

# Supplementary material

## **The unique neuronal structure and neuropeptide repertoire in the ctenophore *Mnemiopsis leidyi* shed light on the evolution of animal nervous systems**

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**Supplementary figure 1.** Workflow for the identification of putative neuropeptide precursors of the ctenophore *M. leidy*.

**Supplementary figure 2.** ML00218a gene specifically overexpressed in C42.

**Supplementary figure 3.** Processing of *M. leidy* neuropeptide precursors.

**Supplementary figure 4.** Sequence alignments of diverse ctenophore neuropeptide precursors.

**Supplementary figure 5.** Developmental profiles of putative *M. leidy* neuropeptides.

**Supplementary figure 6.** Neuropeptides expressed in the subepithelial nerve net.

**Supplementary figure 7.** Neuropeptides expressed in the subepithelial nerve net, in multiple neural cell types and restricted to the aboral organ.

**Supplementary figure 8.** ML02212a, ML199816a and ML056913a expression.

**Supplementary figure 9.** Neuropeptides expressed in the pharynx and mouth area.

**Supplementary figure 10.** ML030511a is expressed in the AO rim and sensory cells in the pharynx.

**Supplementary figure 11.** Neuropeptides expressed in multiple cell types.

**Supplementary figure 12.** ISH with neuropeptide precursors expressed in the AO cells.

**Supplementary figure 13.** ISH of neuropeptide precursor genes expressed in the tentacles.

**Supplementary figure 14.** ML10665a is expressed in the meridional canals and pharynx.

**Supplementary figure 15.** Behavioural experiments with *M. leidy*.

**Supplementary figure 16.** Alignments of *M. leidy* and *H. sapiens* neuronal proteins shown in Table 1.

**Supplementary video 1.** ML02212a localization in the aboral organ of *M. leidy*.

**Supplementary video 2.** ML07842a localization around the pharynx of *M. leidy*.

**Supplementary video 3.** ML07842a localization in the aboral organ of *M. leidy*.

**Supplementary video 4.** ML07842a localization in the aboral organ of an adult *M. leidy*.

**Supplementary video 5.** ML21545a localization around the pharynx of *M. leidy*.

**Supplementary video 6.** ML17711a localization around the pharynx of *M. leidy*.

**Supplementary video 7.** ML17711a localization in the aboral organ of *M. leidy*.

**Supplementary video 8.** 3D reconstruction of a part of *M. leidy* epidermis.

**Supplementary video 9.** 3D reconstruction of a part of *M. leidy* epidermis.

**Supplementary video 10.** 3D reconstruction of a part of *M. leidy* epidermis.

**Supplementary video 11.** 3D reconstruction of a *M. leidy* synapse.

**Supplementary table 1.** Neuropeptide precursors predicted by NeuroPID.

**Supplementary table 2.** NeuroPID scoring for the linear neuropeptide precursors.

**Supplementary table 3.** Neuropeptide homologs uncovered in other ctenophore species.

**Supplementary table 4.** Summary of neuropeptide expression patterns and metacell annotation.

**Supplementary table 5.** ISH probes.

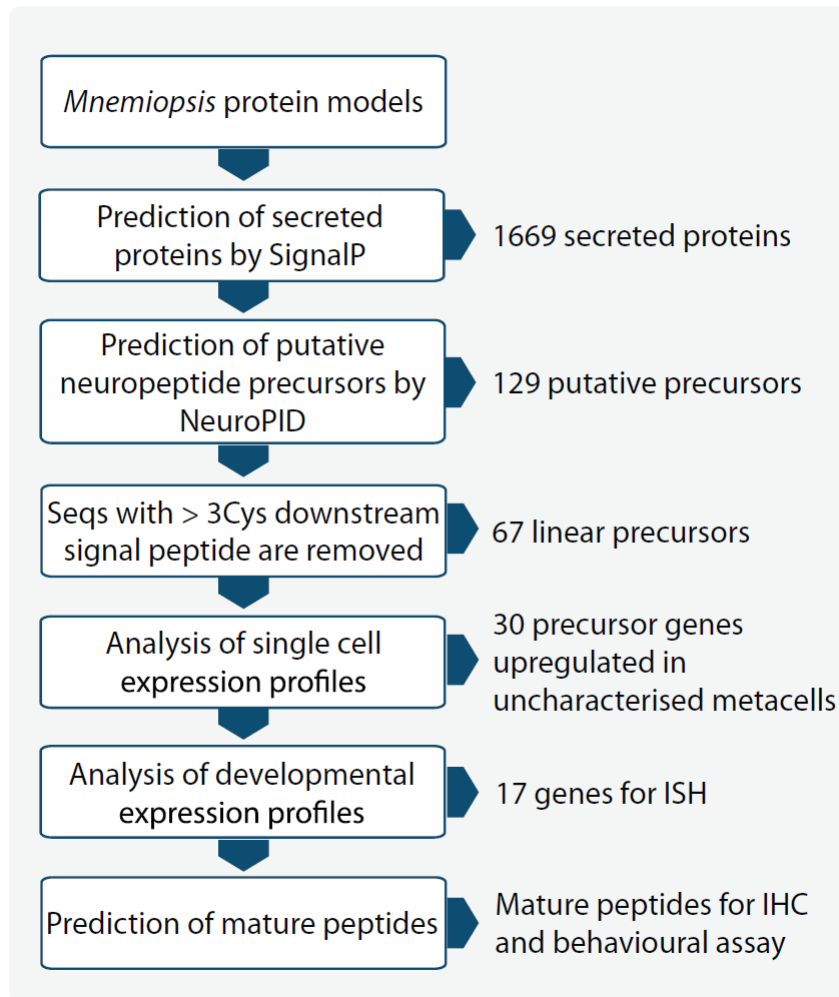
**Supplementary table 6.** GO terms identified in the C33 transcriptome: SNARE binding.

**Supplementary table 7.** GO terms identified in the C33 transcriptome: Ion channel activity.

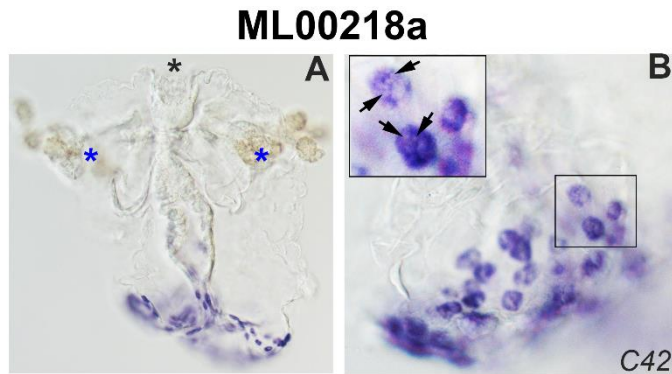
**Supplementary table 8.** GO terms identified in the C33 transcriptome: Actin binding.

**Supplementary table 9.** GO terms identified in the C33 transcriptome: Tubulin binding.

## Supplementary figures



**Supplementary figure 1. Workflow for the identification of putative neuropeptide precursors of the ctenophore *M. leidyi*.**



***Supplementary figure 2. ML00218a gene specifically overexpressed in C42 indicates that this metacell represents gland cells around the mouth and in the pharynx. C42 was not annotated in the original study. (A) Whole cydippid. (B) Close up to the mouth area. Black arrows highlight unstained secretory granules.***

### Repetitive sequences

>ML043317a

*MKTILLISCLLSAVYS*RVLRLNEEWSRNGAMEDSEDSSRNGAMRDSEDWNRNGGMRSEDWSRNGRMEDSEDSWSRNGAMEDSEDSWSRNGAMEDSEDSWSRNGAMEDSEDSWSRNGAM

>ML07842a

*MMKLTVVCLLFASLLVRAE*CGVVERHEEQLFDAEDEQPNFRAGLENKELKRSPNFRFGSKRSAEDAPNLRGRSNEDTNPFRGTKRSAEDSPNFRGAKR  
SAVEAPNFRGAQSEEDAPHFRGAKRFAEDAPHLRGVKRSTVDAPNFRGAERLEEDVPNLRGAERSEGSPNFRGAERAVEDAPQFRG

>ML21545a

*M*SKFLFLTLVGAARAASFASDSNTLADSDECRTGYNMRYDLECRRRRAAAAAAALQLQEDGETEGGEELTKRSAEEQNWNYSARRDRGKRSNEEQ  
DFSGYRRGSGQKRSAEEDDYDIYKRGESEEQDYSGYRGRGRE

>ML017711a

*M*KMFILIGLLITLVLYSAGDLARSLEEENESGINEGAAEEDDESFRGLRESEDESRGREVAEDEELFRGRDFRGRDFRGRDFRGRDFRGRDFRGR  
RDFRGMKSEEEFLVKRDLSRGQ

>ML016347a

*M*ICLNFRVTAVVLVILLAGFCPAPIYSTQENDAFLETGEEKELDIEAPKTPKLRYFYQKRSEEGKDEDPKLQYFQIRSLEDKKKPKLRYFYQKREENKD  
TKPKLRHFYQKREENKDTKPKLRYFYQKREENKDTKPKLRYFYQEREDNKDTKPKLRYFYQKREENKDTKPKLRNFYRKRGEN

>ML11723a (adult specific)

*M*KYFMILAVLITVGSSPFEKRDAENAELASEKRSEADPGEEVLAKRNVDQDAVSLEKRQKYGYKRGE

>ML06405a (adult specific)

*M*RKTLCIQLLVLAIQRFTDGKAFEESENEVLSLEKRAEDLDDEDFDKRETEDRENEVEIDLD

### Non-repetitive sequences

>ML02212a

*M*KLFLVLLGLVALISCETVSEVDSELSSEDSNAMRVKRAFSMSNYRGHKQGNRGWTGGAMQEEE

>ML02736a

*M*KCFVVLFALLALSQSASLSLESVEDVIMADNDNVLEEGALNAEEEARVYKGYNGGNRVWYG

>ML199816a

*M*KLFLTLASLLVLATVTVQTEAREIVAEVAEAESAESASEEDTFVYRKEEDSSAFLAD

>ML056913a

*M*FRLTSILLVLVLAIVFTRTEDSEEIGHGLRMDKNEEIGHGLTDKRSADSVDTEAMADEEELVGHGIKGSHAWRK

>ML01798a

*M*KLLLLTLAVLLACLTAVPVRQEEVPEEIRLERSAESSGETARVEKRAAIDTGSDYPGFEGGKRRWYG

>ML233326a

*M*KTTFLVLTLMICCNYQSVPMSLEEDLSDEEHRGLQKRAGTKFNKADYKSVGEGTRKWFG

>ML065755a

*M*KLAAGIFLVLACLTVVMIPGEAASLGSLDAANSDSNAVLYGADHEILESSLNRKEEAFGALYG

>ML215411a

*M*KQRITILLTLGVIVLAQSKSILVESEDVLLGDNAELVDSNSVDLEELIGSDIKLVPGSGGNPWGRK

>ML124215a

*M*SRMLFAVTLVIFSVLAITSGASLSEEELLTGLEDQMENSEETMMYASDDADNNEAEMAKRGGKARYRRW

*Supplementary figure 3. Processing of M. leidyi neuropeptide precursors. Signal peptides predicted by SignalP tool are shown in yellow and italics, cleavage sites are in purple, Gly residues converted into C-terminal amides are in blue, mature peptides are underlined, negatively charged residues are in red, positively charged residues are in blue. Mature sequences used for antibody production and behavioural tests are in grey. To predict mature peptides, we were guided by the following assumptions: 1) cleavage occurs at dibasic or monobasic motives; 2) mature peptides are the most conserved parts of the precursors (Fig 1D, Suppl fig 3); 3) propeptides tend to be negatively charged); 4) C-terminal Gly is converted into an amide group*



ML233326a  
*Bolinopsis* a sb|12973892|  
*Bolinopsis* i sb|1225922|*Mertensiidae* sp sb|581370|  
*Beroe*\_f\_GHX01353421.1  
*Beroe* sp sb|12857913|  
*Mertensiidae* sp sb|561171|  
*Pleurobrachia* sb|12660472|  
*Pukia* sb|13042259|  
*Hormiphora*\_GHX01067440.1

ML07842a  
*Bolinopsis* i sb|12232314|  
*Bolinopsis* a sb|12925108|  
*Pukia\_f*\_sb|13030337|

ML07842a  
*Bolinopsis* i sb|12232314|  
*Bolinopsis* a sb|12925108|  
*Pukia\_f*\_sb|13030337|

ML14991a  
*Mertensiidae*\_sp\_sb|606751|

ML043317a  
*Bolinopsis*\_i\_sb|12203929|  
*Beroe*\_sp\_sb|12908207|  
*Pleurobrachia*\_b\_sb|11611576|

Adult specific sequences

ML06743a  
*Pleurobrachia* b sb|12652162|  
*Pukia* sb|13031051|  
*Euplokamis*\_sb|10678971|

ML06743a  
*Pleurobrachia* sb|12652162|  
*Pukia* sb|13031051|  
*Euplokamis*\_sb|10678971|

ML218923a-T  
*Pleurobrachia* b sb|11609489|  
*Hormiphora* GHX01041156.1  
*Pukia*\_sb|13091370|

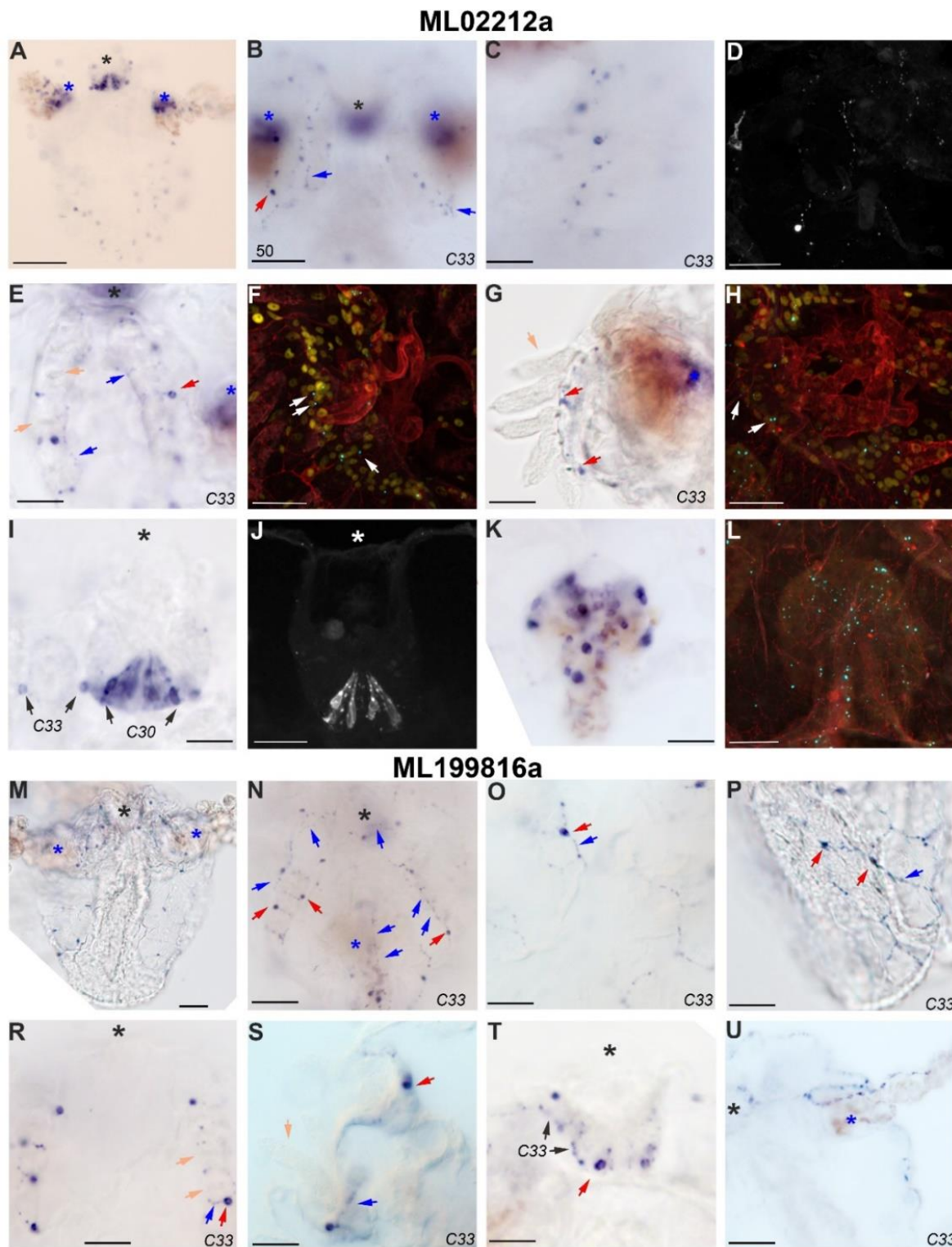
ML218923a-T  
*Pleurobrachia* b sb|11609489|  
*Hormiphora* GHX01041156.1  
*Pukia*\_sb|13091370|

Supplementary figure 4. Sequence alignments of diverse ctenophore neuropeptide precursors.

