Acid cholesteryl ester hydrolase from *Crotalus adamanteus* (Uniprot: J3SDX8, LICH_CROAD) and from *Macaca fascicularis* (Uniprot: Q4R4S5, LICH_MACFA).

[illegible]

		aa	%I	PSI-BLAST E-value
c26308_g1	RDNDKWSSSCAVVYKGGWVDRCHYANLNGQYLHGKHNPWVRGVVWRNWKGHSYSLKGDELKIRPS-----	227	100	
TL5B_TACTR	RDNDKWEKNCAEAYKGGWYNACHHSNLNGMYLRGPHEESAVGVNWNQWRGHNYSLKVSEMKIRPIIFVPGEGLPK *****:..** :*****: **::***** **:* *:: ** * :***** :*****	289	41.9	3e-73

[illegible]

A.3) Veficolin-1

FCNV1_VARKO	-----EACS-----LACQQQEEAGAKDCKELLDRGETLT-GWYMIYPTTG---RGMRAYCDMETDGGGWLVFQRRLDGVSDFYRDWEAYKKGFGRQVSEFWLGNDKIHLLTSSGIQQLR				
c56356_g1	ETSPNALELCNGVSWLPLVTESKGQSMQNPGRHCLDILNSGQSRGNGLYWIDPSGGSPEDSYQALCDMTTESGGWTLVATKVS--VDFVPISSRFSGRAAQTNND--DAASHIHQALKNVWKEIL				
	* * . :: * . : . : * :: : * : : * * * * : * . : * * * * : : * * * : . : : * * * . : . . : . : . : * * . . : : :				
				PSI-BLAST	
		aa	%I	%S	E-value
FCNV1_VARKO	IDVEDFNNSKTFAK	196	100	100	8e-10
c56356_g1	FRFSHRSDVYVIYN	238	24.2	47.2	
	: : : : : :				

		aa	%I	PSI-BLAST E-value
GAPR1_HUMAN	TGHFTAMVWKN TKKMGV GKASASDGS-SFVVARYFPAGNVVNEGFFEENVLPKK-	154	100	3e-26
c22343_g1_i1	TGHFTQLAWKGS KEMGLGIAPSKDKSEYYIVARFRPSGNVQ GK--FVENVGPKVST	138	35.3	
	***** :.***.:*:*:* * *.:** * :****: *:*:* : : * * * * *			

C.3) Venom allergen 3

c18947_g1_i2	MNGGGKNYLVSVLSNATNTTDNATNSCNMPTCAPTTSVPTSAASSASSSGPSNATSGPTSSSHASSAPTSGASASTATGAPSSGGSSGSNDCCQKALAEHNAKRSVHNSPTMTIDPQ			
VA3_SOLRI	-----TNYCNLQSKRNNAIHTMCQYTSPTPGPMCLEYS-NVGFTDAEKDAIVNKHNELRQRVASGKEMRGTN-----GPQPPAVKMPNLTWDPE			
	: * **: * : : : * . : : : . ** : * : * : * : : : : : * : * : *			

c18947_g1_i2	LNAAAQAYAEKLATMKDIIHSPMNERQGQGENLAQRCSLPDTGFDCSKSATDMWYNEVKKYD--WGSPGYTDG-----TGHTQLVWKGTTKLIGIKAPFVNEKNLNCYVIVGRYKMAGNV			
VA3_SOLRI	LATIAQRWANQCTFEHDACRN--VERFAVGQNIATSSSGKNKSTLSDMILLWYNEVKDFDNRWISSFPDGNILMHVGHYTQIVWAKTKKIGCGRIMFK--EDNWNKHLYVCNYGPAGNV			
	* : * * : : : : * : . * * . * : * * . * . . . : * * * * : * * . : * * . * : * * * : * * * * : * * . * * * *			

		aa	%I	%S	PSI-BLAST E-value
c18947_g1_i2	KGQFPDNVQKGSYVARRSLE	211	100	100	
VA3_SOLRI	LGAQIYEIKK-----	253	25.2	44.4	7e-23
	* : : *				

D) Acrohargin I

		aa	%I	PSI-BLAST E-value
c25993_g1_i1	MNQILNIFVLVGMIIYSVESRN-----KACLDACFGDYSSCQMSTSCYDQASC AKKNALYSTCQQS-CGDKRGYVPEAVIDLRRRLRLGQ	64	100	
comp58542_c0	MNQILNIFVLVGMIIYSVESKD-----KACLDACFATYMRCLSNACYDKPSCRCQNTTYRTCVNS-CAKKRSYVPEAVIDLRRQLRLGD	64	64.1	nd
comp66995_c0	MNQILNIFVLVGMIIYSVESKD-----KACLDACFATYMRCLSNACYDKPSCRCQNTTYRTCVNS-CAKKRSYVPEAVIDLRRQLRLGD	64	64.2	nd
U-AITX-Aeq5a	MNQVTIFVLVGVIVYSVESSTPDG--TWVKCRHDCFTKYKSCQMSDSCHEQSC HQCHVKHTDCVNTGCP-----	50	23.9	8e-15
U-AITX-Aeq5b	MNQVTIFVLVGVIVYSVESSLTPSSDIPWEKCRHDCFAKYMSCQMSDSC HNKPSCRCQCVTYAICVSTGCP-----	50	23.3	9e-14
	*****:*****:*:***** * . ** * **:* : : : * : * . : * . : *			