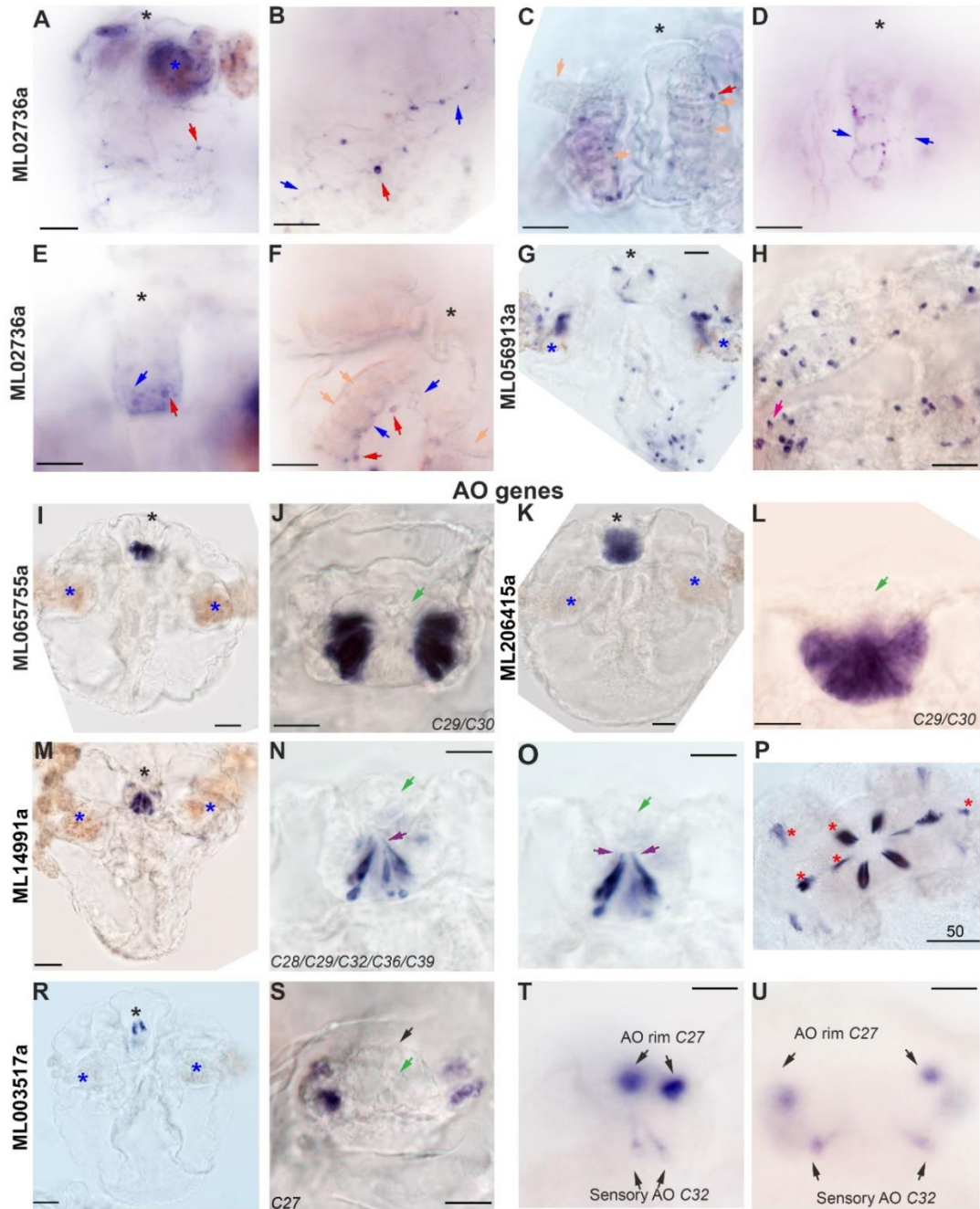


**Supplementary figure 5. Developmental profiles of putative *M. leidyi* neuropeptides** ([https://research.nhgri.nih.gov/mnemiopsis/Mlei\\_expression\\_timecourse/](https://research.nhgri.nih.gov/mnemiopsis/Mlei_expression_timecourse/)). Genes that are not expressed in cydippids are labelled in grey, genes that have expression dynamics which do not correlate with the estimated nervous system development dynamics are labelled in purple.

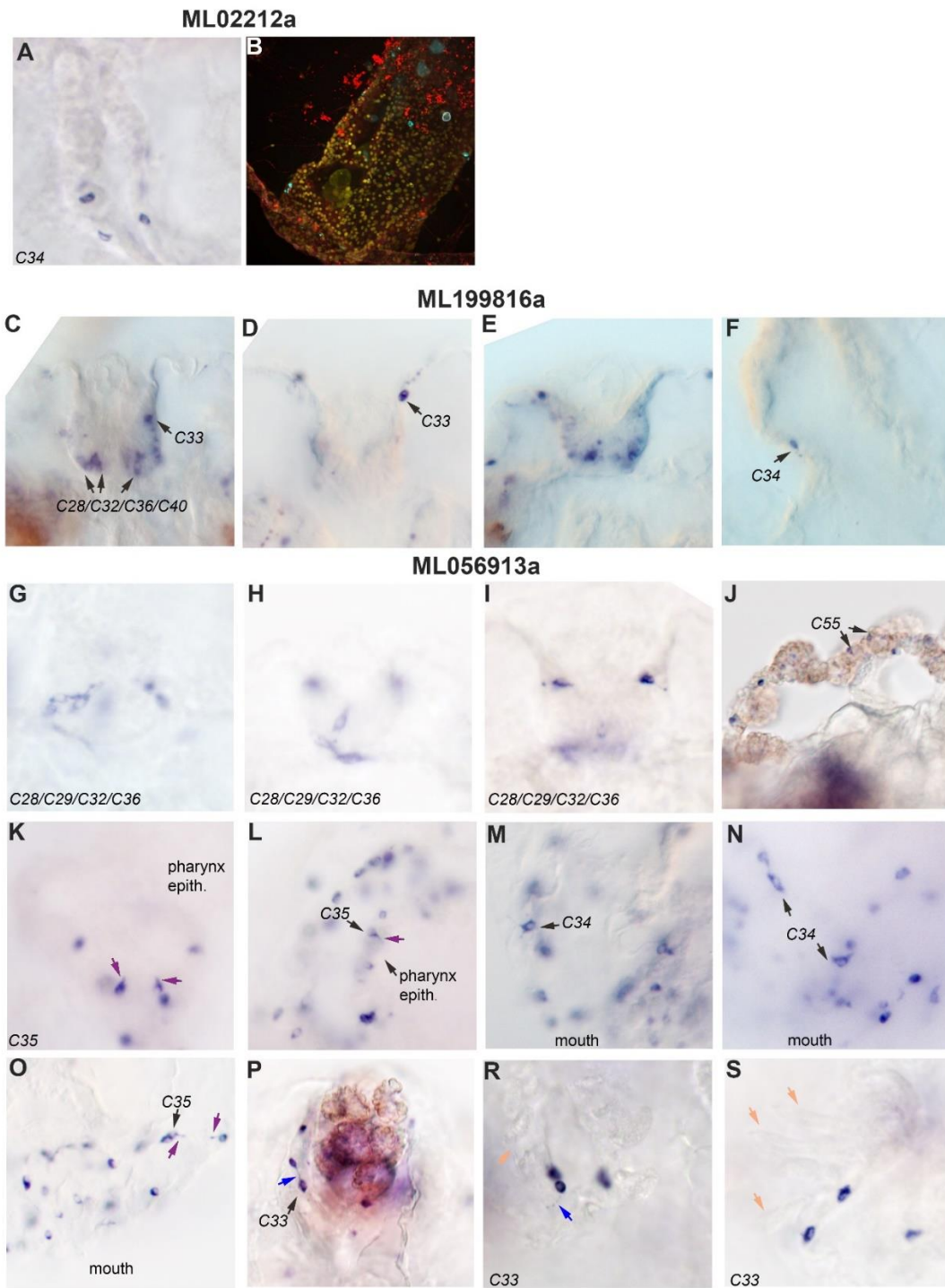




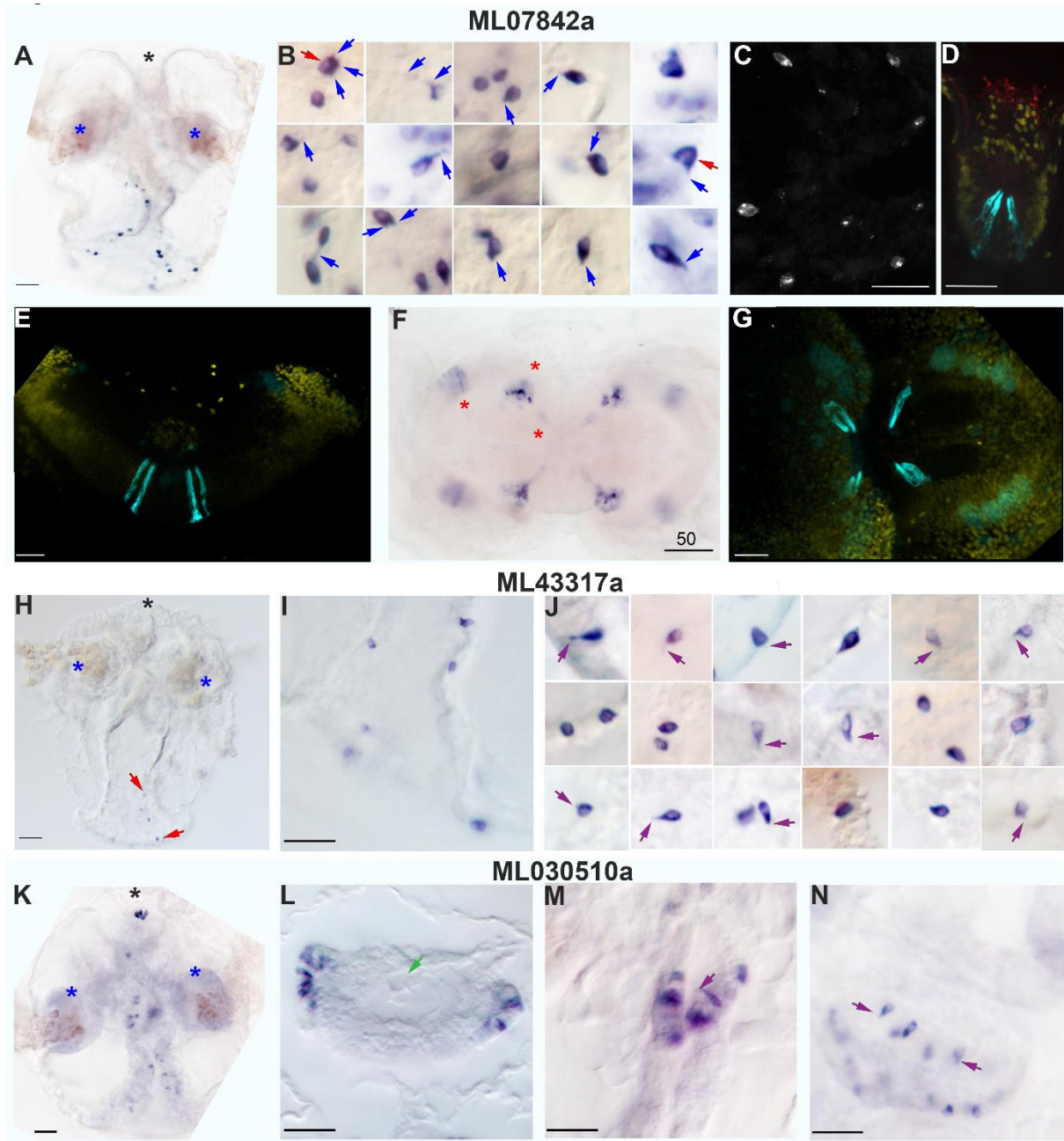
**Supplementary figure 6. Neuropeptides expressed in the subepithelial nerve net.** Black star – aboral organ, blue star – tentacle bulb, red arrow – neuron body, blue arrow – neurite, orange arrow – comb plate. (A-L) ML02212a is expressed in the subepithelial nerve net (B-H, K-L) and in the AO (I, J); (E-H) ML02212a expression around the combs. (M-U) ML199816a is expressed in the subepithelial nerve net (N-T) and in the mesogleal neurons of tentacles; (T) shows the AO and (R, S) show the area around the combs. A-E, G, I, K, M-U – staining by ISH; D, F, H, J, L – staining by IHC, the mature peptide is cyan, tubulin is red, DAPI is yellow. (A, M) Whole cydippid. Scale bars: 50  $\mu\text{m}$  for (A, M, B, U), 20  $\mu\text{m}$  for (C-L, N-T).



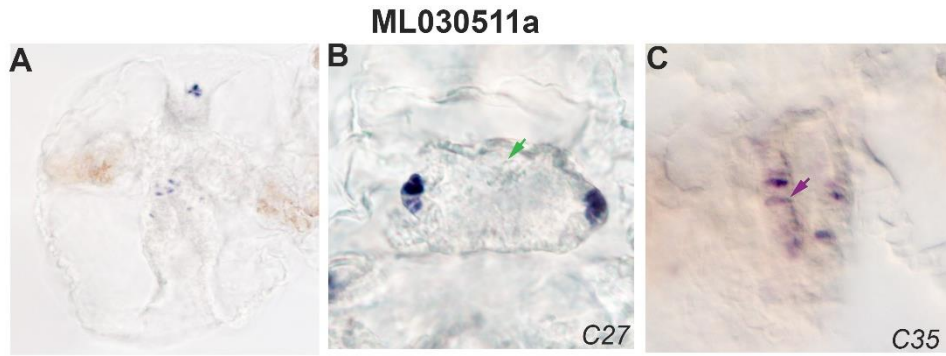
**Supplementary figure 7. Neuropeptides expressed in the subepithelial nerve net (ML02736a, A-F), in multiple neural cell types (ML056913, ML206415a, ML14991a, ML003517a, G-H) and restricted to the aboral organ (ML065755, I-P). Star and arrow labels are the same as at the Fig 3, green arrows – statolith, magenta arrow – sensory cells on the lips, brown arrow - dome. (A, G, I, K, M, O) whole cydippid; (B) epithelial nerve net, (C, D, F) combs, (E, J, L, P) aboral organ, (H) lips. Scale bars: 50  $\mu$ m for (A, G, I, K, M, P, R), 20  $\mu$ m for (B-F, H, J, L, N, O, S-U).**



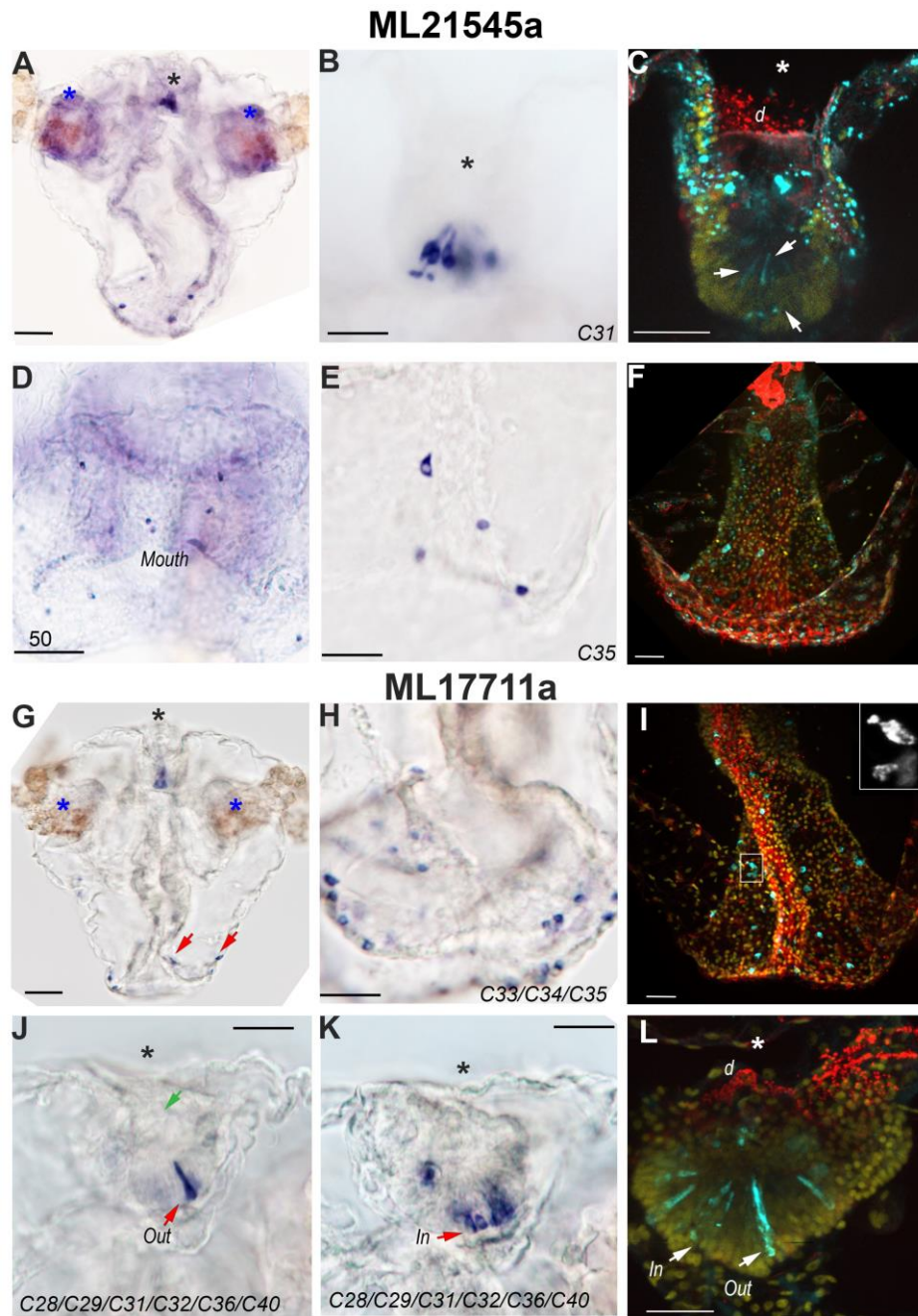
**Supplementary figure 8. ML02212a, ML199816a and ML056913a expression.** Blue arrow – neurite, orange arrow – comb plate, black arrows – corresponding metacells. **(A-B)** ML02212a expression around the pharynx revealed by ISH **(A)** and IHC **(B)**. **(C-E)** ML199816 expression in different cell types of the AO; **(F)** ML199816 expression in pharynx neurons. **(G-S)** ML056913a is expressed in different cell types of AO **(G-I)**, tentacles **(J)**, pharynx and mouth **(K - O)** as well as subepithelial neurons on the body surface and under the combs **(P-S)**.



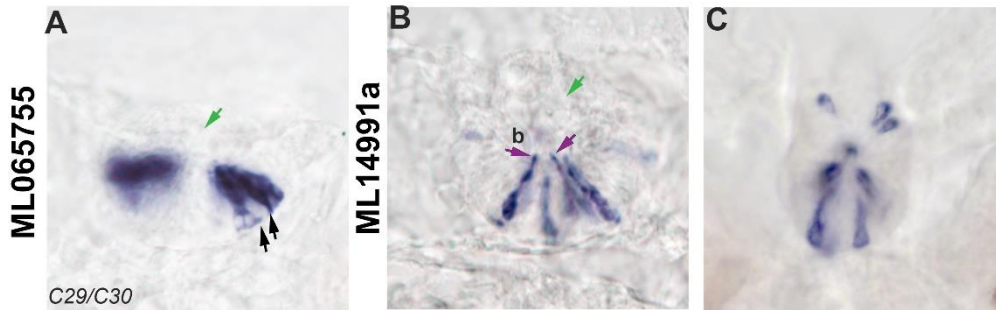
**Supplementary figure 9. Neuropeptides expressed in the pharynx and mouth area (ML07842a, ML43317a, ML030510a).** Star and arrow labels are the same as at the Fig 3 and 4, green arrows – statolith, light brown arrows – cilia. (A-D, H-O) ISH, (E-G) IHC. (A, H, L) whole cydippid, (B, I) close up to individual cells, (C) adult aboral organ, (K, N, O) pharynx, (M) cydippid aboral organ. Scale bars: 50  $\mu\text{m}$  for (A, F, H), 20  $\mu\text{m}$  for (C-E, G, I, L-N).



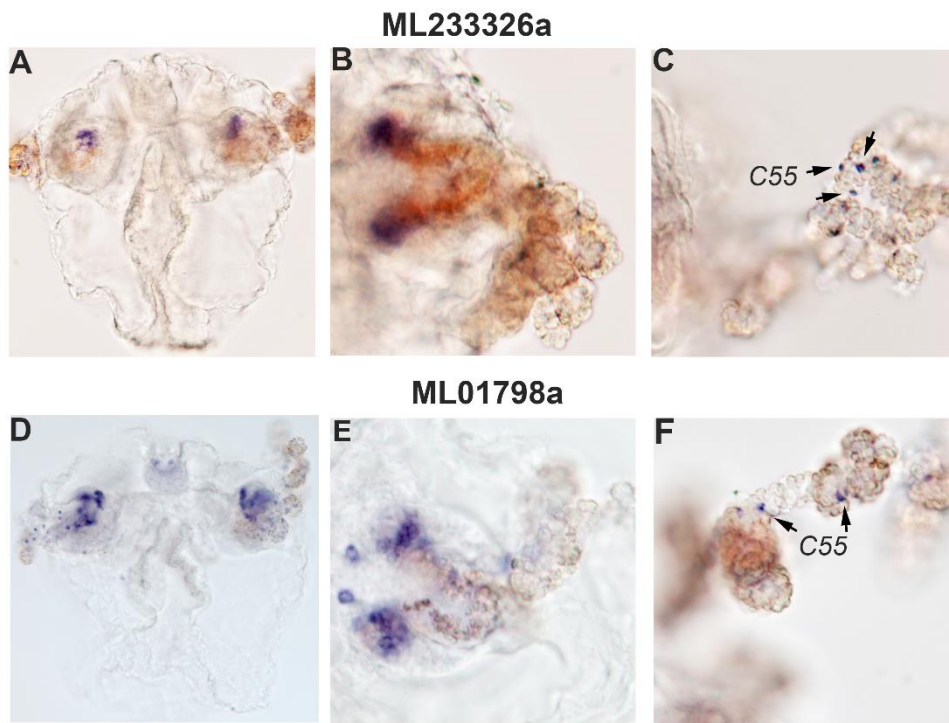
***Supplementary figure 10. ML030511a is expressed in the AO rim and sensory cells in the pharynx. (A) whole cydippid; (B) AO, green arrow indicates the statholyth; (C) pharynx, purple arrow indicates the cilium.***



**Supplementary figure 11. Neuropeptides expressed in multiple cell types (ML21545a, A-H; ML17711a, I-P).** (A, B, D, E) ISH, (C, F, I, L) IHC. (A, I) whole cydippid, (B, C, J, K) aboral organ, (E, H) pharynx and lips area. Scale bars: 50  $\mu$ m for (A, G), 20  $\mu$ m for (B-F, H-L).

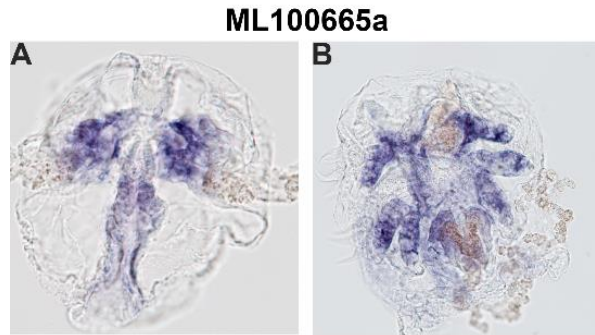


**Supplementary figure 12. ISH with neuropeptide precursors expressed in the AO cells.** (A) *ML065755a*: stained cells appear to have an elongated shape with the cell body close to the base of AO floor and both apical and basal protrusions (the latter is labelled with black arrows). The green arrow indicates the position of the statolith. (B, C) *ML14991a* is expressed in elongated cells with diverse morphology. Purple arrows indicate the cilium at the apical protrusion, green arrow – statolith, *b* – balancer.

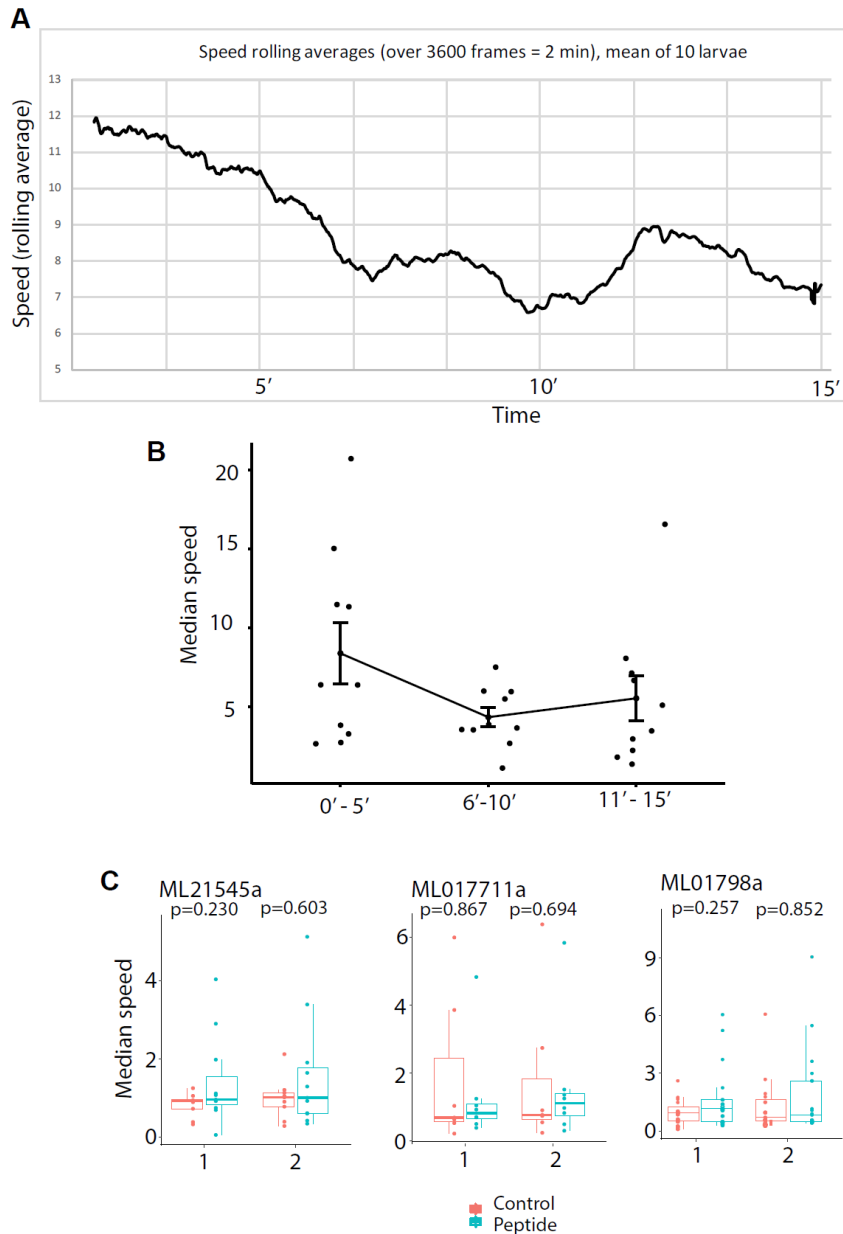


*Supplementary figure 13. ISH of neuropeptide precursor genes expressed in the tentacles. (A-C) ML233326a, (D-F) ML01798a*





*Supplementary figure 14. ML10665a is expressed in the meridional canals and pharynx. (A) whole cydippid, front view; (B) whole cydippid, view from the AO side*



**Supplementary figure 15. Behavioural experiments with *M. leidyi* cydippids.** (A) Speed rolling averages (over 3600 frames corresponding to 2 min) for a cydippid recorded during 15 minutes after being placed into the arena; the mean for 10 cydippids is shown. (B) Median velocity calculated for the three 5 min intervals for the 15 min recordings of cydippids right after placement into arenas. (C) Plots showing median velocity of the cydippids after incubation with peptides or control (related to **Fig 3D**).

**Ferlin (IPR037721)** (Reciprocal Blast eval 0.00)

ML08309a protein model appears truncated since it is missing the transmembrane region (TMR). GFAT01108989.1 cDNA overlaps with ML08309a and has a TMR (highlighted in blue).

|  |   |                   |
|--|---|-------------------|
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | -----MLRVFILYAENVHT-PDTDISDAYCSAV<br>-----<br>MFGSIVRRSRSSDDDDHISSYREYKDVMSKEGLVQVLRNAQNLQNVVERFGYSDPHVVLE  | 27<br>0<br>60     |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | FAGVKKRRTKVIKNSVNPVWNEGFWDLKGIPLDQGSSELHVVKDHETMGRNRFLGEAKVP<br>-----<br>LEGIKRTRV IHSELNPEWNETFTWKRY-RPLTEESMLLIKVYDYEKILKNKLLGEAVYP   | 87<br>0<br>119    |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | LREVLATPSSLASFNAPLLDTKKQPTGASLVLQVSYTPL-----P-----<br>-----<br>LKDLVRLGAQEATV--PLRDRDGKVGESRLNLYLEYTKPTLDPDEEMEEKSGPRPSVAR  | 127<br>0<br>177   |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | -----GAVPLFPPT-----PLEPSPTLPDLVVDVADTGGEEDTEDQGL<br>-----<br>KSTALSHPEIQSLKNAEILPLYHSKRRSTTSAPVSSPEYPAYHPTGVAGAVEETGNP--  | 165<br>0<br>235   |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | TGDEAEPFLDQSGGPGAPPTPRKLPSPPPHYPIKRRKSAPTSRKLSDPKQDFQIRVQ<br>-----<br>IPDEGEQEVEVAPGDAAGAANK-----KKSIVIAAPRSSIDRSKLSLTKKQDFQVRVN  | 225<br>0<br>286   |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | VIEGRQLPGVNIKPVVKVTAAGQTKRTRIHK-GNSPLFNETLFFNLFDSPGELFDEPIFI<br>-----<br>IHEGRKLLGGNIHPVCNVHVKGQSKHTRVQKSTNKPLWDEVLFDFNCSALDLCDEPVTI  | 284<br>0<br>346   |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | TVVDSRSLRTDALLGEFRMDVGTIYREPRHAYLRKWLSDPDDFSAGARGYLKTSLCVL<br>-----<br>EVLNSRKIRSDSLIGAFKFDLGLVYESQDHFVHKWVLLTDPEDKESGAKGYVKISISIL  | 344<br>0<br>406   |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | GPGDEAPLERKDP--SEDKEDIESNLLRPTGVALRGAHFCLKVRAEDLPQMDAVMDNVK<br>-----MK<br>GPGDKLKI PPKSSSTDDLVDIESNLLRPAGVQLQPATYTVKIYKAEDVPKMDTDYFEGMK<br>:*   | 403<br>2<br>466   |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | QIFGFESNKKNLVDPFVEVSFAGKMLCSKILEKTANPQWNQNILPAMFPMCEKMRIRI<br>RVLRMQHGDHDLVDPYMIVSFAGKKLTKVLYKTYTPEWAQELNIGVQMPMSCEQLMLRL<br>RVLRMQHGDHDLVDPYMIVSFAGKKLTKVLYKTYTPEWAQELNIGVQMPMSCEQLMLRL<br>::: :. . .:****: ***** * :*: * * .*: * *::: . :*****: :*:                     | 463<br>62<br>526  |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | IDWDRLTHNDIVATYLSMSKISAPGGEIEEEPAGAVKPSKASDLDDYLGFLPTFGPCYI<br>MDKDHFNRRDDIIATHFLQLTRLSSAD-----PDDEGFLPTFGPAYV<br>MDKDHFNRRDDIIATHFLQLTRLSSAD-----PDDEGFLPTFGPAYV<br>:* *::: :****: * :*: * * * :**** * :* .: . . :. :* * :. :* *   | 523<br>103<br>567 |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | NLYGSPREFTGFPDPYTELNTGKGGVAYRGRLLLSLETKLVEH--SEQKVEDLPADDIL<br>NLYGSPRESI-VDDELEPLNRGCGEGCSFRGRALVELTVNIGQEPSKDEMLRDI DGEDWL<br>NLYGSPRESI-VDDELEPLNRGCGEGCSFRGRALVELTVNIGQEPSKDEMLRDI DGEDWL<br>* :***** . * * * * * * * :**** * :* .: . . :. :* * :. :* *               | 581<br>162<br>626 |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | RVEKYLRRRKYSLFAAFYSATMLQDVEDAIQFEVSI GNYGNKFDMTCLPLASTTQYSRAV<br>RVQPFQRRRRLRFVGFLEGTMIHPVDAPVEFEISIGEYGNKFASTTLPAPSTTQPTNPV<br>RVQPFQRRRRLRFVGFLEGTMIHPVDAPVEFEISIGEYGNKFASTTLPAPSTTQPTNPV<br>** : * * : * * * * * . : * * : * * : * * : * * : * * : * * : * * : * * : * | 641<br>222<br>686 |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | FDGSHYYLPGWQTKPCVMLNSQWEDVMFRIESLNLICRTIDRLEGLKDVKYLMLRAKAP<br>YDGSYYLPGWQTKPCVMLNSQWEDVMFRIESLNLICRTIDRLEGLKDVKYLMLRAKAP<br>:***:*****:*** * :* * * * : * * * : * * : * * : * * : * * : * * : * * : *  | 701<br>282<br>746 |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | TEDVDSLVAQLTDELIAGCSQPLGDIHETPSATHLDQYLYQLRTHHLSQITEAALALKLG<br>LAESAGKLIKLLDELIIDLNPLELPQK-NITELDKKLYALRDEMKRI LIEAVNLRN<br>LAESAGKLIKLLDELIIDLNPLELPQK-NITELDKKLYALRDEMKRI LIEAVNLRN<br>: . : : * * * * * . * * * : : . . * * * : * * * . . : : * * : * * :             | 761<br>341<br>805 |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | HSELPAALEQAEWLLRLRALAEEPQNSLPDIVIWMQLGDKRVAYQRPVPAHQVLSRRA<br>ARDIDQAIIVEIDSYIYRLQQIATEPQNSIPDVIWMLCGNRRVAYHRIPSHQVMFSPK-Q<br>ARDIDQAIIVEIDSYIYRLQQIATEPQNSIPDVIWMLCGNRRVAYHRIPSHQVMFSPK-Q<br>: : * : : : : * * : * * * * * : * * * * * : * * * * * : * * * * * : *       | 821<br>400<br>864 |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1<br>ML08309a | NYCGKNCGLQITFLKYPMEKV----PGARMPVQIRVWLVFGLSVDEKEFN-QFAEGKL<br>DCCGKLCGHVFSVFLKRPSPVDPKSNKRQWKLPAKLQVFWVMGLEDHAKGIQHKPLDGEI<br>DCCGKLCGHVFSVFLKRPSPVDPKSNKRQWKLPAKLQVFWVMGLEDHAKGIQHKPLDGEI<br>: * * * * * : : * * * * * : * * * * * : * * * * * : * * * * * : * * * * * : | 875<br>460<br>924 |
| sp 075923 DYSF_HUMAN<br>GFAT01108989.1             | SVFAETYENETKALVGNWGTGLTYPKFSDVTGKIKLPKDSFRPSAGWTWAGDWFVCP<br>SVFAETYENQ--ISLLSKWTRAMPKPKWSDITGQLKPKESFTTPGGWRWAGWFINPN  | 935<br>518        |