E) Three-finger toxin-like

		aa	%I	PSI-BLAST E-value
c27526_g1	MKLTFLFVLVLAVA-IPIAFSLKCRIC A--GKICGTGPTTCPTG-DTCFTT-TYKNTSSVVKGCVTASACNQTMSCQKYP-NY CVAECCTTDGCN---SSGGFVQINVAMVTLMFAFFASIFYLFSH	70	100	
XP_020916494	MKLALLCLAVFAVV-IPSVFSIKCYN CV--LSVCKETSCLGVG-DRCIHT-SYKNSSKVVKSCATESLCNTTKSACDKVK-NYCTTSCCMTDGCNKGDSGVAALQFN YTMLAFMALLSALLSFVKF	70	48.6	3e-23
3NO23_NAJAT	MKTLLLTLLVVVTIVCLDLGYTLTCLICP--EKYCNKVHTCLNGEKICFKK-YDQKLLGKG---YIRGCADT---CPKLO-NRDVIFCCSTDKCNL-----	65	34.3	0.024
3NO21_NAJAT	MKTLLLSLVVVVTIVCLDLGYTLTCLICP--EKYCNKVHTCLNGEKICFKK-YDQKLLGKR---YIRGCADT---CPVRK-PREIVECCSTDKCNH-----	65	32.4	0.014
3LK6_BUNMU	MKTLLLSLVVVVTIVCLDLGYTRTCHIST--S---STPQTC PKGQDIFRK-TQCDKFCSIRGAVIEQGC VAT---CPEFRSNYRSLCCRTDNCNP-----	66	33.3	0.012
JN112568	--MQLFGPLIFLVT-LSAAFGLRCHSCS--GKSCTGPMTCPQGTDRCAIA-ESNG--AVAKSCMLSALCVSP-----IKCCETDL CNSATPTGSSVLLLVSSGIITLFL-----	62	34.2	5e-05
LYNX1_MOUSE	--MTHLLTVFLVALMGLPVAQALECHVCAYNGDNCFKPMRCPAMATYCMTTRTYFTPYRMKVRKSCVPSCFET--VYDGYSKHASATSCCQYYLCN-GAGFATPVTLALVPALLATFWSLL-----	72	33.8	0.022
	*: : : : * . *			

Figure S10) Other Proteins. The sequences used in the alignment in A.1) correspond to Techylectin-5B (Uniprot: Q9U8W7, TL5B_TACTR) from *Tachypleus tridentatus*, in A.2) to Galactose-specific lectin nattectin (Uniprot: Q66S03, LECG_THANI) from *Thalassophryne nattereri*, in A.3) to Veficolin-1 (Uniprot: E2IYB3, FCNV1_VARKO) from *Varanus komodoensis* and A.4) to Snaclec alboaggregin-B subunit beta (Uniprot: P81116, SLBB_TRIAB) from *Trimeresurus albolabris*; in B) correspond to Translationally-controlled tumor protein homolog from *Anopheles gambiae* (Uniprot: Q7QCK2, TCTP_ANOGA), *Plutella xylostella* (Uniprot: Q60FS1, TCTP_PLUXY) and *Ixodes scapularis* (Uniprot: Q4PLZ3, TCTP_IXOSC); in C.1) correspond to Ectin (Uniprot: B3EWZ8, ECT_ACRMI) from *Acropora millepora*, C.2) to Golgi-associated plant pathogenesis-related protein 1 (Uniprot: Q9H4G4, GAPR1_HUMAN) from *Homo sapiens* and C.3) to Venom allergen 3 (Uniprot: P35779, VA3_SOLRI) from *Solenopsis richteri*; in D) correspond to U-AITX-Aeq5a (Uniprot: Q3C258, ACR1_ACTEQ) and U-actitoxin-Aeq5b (Uniprot: Q3C257, ACR1A_ACTEQ) from *Actinia equina*, and comp58542_c0 and comp58542_c0 from *Anthopleura elegantissima*; in E) correspond to uncharacterized protein (RefSeq:XP_020916494) from *Exaiptasia pallida*, Probable weak neurotoxin NNAM3 (Uniprot: Q9YGI1, 3NO23_NAJAT) and Probable weak neurotoxin NNAM1 (Uniprot: Q9YGI2, 3NO21_NAJAT) from *Naja atra*, Kappa-6-bungarotoxin (Uniprot: Q9W729, 3LK6_BUNMU) from *Bungarus multicinctus*, Ly-6/neurotoxin-like protein (JN112568) from *Epinephelus coioides* and Ly-6/neurotoxin-like protein 1 (Uniprot: P0DP60, LYNX1_MOUSE) from *Mus musculus*.