ML08309a SVFAETYENQ--ISLLSKWTTTRAMPKPKWSDITGQLKLPKESFTTPGGWRWAGEWFINPN 982  
\*\*\*\*\*: :\*:.\* \* .: \*\*:\*:\*:\*\*\*\*:\* \* .\*\* \*\*:\*:\*: \*

sp|O75923|DYSF\_HUMAN KTLHMDAGHLSFVEEVFENQTRLPGGQWIYMSDNYTDVNGEKVLPKDDIECPLGKWKE 995  
GFAT01108989.1 LLSYDLDSGLSSFQDDVFENQLRVPGSDWPTSKLFWTDVTGEEAQSKEDIMCPAGWEWT 578  
ML08309a LLSYDLDSGLSSFQDDVFENQLRVPGSDWPTSKLFWTDVTGEEAQSKEDIMCPAGWEWT 1042  
\*: :\*:.\* \*\* :\*\*\*\*\* \*:\*:\* . :\*\*\*:\*:\* . \*:\* \*\* \*:\*

sp|O75923|DYSF\_HUMAN DEEWSTDLNRAVDEQGWSEYITIPPERKPKHWVPAEKMYITHRRRRWVRLRRRDLQMEA 1055  
GFAT01108989.1 D-IWTVDLNRAVDEEGYEYCLDQ---SVGGFVPEKTYHLRNRVWVTRKRNPDLRQQ 633  
ML08309a D-IWTVDLNRAVDEEGYEYCLDQ---SVGGFVPEKTYHLRNRVWVTRKRNPDLRQQ 1097  
\* \*:\*:\*\*\*\*\*:\*:\*:\* . :\*\*.\* \*: \*\*\*\*\* \*:\*: . :

sp|O75923|DYSF\_HUMAN LKRHRQAEAEGEGWEYASLFGWKHFHLEYRKTDAFRRRRWRRRMEPLEKTGPAAVFALEGA 1115  
GFAT01108989.1 AAHQRMVRAAEEGWEYSRLFTTKFHLKQRTMDMVRRRRWRHRKMVADNPDADAI F I DPT 692  
ML08309a AAHQRMVRAAEEGWEYSRLFTTKFHLKQRTMDMVRRRRWRHRKMVADNPDADAI F I DPT 1156  
:\* . \* \*\*\*\*\*: \*\* \*\*\*\*\*: \* . \* .\*\*\*\*\*:\*:\* : . \*:\* : : :

sp|O75923|DYSF\_HUMAN LG----GVMD-----DKSEDSMSVSTLSFGVNRPTISCFDYGNYHLRCYMQARDL 1164  
GFAT01108989.1 SDAHETVGVSRARSARGKDDHLQ---QRTMITPTVFLTYKEPHTYQLRAYIYQARDL 748  
ML08309a SDAHETVGVSRARSARGKDDHLQ---QRTMITPTVFLTYKEPHTYQLRAYIYQARDL 1212  
. \*\* .:\*:\* . . : \*\* : . : \*:\*.\*:\*\*\*\*\*

sp|O75923|DYSF\_HUMAN AAMDKDSFSDPYAIVSFLHQSQKTVVVKNLNPWTWDTLIFYEIEIFGEPATVAEQPPSI 1224  
GFAT01108989.1 FSADPSGLSDPYARVVFSSRQSQRTKILNETLCPTWDQTLVFEVEFYGNPTMLAESPPIV 808  
ML08309a FSADPSGLSDPYARVVFSSRQSQRTKILNETLCPTWDQTLVFEVEFYGNPTMLAESPPIV 1272  
: \* . :\*\*\*\*\* \* \* :\*\*\*:\* : : : \* \*\*\*\*\*: \* \*:\*:\*:\*: :\*:\*.\* :

sp|O75923|DYSF\_HUMAN VVELYDHDYGADEFMGRICQPSL----ERMPRLAWFPLTRGSQPSGELLASFELIQR 1279  
GFAT01108989.1 VVELFDYDVTGVS-DFLGRAIATPIVKLGGHQAQKLNWHPITRGGEPAGELLAGAFELYLN 867  
ML08309a VVELFDYDVTGVS-DFLGRAIAYPDSEAGR----- 1300  
\*\*\*\*:\*:\* \* :\*:\*\*.\* \*

sp|O75923|DYSF\_HUMAN EKPAIHHPGFVQETSRIIDSESDTDLPPPPQREANIYMPQNIKPALQRTAIEILAW 1339  
GFAT01108989.1 EG-----AELPFMPPTR-GDVYQVPSGIRPVMQLTRIEVLTW 903  
ML08309a ----- 1300

sp|O75923|DYSF\_HUMAN GLRNMKSQYLANISSPSLVVECGGQTVQSCVIRNLRKNPNFDICTLFMEVMLPREELYCP 1399  
GFAT01108989.1 GVRHMKKFQLAAVNSPSEIEICGGVVLSTIKIKNAKKNPNFDTSMLFDVFLPVEELYTP 963  
ML08309a ----- 1300

sp|O75923|DYSF\_HUMAN PITVKVIDNRQFGRRPVVGQCTIRSLSEFLCDPYSAESPSQ---GGPDDVS--LLSPG 1453  
GFAT01108989.1 PLNRLRLDHRSFQVPLVGTTHMKSQLEFYRRDPVAMVQTI REKMLESFGGDAEYAIMDMF 1023  
ML08309a ----- 1300

sp|O75923|DYSF\_HUMAN EDVLIDIDDKEPLI----PIQEEEFIDWWSKFFASIGEREKCGSYLEKDFDTLKVYDTQ 1508  
GFAT01108989.1 ADSAVEAAHQPPATSTSEEGEFKEDVDWWSKYSSSGNEQLGRVYREKGYENMVVFEE 1083  
ML08309a ----- 1300

sp|O75923|DYSF\_HUMAN LENVEAFEGLSDFCNTFKLYRGKTQEE--TEDPSVIGEFGKGLFKIYPLPEDPAIPMPPRQ 1566  
GFAT01108989.1 LEN--YFDNF'TDLAQSFPLFHGKRHEDEDLDEDKAVGYFKGTRVYPLPADGSDP-PPRM 1140  
ML08309a ----- 1300

sp|O75923|DYSF\_HUMAN FHQLAAQGPQECLVRIYIVRAFGLQPKDPNGKCDPYIKISIGKKSVDQDNYIPCTLEPV 1626  
GFAT01108989.1 LKNVPCNLVEVLVRVYIVKAFELQPDPNGLSDPYLALKLGFRKVKVDRENYVPKNLSPT 1200  
ML08309a ----- 1300

sp|O75923|DYSF\_HUMAN FGKMFELTCTLPLEKDLKITLYDYDLSKDEKIGETVVDLENRLLSKFGARCGLPQTYCV 1686  
GFAT01108989.1 FGKMFELDGTLPLESELRVQIFDYDLSGDDLIGETKIDLENRFLSARRGVCGLPKRYV 1260  
ML08309a ----- 1300

sp|O75923|DYSF\_HUMAN SGPNQWRDQLRPSQLLHLCQHRVKAPVYRTDRVMFQ-DKEYSIEEIEAGRIPNPHLGP 1745  
GFAT01108989.1 AGPYKWRDAELPRQILEKWCATQALPPVVRGNSQVYVNGKTCCLRDYETRGQVHKDWGP 1320  
ML08309a ----- 1300

sp|O75923|DYSF\_HUMAN VEERLALHVLQQGLVPEHVESRPLYSPLOPDIEQGLQMWVDLFPKALGRPGPPFNITP 1805  
GFAT01108989.1 PEERLALYTLDDLGLVPEHIETRTLYNPLRPEIQGKIQIFVDIFPKSATI-PPFNITP 1379  
ML08309a ----- 1300

sp|O75923|DYSF\_HUMAN RRARRFFLRCIWNTRDVIDLDDLSLTGKMSDIYVKGWMI GFEEHKQKTDVHYRSLGGEG 1865  
GFAT01108989.1 RAPQDLQLRVIVYVQDVVLSDTSFTEGKMSDIYVKGWLGQD-KKQKTDVHYRSLNGEG 1438  
ML08309a ----- 1300

sp|O75923|DYSF\_HUMAN NFNWRIFIPFDYLPAEQVCTIAKKDAFWRLDKTESKIPARVVFQIWDNDKFSFDDFLGSL 1925  
GFAT01108989.1 NFNWRVYVFPFKYLPAAEVMVIKKKEHFFSLDKHEEKHPVTFCVQIWDNDIFTDDFLGSL 1498  
ML08309a ----- 1300

```

sp|O75923|DYSF_HUMAN      QLDLNRMPKPAKTAKKCSLDQLDDAF--HPEWVSLFEQKTVKGGWPCVAEEGE--KKIL 1981
GFAT01108989.1          ELNLFMFKANKFAKSVSLLDLPDNEKGPVPMVSLFDQKNVKGWPMYEEGGPDQPREL 1558
ML08309a                  ----- 1300

sp|O75923|DYSF_HUMAN      AGKLEMTLEIVAESEHEERPAGQGRDEPNMNPKLEDPRRPDTSLFWFTSPYKTMKFILWR 2041
GFAT01108989.1          TGKVEMELEILSKEDAIAKPAKGQEEFENPHLDPPNRPATSLFWFTSPWKSLRYIIWN 1618
ML08309a                  ----- 1300

sp|O75923|DYSF_HUMAN      RFRWAIILFIILFILLFLAIFIYAFPNYAAMKLVKPFSS 2080    100%
GFAT01108989.1          NYKWYIIGGLVLLLIAMVGLFIYSAPGALSTKLIACL- 1656    46%
ML08309a                  ----- 1300    42%

```

### Secretagoin (Reciprocal Blast eval $9.38 \times 10^{-28}$ )

```

sp|O76038|SEGN_HUMAN      -----MDSREPTLGR-----DAAGFWQVWQRFDADEKGYIEEKELDAFFLHML 45
ML03617a                  MEISGLWNDPQRVPKVKRKMFRISPAFLRNELENNVYNNNYLETVLLDEFLTNLV 60
                          * . * * : * . * : : . * . : : * * * * : : :

sp|O76038|SEGN_HUMAN      MKLGTDDTVMKANLHKVQKQFMFTQDASKDGRI-----R--MKELAGMFLSEDEF 94
ML03617a                  MKE-----YVWQLNRQDIKCFNTEVIGNIKETLGDKLPKINKEVLIAAIPANNY 111
                          ** : : : : * . : . * . * * : : : : * : : : :

sp|O76038|SEGN_HUMAN      LLLFRRENPLDSSVEFMQIWRKYDADSSGFISAAELRNFLRDLFLHKKKAISEAKLEEYT 154
ML03617a                  LVRIG---HRIPSSDFLKLWRNYDTHSGYLEIKELQLLVRDFAQLVGEDVSDKDLNTAL 168
                          * : : * : : : * : : : * : : : * : : : * : : : * : : : * : :

sp|O76038|SEGN_HUMAN      GTMMKIFDRNKDGRDLNLDLARILALQENFLLQFKMDACSTEERKRDFEKIFAYYDVSKT 214
ML03617a                  EELMSEFDVNDGRLELEELSHLMSVEDNFMKAFCSRQ---YLTRKDFDRIFAHYDSDT 225
                          : * . * * * * * * * : : : : : : : : * : : : * * * * * * * *

sp|O76038|SEGN_HUMAN      GALEGPEVDGFGKDMELVQPSISGVLDL---KFREILLRHCDVNDKDKGIQKSELALCLG 271
ML03617a                  GYLDKEEVMALLNDILKYHESSDAHIPVPLKEVYKEVMKACDTNNSNTIQKCELALLLT 285
                          * * : * * : : : * : : : : : : : : * * : : * * * * * * * *

sp|O76038|SEGN_HUMAN      LKINP 276 100%
ML03617a                  SV--- 287 29%

```

### VAMP2 = Synaptobrevin (IPR001388) (Reciprocal Blast eval $3.99 \times 10^{-22}$ , $1.78 \times 10^{-23}$ )

#### SNARE domain, TMR

Residues important for SNARE complex formation are highlighted in grey and cyan.

```

VAMP2_HUMAN      MSATAATAPPAAPAGEGGPPAPPNLSNRRLLQQTQAQVDEVDIMRVNVDKVLERDQKL 60
ML02217a         MAELVAM-----VTLYHPLTSSGGYQTRDTQEQVDQVMGIMRNNIDKVLERSKI 50
ML214317a       -----MSGGYQVNDTQNVDEVMGIMRNNIDKVLERSDKI 35
                          : . . : : * * * * * : * * * * * * * * * * * *

VAMP2_HUMAN      SEIDDRADALQAGASQFETSAAKIKRKYWKNLKMIIILGVICAILIIIVYFST---- 116
ML02217a         QNLNERSDALQVGANQFLQTGTQIKRKMWWKNVKFMIVIGVVVVIVLGVVIVLDFVTIN 110
ML214317a       QNLNERSDALQVGAHQFQQTGQIKRKMWWKNVKFMIIIGVVVVIVGILIGIIVSQTKK 95
                          . : * : : * * * * * * * * : . : * * * * * * * * * * * * : : : : * * :

|VAMP2_HUMAN      ----- 116
ML02217a         RPNVPLWSLQTRSSMNTELYSVSTYLPKHSWLEIKPGLRNCVSKLLLPRLSLRIVSR 170
ML214317a       KKS----- 99

VAMP2_HUMAN      ----- 116
ML02217a         EGLTGVLTLNILRSSLSLPRLVAAANSSSLTDRPTANQPPTTSSTNHRRPFLYSTNKERG 230
ML214317a       ----- 99

VAMP2_HUMAN      ----- 116 100%
ML02217a         IFITVQSTTPASLS 244 45%
ML214317a       ----- 99 51%

```

### Syntaxin1 or Syntaxin-2 (IPR028671) (Reciprocal Blast eval $9.57 \times 10^{-45}$ )

#### SNARE domain, TMR

Residues important for SNARE complex formation are highlighted in grey and cyan.

```

STX1B_HUMAN      MKDRTQELRSKDSDD---EEEVVHVRDH---FMDEFFEQVEEIRGCIKLSQV 53
ML037014a        MRDRINFRLQLDDQEANEGRAVVDVDFHSDTGVEEVKFLKEAQHTREKIVSIEELVNQI 60

```

|                          |  |            |
|--------------------------|--|------------|
|                          | <pre> ** * : * * * : . ** . . * : : * : : : . * * . . . * * : </pre>   |            |
| STX1B_HUMAN<br>ML037014a | <pre> KKQHSAILAAPNPDEKTKQLELEDLTADIKKTANKVRSKLKAIQSI---EQEEGLNRSS REYHGKITGAAARNEEVHKKLNQAMDEIRRLFDTVKEALKKMEQESNALSDDKDAELKRP : : * . * . * : * : </pre>    | 109<br>120 |
| STX1B_HUMAN<br>ML037014a | <pre> ADLRIRKQHTSLSRKFVEVMTEYNATQSKYRDRCKDRIQRQLEITGRTTTNEELEDMLE ADIRIMSSQYTSLQCWFFETWTEYNECQSDYREKCKEKLTRQIQITEKQVTEINTMIE ** : * * . : * : : : * . * . * * * * * * * * : : * : * * * : : * : </pre> | 169<br>180 |
| STX1B_HUMAN<br>ML037014a | <pre> SGKLAIFTDDIKMDSQMTKQALNEIETRHELIKLETSIRELHDMFVDMAMLVESQGEMI SGNFTVFSIN---AQFQPKDIEEMESRHNITKLAKSKQLHEMFKDLALMVEQGEML ** : : : : * : : : : : * : * * * * * * * * * * * * * * * * * : </pre>       | 229<br>236 |
| STX1B_HUMAN<br>ML037014a | <pre> DRLEYNVEHSVDYVERAVSDIKKAVKYQSKARRKKIMIICCVLVGLVGLASSIGGTLGL- NNLEKNVDQARDYVADARECHQAVDLTNKWRKKLICAVVILII---VVIVGAVIIVV : . * * * : : * * * * : : * * . * * : : : : : . : * . . . : </pre>        | 288<br>292 |
| STX1B_HUMAN<br>ML037014a | <pre> -----      288   100% AHLQTK      298   33% </pre>   |            |

**SNAP25** (Reciprocal Blast eval  $2.76 \times 10^{-51}$ )

**SNARE domain**

Residues important for SNARE complex formation are highlighted in grey and cyan.

|                         |   |            |
|-------------------------|---|------------|
| SNP25_HUMAN<br>ML26853a | <pre> MAEDADMRNELEEMQRRADQLADESLESTRRLQLVEESKDAIGIRLLVMLDEGEQLERI --MSGRTFPVQMSDIEIRGNALTDSTLEATREMKRLAAETREIQAATAQNIDRGEQLNNI . . : : : : * . : * : * : * : * : * : * : * : * : * : * : * : * : </pre> | 60<br>58   |
| SNP25_HUMAN<br>ML26853a | <pre> EEGMDQINKDMKEAEKNITDLGKFCGLCVPCNKLKSSDA-----YKKAAGNNQDGVV ENNIDEINADLHKAKEKHTNMEKCCGICLPCARPkgvggTKTRNDKWKAAQSVNNGGTV * : : * : * * * : : * : * : * : * : * : * : * : * : * : * : * : </pre>      | 113<br>118 |
| SNP25_HUMAN<br>ML26853a | <pre> ASQPARVVDEREQMAISGGFIRRVVNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDT TTQPHGYQK--EEVAKTGYIKRITNDAREDEMENDLAVVADVVDLKMAMDMGSELER : * * . : . . * : * : * : * : * : * : * : * : * : * : * : * : </pre>       | 173<br>175 |
| SNP25_HUMAN<br>ML26853a | <pre> CNRQIDRIMEKADSNKTRIDEANQRATKMLGSG      206   100% CNAQLDRINVKITDCNVNRVQDAEARTNKLNS-      207   42% ** * : * * * * * : * . * . * : : : * : * : * : * : </pre>                                      |            |

**Synaptotagmin-7** (Reciprocal Blast eval  $1.05 \times 10^{-21}$ )

**TMR, InerPro C2\_dom**

|                        |   |  |
|------------------------|---|--|
| SYT7_HUMAN<br>ML16217a | <pre> MYRDEAASPGAPSR-DVL--LVSAIITVSLSVTVVLCGLCHWCQRKLGKRYKNSLETVG 57 -----MSLSLSDLELTVLLCVLVGVIIFIF--FVMFVLCFECLRQKEN----- 40 * . . . * * : : : * * : * : * * * * : </pre>                                |  |
| SYT7_HUMAN<br>ML16217a | <pre> TPDSGRGRSEKKAII--KLPAGGKAVNTAPVPGQTPHDESDRTEPRSSVSD---LVNSL 111 EPEGGAGDNLPSFSLSVNQGDNSEIRIGNKNI FSKRKEQPPAAVPTETVYVNDISI 100 * . * * . : : * . . * . * : : . . . * . * : * : * * * : * : </pre>    |  |
| SYT7_HUMAN<br>ML16217a | <pre> TSEMMLSPGS-----EEDS---AHEGCSRENLGRIQFSVGYN 146 KSSYVDIVPQSKVIYKVAQDSDESQFSFTSEPDQRRLSHFAPLEASTCGTIVCSIKFY 160 . * . : : * * * * * * * : * * : . . . * * * * : : </pre>                              |  |
| SYT7_HUMAN<br>ML16217a | <pre> FQESTLTVKIMKAQELPAKDFSGTSDPFVKIYLLPDKKHL--ETKVKRKNLNPWNETF 204 HFANRLAVRVGEVQLNL--VENLAVNPYVKLHLLPEYKRGNRQTRVKNRNTLFCDEDF 218 . . * : : : : * . : : * : * : * : * : * : * : * : * : * : * </pre>    |  |
| SYT7_HUMAN<br>ML16217a | <pre> LFGFPPYKVVQRILYLQVLDYDRFSRNDPIGEVSIPLNKVDLTQMOT---FWKDLKPCS 261 LF-GVGSREVRTKSLSLQVYDYKSNTRHLCIGKVINLGDYDFKDEDKPLSLKRHIIPYR 277 ** * . : * : * * * * * . : : * : * * * * . . * : : : . : : * </pre> |  |
| SYT7_HUMAN<br>ML16217a | <pre> DGSGRGELLLSLCYNPSANSIIVNIKARNLKAIDIGGTSDPYKVVWLMYKDKRVEK 321 ESQHFAGAIQV--AVSIASETLRIGIKAEGLVVDMGSLTEPYCRILVHVGSELIHKK 335 : . . * : : . . : : : : : * * * . * : * : * * * * : : : : : * </pre>     |  |
| SYT7_HUMAN<br>ML16217a | <pre> T-VTKRNLNPIFNESFAFDIPEKLRER-TIIITVMDKDKLS---RNDVIGKIYLSWKS 376 TCIAEAINRSPIEWEFFTLDPKNTLLCETSITIEVRDHLNRSRSTSYLLMGRVILSNTA 395 </pre>   |  |

```

* :: * .**:* * :*:*.:.* :* * * * : : * :*: : ** .:
SYT7_HUMAN      GPGEVKHWKDMIARPRQPVAQWHQLKA      403      100%
ML16217a       PGGQAHWEHASAQRGTMITTEWQPLLS      422      27%
                **: . * : :*: : * :

```

**Dematin** (Reciprocal Blast eval  $1.17 \times 10^{-09}$ )

**Villin\_headpiece domain**

```

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                MSRSFQDPPTTPSRPVVLGGSFIFSNDCGYISPTVIEKYESLAGDLSLDKENLLNIEKSL 60

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                DKGIVTEDVGANQDIISFTTSPPCVVESSPAMAEKPANPKKVELVGPYISPHKDIITFFL 120

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                TDIGRQKTMEQDGACYGTSVSVETVGETTPDCVTAERDDKKDENNKDIISFLTAGTNVDA 180

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                DNSRKLSSLSVPPPKSKADLRKPYFSLNFSDIISFYNSEESLLHACSMNSDQEPQGLDS 240

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                QKEADDIVQDPKSPDKEKIPANNPDQFVFQNDRSANANKVLTSTPKSTLKKRTPMMIHQ 300

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                GSVISFYSKESFLSALEVSSVDGDDINASAEDQDIEEAFKQNKDKCESTVSTANEQEIS 360

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                NSDIKVFNSRATEPLPNSFLKQPFKSEFQLRKSNSVLVVTEEFPDIIISFYNPGADDTDPT 420

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                SPAGATLEVKDSMRKRENSTSLDTAEFGIIELTQLNENMAQVDTEVATAPDEEPIVIEIN 480

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                PASEEADEVNPKFVFRNDRSGFVEKNVISPANQNVRTTEKQTPMMINQGSVITFYRNET 540

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                SFALTALNSPNTVQTDESIENDINSPVDVAEDEADKNVTSESNFDIKVYENTVLEHDTSM 600

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                EDDNECLKRSLPDDDEEAPIPEKIEIEDQISKPVTTNIKVDASIPDVVKETEKEDIERL 660

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                VHIVEMNEHNQDSYDDMPGLEECPKSIHESDLSENQDSLVVVEDSISEDGIPIRKLQD 720

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                IENLPSIEKAIMVNAIGGALDENLGMVPEPLDDDYMYDDEEFERDITEIDSLISEAE 780

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                QLMMPTDSADNDALCDDLDRFDEVDDVDELLKAEVPEVLDLQIRNVSQNGETEISPRD 840

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                SSSESATINFITQNDIKYMESTS AVDAAVATAPPTNVDPSTDDADDLVARIDELLDVEDY 900

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                LDIPGCETPEPPSPLRDTPTPQPHPTVTRHLIRSTSLGEQALGLSLERTKGSFSAEDDG 960

sp|Q08495|DEMA_HUMAN      ----- 0
ML334211a                GSDEEYHTLFEALNKPILPPIPRVEYDEEDNQIAPAKSLTALQDYVDPANLSLQPSNNP 1020

sp|Q08495|DEMA_HUMAN      ----- 9
ML334211a                -----MERLQKQPL-----
CDPDSKVLSTGLLSEIVRHPLAGSLKRSASSGDAPGYHRRNPVTRSQKNDLLDEAHLFFL 1080
                :. . : :**

sp|Q08495|DEMA_HUMAN      ----- 30
ML334211a                -----TSPGSVSPS-----RDSSVPGSPSSI
QNNIGVPSRGGDDPSNREKKPSEDDQELSPISSLAQTLTERLTAHTAGRAGVKMVKPFD 1140

```

```

      . .:**          :.*  *
sp|Q08495|DEMA_HUMAN  VAKMDNQVLGYKDLA-AIPKDK-----AALDIERPDLMIYEPHF 68
ML334211a             VVKIDKQLFGLQKFKSKPKKMSLRSKYKNRKKTANKWVPVQVPSQVNHTSLYQVDI 1200
      *.*.*.*.* : : **.*          : : : : : : : : : :
sp|Q08495|DEMA_HUMAN  TYSLLEHVLELP---R---SRERSLSPKSTSPFPSPVWADSRSPGIISQASAPRTTGT 120
ML334211a             SYDEVNPDVDEVRIPLDTPVDSRRRPVSP-----GPESK-----YLGSLENVADPEDSHD 1249
      :* : : *:*          **.* :**          * :          * : : : * : :
sp|Q08495|DEMA_HUMAN  PRTSLPHFHHPET-----SRPDSNIYKKPPIYKQRESVGGSPQTKHLIEDLIESSK 172
ML334211a             ----CECKTHPGKLTRQSRNWSQDSGLYDGT-----KPVSAK-HTEMFQP-----T 1293
      ** .          **.*.          : *..          . : : : .
sp|Q08495|DEMA_HUMAN  FPAAQPPDPNPAKIEETDYWPCPPLA--VETEW-----RKRKASRRGAE 216
ML334211a             WKR-NSPDPVEERPRSTSP-YCQPFSEAAFGVNGSYIDNHVPASVRHPSRARNLSSDSNR 1351
      : : **.* : : *.* * * * * * * : : : : * * * * * .
sp|Q08495|DEMA_HUMAN  EEEEEEDDSDGEMKALRERQREELSKVTSNLGKMLKEEMKSLPIR----- 264
ML334211a             -ENRIVQNSIGSQNT---HVDRLARSGS---AASLAVVMASFPNGGDPNFDLAGTAA 1403
      *.. : : *.* : : : : : : : * * * * * : : :
sp|Q08495|DEMA_HUMAN  ---RKRTRSLP---DRTPFHTSLHQGTSKSSSLPAYGRT---TL SRLQSTEFSPSGSE 312
ML334211a             KISQVCKSLSSQTDITSCGVNLRSRSMNSGMDVIHSTEVKRPTRPIYFDRNYSPPSSAM 1463
      : : **          * *          . * : . * * . : . * *          . : : **.* :
sp|Q08495|DEMA_HUMAN  TGSPGLQNGEGQRGRMDRG-NS-----LPCVLEQKIYPYEMLVVTKGRKLPVGVDR 364
ML334211a             RIRTPENRVGQPVKAKKATTSYREILKIQEK IKDANI ISYQDL--VRCPRNKLPHPVDK 1521
      :* ** : : : . *          : : * * * : * . . * . * * * * * :
sp|Q08495|DEMA_HUMAN  MRLEHLSAEDFSRVFAMSPPEEFGKLALWKRNLKKKASLF 405
ML334211a             LQLQKYLSDTEFVDVFKMPREEFDKMAPWKQANLKNVSLY 1562
      : : : : * * * * * * * * * * * * * * * * * * * * * * * * * * * *

```

**Two pore domain K<sup>+</sup> channel (IPR003280) (Reciprocal Blast eval  $2.65 \times 10^{-31}$ )**

```

sp|Q9NPC2|KCNK9_HUMAN  ---MKRQNVRTLILVCTFTTYLLVGAAVFDALESDEMHEEKKLKAEEIRIKGKYNISS- 56
ML17562a             MSKLGKGVIAAFATFIAVLTLYLAIGAAIFQAIQEHEIEQREEYDQQLNLLLDKVDVDFH 60
      : : : : : : : : : : * * * * * * * * * * * * * * * * * * * * * *
sp|Q9NPC2|KCNK9_HUMAN  ED-YRQLELVILQSEPHRAGVQWKFAGSFYFAITVITTIYGHAAAGTDDAGKAFCMFYAV 115
ML17562a             DELKAPCHMIEILEANFNNTAQWDFVNSVIFCLTIVTTIGYGATYVPTDEGRGFCIFAL 120
      : :          : : : . . . . . * * . * * . * * * * * * * * * * * * * *
sp|Q9NPC2|KCNK9_HUMAN  LGIPLTLVMFQSLGERMNTFVRYLLKRIKKCCGMRNTDVS-MENMVTGFFSCMGTLCIG 174
ML17562a             IGLPLFMACLAVYAQHTANLIRIMKKLGLTNGLEDEQTEKMQQLITAAF--CLTVILTF 178
      : * * * * * : : :          : : : : * * * * * * * * * * * * * * * *
sp|Q9NPC2|KCNK9_HUMAN  AAASFQCEEWSFFHAYYCFITLTTIGFGDYVALQTKGALQKKPLYVAFSFMYLVLGLTV 234
ML17562a             SGYLSYKENWDYSVYFTFISFTTIGFGDLYPSSNTDFH-----IIFICFLILGLIS 232
      : . * * * * * : : * * * * * * * * * * * * * * * * * * * * * * * *
sp|Q9NPC2|KCNK9_HUMAN  IGAFNLVLRFLTMNSEDERRDAEERASLAGNRNSMVIHIPEEPRPSRPRYKADVPDLQ 294
ML17562a             LGTVIEAQT-----NFGNLLRTIS 252
      : * : : : .          . : : : .
sp|Q9NPC2|KCNK9_HUMAN  SVCSCTCYRSQDYGGRSVAPQNSFSAKLAPHYFHSISYKIEEISPSTLKNLSPSPSSI 354
ML17562a             SSCDCLCKNR-CFGGDRVPVDE----- 273
      * * * * . : * * * :
sp|Q9NPC2|KCNK9_HUMAN  SPGLHSFTDHQRLMKRRKSV 374 100%
ML17562a             ----- 273 25%

```

**Innexin (IPR000990) (Reciprocal Blast eval  $1.10 \times 10^{-15}$ ,  $1.18 \times 10^{-14}$ )**

```

sp|P33085|SHAKB_DROME  ML--D-----IFRGLKNLVKVSHTKDSIVFRLHYSITVMILMSFSLIITTRQY 47
ML036514a             MLLLG-----SLGTIKNLSIFKDLSDLDWLDQMNRTFMFLLCFMGTIVAVSQY 49
ML32831a             MRLSEKSTSHDCKACITRSHNEDCARRWGITIDGWDQLNRSFMFGLLVVMGTTVTVRQY 60
      *          : :          : . * .          : : : : * * . : : . * *
sp|P33085|SHAKB_DROME  VGNPIDCVHTKDIPEVNLNTYCIQSTYTLKSLFLKKGQVSVPPYPIGNSD----- 98
ML036514a             TGKNISCDGFTKFGEDFSQDYCWTQGLYTIKEAYDL-PESQIPYPIIPENVPACREHAL 108
ML32831a             TGSVISCDGFKKFGSTFAEDYCWTQGGYTVLEGYDQ-PNQNI PCVPRPPSRRGSTLNTM 119
      . * . * . . : . . : * * * * * * * * : :          . : * * .
sp|P33085|SHAKB_DROME  -----GDPADKHKYKYQVVCFLFFQAILFYTPRWLWKSWEQGIHALIMD 145
ML036514a             KNGGKIVCPPEQVQPLTRARHLWYQWIPFYFWVIAPVYLYPYMFWKRMGLDRMKPLKI 168
ML32831a             SQTQGFLLHPVE----- 131
sp|P33085|SHAKB_DROME  L-DIGICSE-AEKKQKKKL-----LLDY-----LWENLRYHNWWAYRYVCELLALI 190
ML036514a             MSDYYHCTTETPSEEIIVKCADWVYNSIVDRLSEGSSWTSWRNRHGLGLAVLVSKFMYLG 228

```



```

ML32831a      -----SDQELKMKTDKAAWLFYKFDLYMSEQSLLASLTNKHGLGLSVVFKILYAA 183
              ::                :                :                :                :
sp|P33085|SHAKB_DROME  NVIGQ-MFLMNRFDGFEFITGLKVIDYMETDQEDRMDPMIYIFPRMTKCTFFKYGSSGE 249
ML036514a     GSVLVMMMTLMFQVGDGFKTYGIEWLRQFPNPNENYSTSVKHKLFPKMVACEIKRWGTTGL 288
ML32831a     VSGFCFLTADMFSGDFKYGSEWINKLKLEDNLATEEKKDLFPKMVACEVSRWASGI 243
              . : : * * * * * : : : : : : : : : * * * * * . : : * * * * *

sp|P33085|SHAKB_DROME  VEKHAICILPLNVVNEKIYIFLWFWFILLTFLTLTLIYRVVVIIFSPRMRV-YLFRMRF 308
ML036514a     -EEENGMCVLPNVIYQYIFLIMWFALAITICTNFGNIFFYLFKLTATRYTYNKLVTAGH 347
ML32831a     -EEEQGMCVLAPNVIQYLFLLWFLVFMFCNIVSIFASLIKLLFTYGSYRRLST-A 301
              * : : * * * * * : : : : : * : : : : : : : : * .

sp|P33085|SHAKB_DROME  RLVRDAIEIIVRRSKMGDWFLLYLLGENIDTVIFRDVVQDLANRLGHNQHRVPLKGE 368
ML036514a     FSHKHPGWKFMYYRIGTSGRVLNIVAQNTNPIIFGAIMEKLTSPVIKH--LRIGHVPE 405
ML32831a     FLRDDSAIKHMVFNVGSSGRLLHLVLANNTAPRVFEDILLTLAPKLIQR--KLRAKDYD- 358
              . : : . : : * * * * * : * : : * : : * : : .

sp|P33085|SHAKB_DROME  IQDA--                372    100%
ML036514a     YLTDPA                411    21%
ML32831a     -----                358    20%

```

**Munc13 (Protein Unc-13 (IPR027080)) (Reciprocal Blast eval  $2.11 \times 10^{-174}$ )**

```

sp|O14795|UN13B_HUMAN  -----0
ML24335a     MGLLYASYAPLNCFGHGNSPQYNKLSQLNLRILIKHIGSEIALDIYKKAVALDVPQT 60

sp|O14795|UN13B_HUMAN  -----0
ML24335a     ESSLNVYKEMKWLPLHLTRQLHLSNYMFRIIHDDCPTNFMNKFSDIIDNERVQNRRIAN 120

sp|O14795|UN13B_HUMAN  -----0
ML24335a     EFNKYFASIASNLNEVSSSDQVRISLPSFTDYLPKSESSSIYLKESDYDEVSGIIGDL 180

sp|O14795|UN13B_HUMAN  -----0
ML24335a     KNGKSSDIPIHVIKSSNVIAPFLSKFFNECMSGHPDELKTGRISPIYKKEQELLEEN 240

sp|O14795|UN13B_HUMAN  -----13
ML24335a     YRPVSTLPVFGKILEKLIYTRLYSFLIAKGIHENQYGRKGGHSTSHALNYSVQHIESMT 300
              * * . : : *

sp|O14795|UN13B_HUMAN  -----59
ML24335a     KNGKQHVLFIFDLSKAFDITDHRKL-I TKLNNGYIRGNALKLIKSYLSNRTQFVSVLDIE 359
              . * * * * * * . * . . * * * . : : : * * *

sp|O14795|UN13B_HUMAN  -----103
ML24335a     LSVEVWNKGLIWDTMVGTWVIALKTIHQSDDEEGPGEWSTLEAET-----103
              . : * : * * * : * . : * * : *

sp|O14795|UN13B_HUMAN  -----135
ML24335a     NEVLLAVISRFRYKTLCFSEVPMTVTHVIVELWEKKTFFHSVNSSVLQLELIDIPFNKK 479
              : : * * * . * . : * : * * . :

sp|O14795|UN13B_HUMAN  -----507
ML24335a     -EEARYWYKWEQINALGADNEYSSQEEQRKPLPTAAAQCSFEDPDSAVDDRSDYRSE 194
              FRTFGCWAYSISN--TVSDS-----SGCEDNEL--FL- 507
              . * * . : : * * * . * * * .

sp|O14795|UN13B_HUMAN  -----551
ML24335a     TSNFPPPP-YHTASQPNASVHQFVFPVRSPOQLLQGSRRDSCNDSMQSYDLDYPERRAI 253
              QNIVFAPSCYTSYVSRDCENKLVVL-----LVIDSVSKE---E-----LALLEQKM- 551
              . * * * : . . . : : * * : : * * : . * * :

sp|O14795|UN13B_HUMAN  -----313
ML24335a     SPTSSSRYGSSCNVSGSSQLSELDQYHEQDDHRETDSIHSCHSSHLSRDLGAGFGGEQ 313
              -NVLSKVQDEDECLLFNGE-----SFCL-----KDG-----ST 578
              . * . . * : * . * * : * * :

sp|O14795|UN13B_HUMAN  -----351
ML24335a     EKPLEVTGQAEK-----EAACEPKE-MKEDAT--TH-----PPDLVLQKD 351
              GDFPFLAGNDVFTGIDLVIHLGAIAPQPERNDSFMTIDSGSDFRDAVTNETGMMQAE 638
              . * : * * : : * * : * * : . : :

sp|O14795|UN13B_HUMAN  -----409
ML24335a     HFLGPQESFPEENA--SSPFTQARAHWIRAVTKVRIQLQEIPDDGDFSLPQWLPFGFAG 409
              HFKSLIKTFDSSNFKITAPITPTSPRTASQNGELDMI SMS-MSHRSRQSSMSQNSADG 697
              * * . : * * * * * * * : * * : : . * . : : * *

sp|O14795|UN13B_HUMAN  -----731
ML24335a     LYGIDSMPLRRKKPLPLVSDLSLVQSRKAGITSAMATRTSLKDEELKSHVYKTLQALI 469
              VYSVSSQPLHPRI SNLIH-SDGSVTRQQSRSTSQ-----731
              : * . * * * * * * * * * * : : * *

sp|O14795|UN13B_HUMAN  -----516
ML24335a     YPISCTTPHNFEVWTATTPTYCYECEGLLWGIARQGMRC-----ECGVKCH 516
              FLSMSDDHEAE-----TEEVSKALMWSAVQRIKNIYMRNVENTAKEGEEGEEGE 784
              : * : * * * * * * * * * * * * * * * * * * .

```

sp|O14795|UN13B\_HUMAN  
ML24335a EKCQDLLNADC-----LQRAAEKSC----KHGAEDRTQNIIMAMKDRMKIRERN 561  
GKGEELKENGAYPTADGEVGLTRHENNS TVNSDNSSDMFDSKVKSTAARQRMKVTEA 844  
\* : : \* : . . \* \* : \* . . \* : \* : \* : \* : \*

sp|O14795|UN13B\_HUMAN  
ML24335a KPEIFEVIRDVFTVKNAAHVQMKTVKQSVLDGTSKWSAKITITVVCAGLQAKDKTGSS 621  
SKDMFELLRLAFGESEKLDVSKVKEVKHS LLTGSSKWSAKIDIEVVEAQLTGKDKSGTS 904  
. : : \* : \* : \* : . . \* \* : \* : \* : \* : \* : \* : \* : \* : \* : \*

sp|O14795|UN13B\_HUMAN  
ML24335a DPYVTVQVSKTKKRTKTFIGNLNPVWEEKFHFECNNSDRIKVRVWDEDDDDIKSRVKQRL 681  
DPYVTVQVQKIKKTTATIQDLNPKWNEFSDCNNSDRIKVRVWDEDDDFKSRVMTHL 964  
\*\*\*\*\* \* \* \* \* : \* \* : \* \* : \* \* : \* \* : \* \* : \* \* : \* \* : \* \* : \*

sp|O14795|UN13B\_HUMAN  
ML24335a KRESDDFLGQTIIEVRTLSEMDVWVYNLEKRTDKSAVSGAIRLQISVEIKGEE-KVAPYH 740  
KREADDFLGQAIIDVKQLCGETDVWLDLQRTDRSDVSGQVHLRMTIKIEGEEQNMSYH 1024  
\* \* : \* \* : \* : \* : \* : \* \* : \* : \* \* : \* : \* : \* : \* : \* : \*

sp|O14795|UN13B\_HUMAN  
ML24335a VQYTCLENLHFHYLTDIQGS---GGVRIPEARAGDDAWKVYFDETAQEI VDEFAMRYGIE 796  
IQYQLLHETLFNHLCEVNSGVNIPPGTRKLGDELDEWPTFFEGPAQYIVVEEFATRFGIE 1084  
: \* \* \* \* : \* : \* : . . \* . : . \* \* : \* : \* \* : \* \* : \* \* : \* \* :

sp|O14795|UN13B\_HUMAN  
ML24335a SIYQAMTHFACLS SKYMCPCG--VPAVMSTLLANINAYAHHTASTNVSASDRFAASNFGK 854  
SIFMAMTQFSCLTQRFITKKDAPPQDVSKLLALINSHYRRN-----NGQEVNVSFGK 1137  
\* \* : \* \* : \* \* : \* : \* : \* \* : \* \* : \* : . . : \* \* : \* \* : \* \* :

sp|O14795|UN13B\_HUMAN  
ML24335a ERFVKLLDQLHNSLRIDLSTYRNNFPAGS-PERLQDLKSTVDLLTSITFFRMKVQELQSP 913  
QKFTTVLDRLQSSLRENLASVAVYPSNRGQEKLDLLENSIALLSIVFFRLK-----1190  
: \* : \* : \* : \* \* : \* : \* : \* : . . \* : \* : \* : \* : \* : \* : \* : \*

sp|O14795|UN13B\_HUMAN  
ML24335a PRASQVVKDCVKAACLNSTYEIFNNDLYSRQYQLKQELPPEEQGPSIRNLDLFWPKLIT 973  
-----LCLENTYDFISTKTEVYAKYA-----NAEENTEAKIAYWKKLIT 1231  
\* \* : \* \* : \* : . . : \* : \* : \* . . : \* \* \* \* \*

sp|O14795|UN13B\_HUMAN  
ML24335a LIVSII EEDKNSYTPVLNQFPQELNVGKVAEVMWHLFAQDMKYALEEHEKDHLC--SA 1031  
LILVEMKEDKMFYEPIFNRFPPH--AALSAQTFWELLSRDLKDLTENLDTWLSETAAS 1288  
\* \* : \* \* \* \* \* : \* : \* . . : \* \* : \* \* : \* : \* \* : \* : \* : \*

sp|O14795|UN13B\_HUMAN  
ML24335a DYMNLHFVKWHLHNEYVRDLVPLVQGGQVPEYPAWFEQFVLQWLDENED-VSLEFLRGALER 1090  
DVMGFQMTVKFVYDKKISHIPEYENSLDPYKWFEPFVMKHLQESDSKIKNSFLIKSLDK 1348  
\* \* : \* : \* : \* : \* : . : \* : \* : \* : \* \* \* \* : \* : \* . . : \* \* : \* \* :

sp|O14795|UN13B\_HUMAN  
ML24335a DKKDGFQQTSEHALFSCSVVDVFTQLNQSFEIIRKLECPDPSILAHYMRFAKTIGKVL 1150  
DTFT--VQPNSSIKHSSSIDIFSSLRATYDSLDMKCPIPALRDKYHNRFCETIDAVLI 1406  
\* . \* . . \* . \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \*

sp|O14795|UN13B\_HUMAN  
ML24335a QYADILSKDFP---AYCTKEKLPCILMNNVQQLRVQLEKMFAMGGKELDLEAADSLKEL 1207  
EYTKRIIEVFKGLGLTSETTSVCVILCNHVRREELSESIFKTMGGELLDITAKQTLEGT 1466  
: \* . : : \* . \* . \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \*

sp|O14795|UN13B\_HUMAN  
ML24335a QVKLNTVLDLDEL SMVFNFSQVRIDECVRQMADILGQVRGTGNASPDARASAAQDADSVLR 1267  
QKRLKDARNVSVISDLVKDMKQIEKCIIRDIKSRLRNVR-----KNGEDYTEIVS 1516  
\* : \* : . : : : : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \*

sp|O14795|UN13B\_HUMAN  
ML24335a PLMDFLDGNLTLFATVCEKTVLKRVLKELWRVVMNTMERMIVLPPLTDQGTQLIFTAAK 1327  
PLIEYFDVVFKIFVDNLYDDVRKPLLQQTWKRTLKLFEEIILPDINAIA-----1566  
\* : \* : \* : \* : \* . . \* \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \*

sp|O14795|UN13B\_HUMAN  
ML24335a ELSHLSKLDHVMVREETRNLT PKQCAVLDLALDTIKQYFHA-GGNGLKKTFLKSPDLQS 1386  
-----HDEVQELNSKQSVVEAMLILKVYFTDSSGCKLAKNLEKTTEMRD 1613  
: \* : \* : \* . \* \* : \* : \* \* : \* \* . \* : \* \* . \* \* : \* : :

sp|O14795|UN13B\_HUMAN  
ML24335a LRYALSlyTQTTDTLTKTFVRSQTTQG-SGVDDPVGVEVS IQVDLFTHPGTGEHKVTVKVV 1445  
LRKVLQYRLTDTLTKNFTVQADNRFAEDSQGEIQLQVDLFTPPGQEHHDCTVKGL 1673  
\* \* . \* \* \* \* \* \* \* . \* . . : \* \* : \* \* : \* \* : \* \* : \* \* : \*

sp|O14795|UN13B\_HUMAN  
ML24335a AAN---DLKWQTAGMFRPVEVMTVGPQSDKRRKFTTKSKSNWAPKYNETHFLFLGN 1501  
FSFYYSKFLPWCLELSHS-----VSVP-----1695  
: \* \* . . : \* : \* : \*

sp|O14795|UN13B\_HUMAN  
ML24335a EEGPESYELQICVKDYCFAREDRVLGLAVMPLRDVTAKGSCACWCPLGRKIHMDETGLTI 1561  
-----1695

sp|O14795|UN13B\_HUMAN  
ML24335a LRILSQRSNDEVAREFVKLKSERSSTEEGS 1591 100%  
-----1695 33%

**Munc18 (Sec1-like protein (IPR001619)) (Reciprocal Blast eval  $2.59 \times 10^{-22}$ )**

sp|P61764|STXB1\_HUMAN  
ML005115a -MAPIGLKAVVGEKIMHDVKKVKKGEWKVLVVDQLSMRMLSSCCKMTDIMTEGITIVE 59  
MAADVTRQIDAVKHM-LNLSPKSESTWIKLVFDEYGRDIAPLLTVKELRECGVTLNL 59  
\* : : : \* \* \* : \* \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \*

sp|P61764|STXB1\_HUMAN  
ML005115a DINKRREPLPSLEAVYLITPSEKSVHSLISDFKDPPTAKYRAAHVFFTDSCPDALFNLV 119  
LIADKRDPIDVVPVYFVMPKQNI DLISQDCKNQMYEKFY---INFITAVSRQLLEDLA 116  
\* . : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \*

sp|P61764|STXB1\_HUMAN  
KS---RAAKVIKLTLEINIAFLPYESQVYSLDSADSF-QSFYSPHKAQMKNP---ILE 170

ML005115a QATIESDSVARVEKIFDQYLSFCMLEQNLFTVSAYDAQSCSYALNRPDADADIEKICIN 176  
 : : : : : : \* \* : : : \* : \* : : : \* : : :

sp|P61764|STXB1\_HUMAN RLAEQIATLCLATLKEYFAVRYRGEYKDALLAQLIQDKLDAYKADDPMT----GEGPDK 225  
 ML005115a AITDSVFLFVTLRELFPVIRCPKGNAAEIVAEER-LEKKMRDAR-RDPKSELFKDQAITSF 234  
 : : : : \* \* \* \* : : : : \* \* .

sp|P61764|STXB1\_HUMAN ARSQLLILDRGFDPSSPVLHELTFQAMSYDLLPIENDVYKYETSIGIGEARVKEVLLDEDD 285  
 ML005115a QRPILLILLDNRMDICSTLHHTWTYQALIHDLFNLNLRCKV---EVDEKVKNYDLGPDD 290  
 \* \* : \* : \* \* \* : \* : \* : : \* : : \* : \* : \* \*

sp|P61764|STXB1\_HUMAN DLWIALRHKHIAEVSQEVTRSLKDFSSSKRMN-----TGEKTTMRDLSQMLKKMPQ 336  
 ML005115a QFWAKNKGGPFPEVADAVHVELEACRAAEQEIKRKLDVMGESGVENANDQIANTVSSLPE 350  
 : \* : \* \* : \* \* : \* \* : : : : \* : : : : : \* : :

sp|P61764|STXB1\_HUMAN YQKELSKYSTHLHLA--EDCMKHYQGTVDKLCRVEQDLAMGTDAEGEKIKDPMRAIVPI 393  
 ML005115a LMERKKRVDMHINIALTALSDCIRA--RNLDKFFEVEEKIMTKTLEES-----VLDL 400  
 : . : . \* : : \* . \* : : . \* : : \* : : \* \* . : :

sp|P61764|STXB1\_HUMAN LLDAN-VSTYDKIRIILLYIFLKNGITENLNLKLIQHAQIPPEDSEITNMAH-----L 446  
 ML005115a LKNPSVGTAEADKRLRFIIYYLTSDLPDNLQYIEALQEAGCDTSCIEYLAKLKSIVSSL 460  
 \* : . : \* : \* : \* : : : . : : : : \* : \* \* : \* : \* :

sp|P61764|STXB1\_HUMAN GVPIVTDSTLRRRSKPERKERISEQTYQLSRWTPIIKDI-MEDTIEDKLDTKHYPIYISTR 505  
 ML005115a NVPAQTKLTSSSGSYS---SMS---NMFKYVKQSSKFMMEGVKSLVGHRRKLPVTRTV 512  
 . \* \* \* \* \* \* \* : \* : : : . : : \* \* . : : : \* \* \*

sp|P61764|STXB1\_HUMAN -----SSASFTTAVSARYGHWKPKAPGEYRSGPRLIIFILGGVSLNEMRCAYE 555  
 ML005115a DCLSELKQTPETDSFL--ALDPKIYRKTEMLPALKNTFNDVYVFVVGGGSYVEYQNLMT 570  
 . : \* \* \* \* . : : : \* \* \* . : : : \* : \* \* \* \* : :

sp|P61764|STXB1\_HUMAN VTQANGKWEVLIGSTHILTQKLLDTLKKLNKTDEEISS 594 **100%**  
 ML005115a YSEQHPGKRIYVGSSEMMDSKNFDQLTKLGSSSS--- 605 **21%**  
 : : : : \* : : : : \* \* \* \* . . . .

**Complexin (Synaphin (IPR008849))**

Complexin was identified de-novo using O14810|CPLX1\_HUMAN as a query (BlastP evalue =2.64 × 10<sup>-04</sup>)

sp|O14810|CPLX1\_HUMAN MEFVMKQALGGATKDMGKMLGGD-----EEKDPDAK--KEEERQEALRQEEERKA 50  
 ML08643a MNFIKQVLSKKTGALTDKLDVSKKCKELLESDPEDAAPQAQNLSEEEQMKQEAADRKE 60  
 \* : \* : \* \* . \* : . \* . \* : \* : \* : \* : : : \* \* : : \* \* : : \*

sp|O14810|CPLX1\_HUMAN KYAKMEAEREAVRGIRDKYGIKKKEEREAEQAAMEANSEGSLTRPKKAIIPGCGDEV-109  
 ML08643a HYNFNAEREEQRNMREKYGLRSDCPKSTGNE----SGADNCVNEASEPESKEDHK 115  
 : \* : : \* \* \* \* \* : : \* : \* : \* : . . . : . \* : . : \* \* . : . :

sp|O14810|CPLX1\_HUMAN ---EEDESILDTVIKYLPGPLQDMLKK 134 **100%**  
 ML08643a DSEKKDGDCVM----- 127 **27%**  
 : : \* : : :

**ABLIM3 (reciprocal eval 0.00)**

**Villin\_headpiece domain**

sp|O94929|ABLIM3\_HUMAN MNNTSIPYQQNPYNPRGSSNVIQCYRCGDTCKGEVVRVHNNHFHRCFTCVCGCGLAQSG 60  
 ML435828a ----- 0

sp|O94929|ABLIM3\_HUMAN FFFKNQEYICTQDYQQLYGRCDSCRDFITGEVISALGRTYHHPKCFVCSLCKRPFPIGDK 120  
 ML435828a -----MSAVE-----VVPPPLMED 14  
 : \* : : :

sp|O94929|ABLIM3\_HUMAN --VTFSGKEVCVCTCSQSMASPKPIKIRGSPSHCAGCKEE--IKHGQSLALDKQHWVSCF 176  
 ML435828a CAVPPLGEAC---CDPGLPDP-----CPPECQPPPEQASLLAGFYALSGLGAYGTTLI 64  
 \* \* : \* \* \* . : . : . \* \* \* \* : : \* \* \* : \* : : :

sp|O94929|ABLIM3\_HUMAN KCQTCQSVILTGEYISKDGVPIYCESDYH-AQFGIKCE-TCDRYISGRVLEAGGKHYHPTCA 234  
 ML435828a RLSN-----DQGTLKFVLPQLSEQAVQTECEEECEEKKE---EAAAAEE---AAA 107  
 : . : . : : : : \* : \* : \* . \* : \* : \* : \* : \* :

sp|O94929|ABLIM3\_HUMAN RCVRCHQMFTEGEEMYLTVSEVWHPICKQARAARKLKHRRRTSETGISPPGSSIGSPNRV 294  
 ML435828a EEGKGAEVSLADNRDLDSISGELSTPLCDDSDL-----PPP-----A 143  
 . : : : : : \* : \* : \* : \* : \* : \* :

sp|O94929|ABLIM3\_HUMAN ICAKVDNEILNYKDALAALPKVKSIIYEVQRPDILSYEPHSRYMSDEMLERCYGESLGLTSL 354  
 ML435828a ECDEERDM-----PDPPI----- 158  
 \* : : : \* : :

sp|O94929|ABLIM3\_HUMAN PYSQDIYENLDRQRRASSPGYIDSPTYRQGMSPTRFSRSPHHYRSRSGPESGRSSPYHSQ 414  
 ML435828a -----ECPDQVQKPVGRKESVA-----FD--P----- 178  
 . \* \* : \* \* . : : : : : \* :

sp|O94929|ABLIM3\_HUMAN LDRVRSSTPTSYPQPKHFIIPAGDSNIYRKPPIYKRHGDLSTATKSKTSEDIS---QTSK 470  
 ML435828a -----ENNPNAVNFHTPKAV-----NKFQNYTQVQM--LGEDLHAPSTRRP 219  
 . . : \* : \* \* \* . : : : \* : : . : \* : \* : :

```

sp|094929|ABLM3_HUMAN      YSPIYSPDPYAYASESEYWTYHGSFKVPRARRFSSGGEDDFDRSMHKLQSGIGRLILKEE 530
ML435828a                  MSPV-----VSQPIRWCNRSQKGSPPRITKGFNKNTPVRRHRTPS----- 262
                          **:      .*:  * : * *      *::.*  ::.  * : *

sp|094929|ABLM3_HUMAN      MKARSSSYADPWTPPRSSTSSREALHTAGYE-----MSLNGSPRSHYLADSDPLISK-- 582
ML435828a                  ----PQRFKSPDRGPRVRSNGL-PAGTAYKASGEIDPKIKESPPKDIVNKIRNTIESPS 317
                          . : .*  **  .*.      ::*:      .::  **  .. : .  *..

sp|094929|ABLM3_HUMAN      -SASLPAYRRNGLHRTPS-ADLFHYDSMNAVNWGMREYKIYPYELLVLT-----TRGRNR 635
ML435828a                  RVKSPPKP-----RSPSPVKPFDTDAFRLARKLAQEVADCPDPCIMVRVKDLQRCPKAL 371
                          * *      ** ** .. * .*:.. ..  *      * : : **

sp|094929|ABLM3_HUMAN      LPKDVRTRLRLRHLSQEEFYQVFGMTISEFDRLALWKRNLKQARLF 683
ML435828a                  LPELDPKARLEEYISDTEFRRTLGLSRSEYESFSEWKQOEIKKELGLF 419
                          ** :*:***:***: ** ..*: : ** : : ** :*:** : **

```

**Contactin-5** (reciprocal eval  $1.19 \times 10^{-17}$ )

```

sp|094779|CNTN5_HUMAN      -----MASSWKLM-----LFL 11
ML087115a                  MNSTESMPCKEAQSLFSAKNSVDIFQDEDGTFLLTSIHTANVARRDSQPFCTGDLSLAN 60
                          .::.*:      *

sp|094779|CNTN5_HUMAN      SVTMCLSEYKSLPGLSTSYAALLRIKSSSSSLFGSKTRPRYSPPSLGTLSSASS----P 67
ML087115a                  DASICIVTC--SLPDYE-----CPREFKQRCACPWDKPIKLDIDKGCIVKSI 105
                          .:***:      .      * .:      .:.* * .: .

sp|094779|CNTN5_HUMAN      SWLGAAQNYSPINLYHSSDAFKQDESVDYGPVVFVQEPDDIIFPTDSDEKKVALNCEVRG 127
ML087115a                  RDCPPYNTYILPIKGLK-----QFNFTKQPEDLVK---KRGDKIRMQCTVNG 149
                          :.* **:  :      *::*:** : . .*: :*: **

sp|094779|CNTN5_HUMAN      NPVPSYRWLRNGTEI-----DLESYRSLIDGTFIISNPSEAKDSGHYQCLATNTVGS 181
ML087115a                  DTNYQYFWYKSPSLAMGSHSVSRSSDKYLKQTNPFYDINSVQPSDSGYHCVIRTGDTV 209
                          : . * * : . :      . . ** . . . : * : .***:*:*..

sp|094779|CNTN5_HUMAN      -----ILSREATLQFAYLGN-FSGRTRSAVSVREGQGVVLMCSPPPHS 223
ML087115a                  AGVQRDPKYGSRDAKYSLVSNIGYLKVEYFDVPQLGETASIVTQKGTLLTVLPCDLPKSE 269
                          :* . . .*: .*.      *.* * * : :      .** * . *

sp|094779|CNTN5_HUMAN      PEI IYSWVFNEFP----SFV-AEDSRRFISQETGNLYISKVQTSDVGSYICLVKNVTVN 277
ML087115a                  PPVEAVWYKDDQIVSSKRMFVVPPAQKQKPDNDVNRKGSPLYIEMAETGDAGVYTCKTTYGDQT 329
                          * : * : :      ** : : . : * .*** .:*. * * * . .

sp|094779|CNTN5_HUMAN      ARVLSPTPLTLRNDGVMGEYEPKIEVHFPTVTAAGKTVKMECFALGNPVPTITWMKV 337
ML087115a                  YE---VAKVNLQVQGIIGQPTSDPEIVVQVAGRANVGETATFFCAGVGNPVPDVSWSKE 385
                          .      : :*: :*:** : * : . : * * * .: * .:***** :* *

sp|094779|CNTN5_HUMAN      NGYIPSK---ARLRKSQAVLEIPNVQLDDAGIYECRAENSRGKNSFRGQLQVYTYPHWVE 394
ML087115a                  DGTSIFESDRVALSDFNRKLT IADVRPEMSRDFACTVSSENSANSRKTILYLSIMPASYE 445
                          : *      . * . : * * : * : : * * . . . . . * * : * *

sp|094779|CNTN5_HUMAN      -KLND-----TQLDSGSPLRWECKATGK---PRPTYRWLKNGVPLSP--QSRV----- 436
ML087115a                  INFQETPVSHVIKPNVYTPFTIQCAITVDFVIEAPVMYWIKNGLASLDMTPPTRIRTVTDN 505
                          : : :      : : * : * * .      * .***. * .      * :

sp|094779|CNTN5_HUMAN      -----EMVNGVLMIHNVNQSDAGMYQCLAENKYGAIYASAEKILASAPTALNQLKK 489
ML087115a                  QKILNKVTIRTSRLIFDTPNESDKGVYQCIVENKEQMRQATAYVDVSKSPSSYDVYDQE 565
                          : . . * : . . * . * * . * . * . * . * * * * * * * * * * * * * * * *

sp|094779|CNTN5_HUMAN      TIIVTKD---QEVVIECKPQGSFKPT----- 512
ML087115a                  YEVFTEKKIDEAAEHCTKKWGRGNLVTITNKKESDQVFLVQAGVTRAWIGLTSESP 625
                          :.*: :      :*..* . : * : .

sp|094779|CNTN5_HUMAN      -----ISWKKGDRAVRENK-----IAILPDGSLRILNASK-----SDEG--KYVC 551
ML087115a                  IEQTGIWKWQAGSHVRDDFSYWYSGNPDNALGNESYAIMDVSRAHGLDWNNEGSYFPVC 685
                          .*: .: . : .      * : * * : : * :      .: **  : **

sp|094779|CNTN5_HUMAN      RGENVFGSAEIIAS-LSVKEPTRIELTPKRELTIVGESIVLNCKAIHDASLDVTFYWTLK 610
ML087115a                  SRYRA--KCPVAKFFNNSARPISSGLETEGTEYEVGKEITVKCVEKEESNVSQKIVCHPS 743
                          .. .. * : . . .      * : ** ** : * : * * . : : . : .

sp|094779|CNTN5_HUMAN      GQPIDFEEEGGHFESIRAQASSADLMIRNILLMHAGRYGCRVQT TADSVSDEAELLVRGP 670
ML087115a                  G-----TF-----MPSSIPCVPKSRQHVTTSL----- 766
                          *      *      .      * * : * : * : .

sp|094779|CNTN5_HUMAN      PGPPGIVIVEEITESTATLSWSPAADNHSPISSYNLQARSPFSLGWQTVKTVPEIITGDM 730
ML087115a                  ----- 766

sp|094779|CNTN5_HUMAN      ESAMAVDLNFWVEYFRVATNP IGTGDPSTPSRMIRTNEAVPKTAPTNVSGRSGRRHEL 790
ML087115a                  -CHVTVGLFLFLLYR----- 780
                          . : * . * : : * .

sp|094779|CNTN5_HUMAN      VIAWEPVSEFQNGEGFGYIVAFRPNGTRGWKEKMTVSSEASKFIYRDESVPLTPFEVK 850
ML087115a                  ----- 780

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sp | 094779 | CNTN5\_HUMAN | VGVNNKGDGPFQSQVIVVICSAEAGEPSAAPTDVKATSVSVSEILVAVKHIKESLGRPQGF 910  
ML087115a | ----- 780

sp | 094779 | CNTN5\_HUMAN | VGWYKMEQEDTAEIVKTRGNESFVILTLGLEGNTLYHFTVRAYNGAGYGPSSSEVSATK 970  
ML087115a | ----- 780

sp | 094779 | CNTN5\_HUMAN | KSPSPQAPSNLRWEEQGSQVSLGWEPV I PLANESEVVGKYVFYRQEGHSNSQVIETQKLQ 1030  
ML087115a | ----- 780

sp | 094779 | CNTN5\_HUMAN | AVVPLPDAGVYIIIEVRAYSEGGDGTASSQIRVPSYSGGKITSAQSTLHSLSTSSSSVTL 1090  
ML087115a | ----- 780

sp | 094779 | CNTN5\_HUMAN | LALMIPSTSW                   1100     **100%**  
ML087115a | -----                   780     **22%**

**Calcium-activated potassium channel (Reciprocal Blast eval 0.00, 3.84 × 10<sup>-177</sup>)**

sp | Q12791 | KCMA1\_HUMAN | MANGGGGGGSSGGGGGGGSSLRMSSNIHANHLSLDASSSSSSSSSSSSSSSSSSSSSSSSSSSSS 60  
ML04056a | ----- 0  
ML128229a | ----- 0

sp | Q12791 | KCMA1\_HUMAN | VHEPKMDALII PVTMEVPCDSRGQRMWAF LASSMVTFFGGLF I ILLWRTLKYLWTVCC H 120  
ML04056a | -----MSCCD 5  
ML128229a | ----- 0

sp | Q12791 | KCMA1\_HUMAN | CGGKTKEAQ-----KINNGSSQADGTLKPVDEKEEAVAAEVGWMTSVKD-WAGVMISAQT 174  
ML04056a | EFVNIDISLQFKNRDLYENTSQISRMPFNHYDRD-KLDEVELHNKLRHYIVNEVISLQT 64  
ML128229a | ---MRKRRRQDSEIEYFGCIRFIRRVYNIQR-----RV-VQFAEDISYPKT 43  
. . . . . : : : : : \* : . . . : \*

sp | Q12791 | KCMA1\_HUMAN | LTGRVLVVLFALSIGALVIYFIDSSNPIESCQNFYK--DFTLQIDMAFNVFFLLYFGLR 232  
ML04056a | NKGMLVAILYLFNIVSVTLYINQSDQPLEQCEDVLNTCNWTLYADIGLNVFFLFHFLR 124  
ML128229a | KKGRAMTWVQLLMNLIAIGSFAAQTPEEIERCVELT---EITIVDLICNIFFLWRVVM 100  
. \* . . . : : . : : : : \* \* . . : \* : \* : \* : \* : \*

sp | Q12791 | KCMA1\_HUMAN | FIAANDKLVWFLEVNSVVDFFTVPVFFVSVYLNRSLGRLRFLRRLRIQFSEILQFLNL 292  
ML04056a | LIAAPNRLKFWFQMGSIVDFCTIPPCALALILERNWLGMRFMRALRFMGMGEILMFTNST 184  
ML128229a | YIVSKDKLCFVWEIGSLIDFCTIPPALVTFGIRKSWLGLRFVRCCLKLLSFGDDIAAVKLI 160  
. : : \* : \* . . . : : \* : \* . . . : \* : \* . : : \* : \* . : :

sp | Q12791 | KCMA1\_HUMAN | KTSNSIKLVNLLSIFISTWLTAAGFIHLVENS G DPWENFQ--NNQALTYWECVYLLMVTMS 351  
ML04056a | GTS-IVQLLVMLDFVSVWLFAAGFVHLVENS G DPWKADSAKDNTFYFDSVWLTMTVMS 243  
ML128229a | SSHKMLTLSRTLQCFVSWFLTAAGLYFLAARMSD-----SGNKIHFFECMYFLLVITIS 213  
: \* : : \* \* \* : \* : \* . . . \* : : : : : : : \* \* \*

sp | Q12791 | KCMA1\_HUMAN | TVGYGDVYAKTTLGRFLMVFIFLGLAMFASYPVEIIEIIGNRKYGGYSYAVSGRKHIV 411  
ML04056a | TVGYGDVYPTTGIGRSFMVYIVCGLAMFATYTPYLYEFYRSRSPYAGRERADSKKYVV 303  
ML128229a | TIGYGLKPETTTRLVVIVLIAVGLAVFASFGPAMIEFKKSPPPYTLDDYDSK-SHV 272  
. \* : \* \* : \* \* . . . : \* \* : \* : \* : \* . . . : \* :

sp | Q12791 | KCMA1\_HUMAN | VCGHITLESVSNFLKDFLHKDRDDVNVVEIVFLHNSPNLELEALFKRHFQVEFYQGSVL 471  
ML04056a | VCGHITYNVKSF LADLPDRDRTSRVFLDNKRPEPELTGLIKRYFLSVQYFEGSAL 363  
ML128229a | VCGYINTSVSNFMRF LHPENEDHETAVFLNTIPPEDLQNLMRHNFYRCQQYQGSPL 332  
. \* \* : \* . . . \* : \* : \* : \* \* : \* : \* : \* : \* : \* : \* :

sp | Q12791 | KCMA1\_HUMAN | NPHDLARVKIESADACLILANKYCADPDAEDASNIMRVISIKNYHPKIRIITQMLQYHNK 531  
ML04056a | NHDNLRVQLEFSDAVILLCNKSDDTKSEDAATILRAISVKNYCSKARLIMQLLNYKSK 423  
ML128229a | RASDLARVKLSTAKACLVIANKHSAPEDAEDAAANILRVISIKNYKSDVRVILNLYHNE 392  
. \* \* \* : \* . : \* . : \* \* : \* . . : \* : \* : \* : \* : \* : \* : :

sp | Q12791 | KCMA1\_HUMAN | AHLNIPSWNWK-EGDDAICLAELKLGFI AQSCLAQGLSTMLANLFSMRSEFIKI--EEDT 588  
ML04056a | SFLQTI PNWDPI NYRDENICISEFMYGLVAQSCLCPGFSTLMINLISTRSYIPGINENFD 483  
ML128229a | EHLFNVPDWNHQLYGDEVICINESK-----VRSN 422  
. \* . : \* : \* : \* : \* : \*

sp | Q12791 | KCMA1\_HUMAN | WQKYYLEGVSNEMYTEYLSAFVGLSFPTVCELCFVKLKLMMIAIEYKCSANRESRILINP 648  
ML04056a | WKSDFAYGCDHEIYTMISDFNGMTPEAAEICYKQLNLLMIAVENFDNS---GLAINP 540  
ML128229a | WEYEGYGASNELYTGSLSDFLDMTFPEVAEICLIKHLILLIGVETNS--SSTGILFNP 480  
. \* : \* \* . : \* \* : \* \* . : \* \* . : \* \* : \* \* : \* : \* : \* : \* :

sp | Q12791 | KCMA1\_HUMAN | -GNHLKI QEGTLGGFIASDAKEVKRAFFYCKACHDDITDPKRIKCKCRPKMSIYKRMR 707  
ML04056a | LPDQFTIRKECLGYFIASSYKDCRARFYCALCLNEGIEI-GFKPKCRLEAVKKSRSNV 599  
ML128229a | SPHVFREFRQGTGIFIAQNPTVVKSAAALFCFKCHEYAIQS-EIVKCTCDKS DSGYTN SRT 539  
. . : : : \* \* \* : \* . : \* : \* : \* : \* : \* : \*

sp | Q12791 | KCMA1\_HUMAN | RACCFDCGRSERDCSCMSGRVR-GNVDTLERAFPLSSVSNVDCSTSFRAFEDEQPSTLSP 766  
ML04056a | QLIPLSEHKSFN--NNEGLTRVGSIDS KS---STATDVNQLRVTRHLSQHS--- 648  
ML128229a | -----N-----SNA-----NTTVP 548  
. \* . : \* . : \* . : \* . : \* . : \* . : \* . : \* . : \* . : \*

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sp|Q12791|KCMA1_HUMAN      KKKQRNGGMRNSPNTSPKLMRHDPLLI PGNDQIDNMDSNVKKYDSTGMFHWCAPKEIEKV 826
ML04056a                   -----KTSVDRGTLA-----GAGMSSTFDPTGNYHWAPEKKFEDV 684
ML128229a                  KKKRKKQS-EYVPYW-KRLSQEER-----AKMDERLTLDGSGTFHWRESCLEEVEV 596
                               :   :                               .   * : * : * *   : * . *

sp|Q12791|KCMA1_HUMAN      ILT-----RSEAAMTVLSGHVVVCI FGDVVSALIGLRNLVM 862
ML04056a                   DLAGYITKEYQYKPDAAEAINQRVVIKYINEKDHELNNHIVICAFGDDKTPISGLSSLIK 744
ML128229a                  TMT-----KEDVATLTDHII VCVFGDNNAPT VGLRNL 630
                               : :                               :   * . * : : *   * * *   : :   * *   . * :

sp|Q12791|KCMA1_HUMAN      PLRASNPHYHELKHIVFVGSIEYLKREWETLHNFPKVSI LPGTPLSRADLRVNLINLCDM 922
ML04056a                   PLRASNLPYKKLKVVLLLAEKDFLLKAWKELRHFPKIRVLCGSALDRSKLKRAFINRASM 804
ML128229a                  PLRNSNLPTEVKKVLLGKKKEY IEKEWKDIDEFQDVYFMEGSP IRREDVISAGVQNCLM 690
*** ** :   : * : : : : . : : : * : : * : : * : : * : : * : : . : : . *

sp|Q12791|KCMA1_HUMAN      CVILSANQNNI--DDTSLQDKEC ILASLNKSMQFDDSIGVLQANSQGFTPPGMDRSPD 980
ML04056a                   VVILSNYGKRMAYKDPFLLDKEPILACLNLQPVA-----GK--- 840
ML128229a                  CLILSSALQSK-ATDPNLVKEITILSFLQIKGCRGTESSD-----T 730
:***   :   * * * * * * : :

sp|Q12791|KCMA1_HUMAN      NSPVHGMLRQPSITTG VNIPIITELVNDTNVQFLDQDDDDDPTELYLTQPFACGTAFAV 1040
ML04056a                   -----SENSKPVFIAELVNDSNVHFLDQDNEDEPDIELHLTMKFAQGGSCITA 888
ML128229a                  SNTTKYRLSEKPIRNRAQIPI ISEIVNDSNVQFMEKSKDS-SVGALYMALPFFTRGQAFIV 789
                               .   : : * : * : * : * : * : : : .   * : :   * : *   . : .

sp|Q12791|KCMA1_HUMAN      SVLDSLMSATYFNDNILTIRTLVTTGGATPELEALI---AEENALRGYSTPQTLANRDR 1097
ML04056a                   TALDITLMSEAYYNDEVMTLVRAIAGANVPEYDAE-----DEEHSGPLQV PANALCGSQ 942
ML128229a                  SVLDAILSLTFYNEKLM SII RTLITIGI GNSHKNETADNYLPENSEDDVMYYQPWLRTMS 849
:*** : : * : : * : : : : * : : * : :   :   :   :   :

sp|Q12791|KCMA1_HUMAN      CRVAQLALLDGPFDLGDGGCYGDLFCKALKTYNMLCFGIYRLRDAHLSTPS-----QC 1151
ML04056a                   CRVIRIKAEEPSLSEHIK GKAYKDVVELLQKFNLLCLGLHRAIDWHLDVSV-----E 995
ML128229a                  CRIAQISLRDERFSRF---RVYGE L FVYLLHNY SMLALGLYRSYQWANKGKSTKARDNHN 906
** : :   :   : :   * : *   * : : : * : : * : : * : :   :   .

sp|Q12791|KCMA1_HUMAN      TKRYVITNPPYEFELVPTDLIFCLMQFDHNAGQSRASLSHSSHSS-----QSSSK 1201
ML04056a                   HKRFVYINPPGETKIVASDYLVI VQT SKLQPPTEVMLNKIRD TMLRKGTPPEHEQSADS 1055
ML128229a                  EDRYVTTAPSYDAKLRPN DKVFVLAQSEMELPFPLEMGNEMD-GLDDDGMSYQTSRETS 965
. * : *   * : : : * : : : * .   . :   .   .

sp|Q12791|KCMA1_HUMAN      -----KSSSVHSI PSTANRQNRPKSRE-----SRDKQKYVQE---ERL- 1236
ML04056a                   KLTRQNKVDNESVRFESVSTRSVSSVAPS PRTPLS-----PHSPPAAGE---ERFY 1103
ML128229a                  PPTVMKPKPDVSVPIA VEEIQPV TQPNNQPSNPTTDTDTDHSSPLKEPVTMETKTD DTL 1025
                               . : : .   * :   .   . *   : :

sp|Q12791|KCMA1_HUMAN      ----- 1236 100%
ML04056a                   NPLHA-----AANHTSSKTTQHILENFRNSYASYSDGH 1136 38%
ML128229a                  HPVDLPVYTTDP TENLKPNNTTTSNDIAHLIA----- 1059 35%

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**Supplementary figure 16. Alignments of *M. leidy* and *H. sapiens* neuronal proteins shown in Table 1 (<https://www.ebi.ac.uk/Tools/msa/clustalo/>).**

## Supplementary videos

*Supplementary video 1. ML02212a localization in the aboral organ of M. leidy. Neuropeptide: cyan, DAPI: yellow.*

*Supplementary video 2. ML07842a localization around the pharynx of M. leidy. Neuropeptide: cyan, DAPI: yellow, Tubulin: red.*

*Supplementary video 3. ML07842a localization in the aboral organ of M. leidy. Neuropeptide: cyan, DAPI: yellow.*

*Supplementary video 4. ML07842a localization in the aboral organ of an adult M. leidy. Neuropeptide: cyan, DAPI: yellow.*

*Supplementary video 5. ML21545a localization around the pharynx of M. leidy. Neuropeptide: cyan, DAPI: yellow, tubulin: red.*

*Supplementary video 6. ML17711a localization around the pharynx of M. leidy. Neuropeptide: cyan, DAPI: yellow, tubulin: red.*

*Supplementary video 7. ML17711a localization in the aboral organ of M. leidy. Neuropeptide: cyan, DAPI: yellow.*

*Supplementary video 8. 3D reconstruction of a part of M. leidy epidermis. Colours coded as in Fig 6A.*

*Supplementary video 9. 3D reconstruction of a part of M. leidy epidermis. Neuron is shown half-transparent. Colours coded as in Fig 6B.*

*Supplementary video 10. 3D reconstruction of a part of M. leidy epidermis. Neuron is not shown. Colours coded as in Fig 6C.*

*Supplementary video 11. 3D reconstruction of a M. leidy synapse.*

# Supplementary tables

## Supplementary table 1. Neuropeptide precursors predicted by NeuroPID.

| <b>Linear precursors</b>  |
|---|
| <b>-Enriched in uncharacterised metacells</b>   |
| >ML043317a<br>MKTILLISCLLSAVYSRVLRLNEEDWSRNGAMEDSEDSWRNGAMRDESDWNRNGGMRDSEDSWRNGRMEDESDWSRNGAMEDSEDSWRNGAMED<br>SEEWSRNGLENSEDWSRNGAMRDESDWSRNGAIKDESDWSRNGAMRDESDWSRNGAMKDESDWSRNGMEDSEDSWRNGA                   |
| >ML21545a<br>MSKFLFLTLVGAARAAS FASDSNTLADSDECRGTGYNMRYDLECRRRRAAARLQLQEDGETEGGEELTKRSAAEQNWYSARRDRGKRNS<br>NEEQDFSGYRRSGQKRSAEEDDYDIYKRGESEEQDYSGYRGRGRGE   |
| >ML016347a<br>MICLNFRVTAVVLFVILLAGFC PAAPYIYSTQENDAFLETGEEKGELDIEAPKTPKLRIFYQKRSEEGKDEDPKLQYFYQIRSLLEDKEKKPKLRY<br>FYQKREENKDTKPKLRHFYKREENKDTKPKLRYFFQKREENKDTKPKLRYFYQEREDNKDTKPKLRYFFQKREENKDTKPKLRNFYRKRGEN   |
| >ML07842a<br>MMKLTVVCLLFASLLVRAECGVVERHEEQLFDAEDEQPNFRAGLENKELEKRS PNFRFGSKRSAEDAPNLRGKRSNEDTPNFRGTKRS AEDSPN<br>FRGAKRS AVEAPNFRGAQKSEEDAPHFRGAKRFAEDAPHLRGVKRSTVDAPNFRGAERLEEDV PNLRGAERSEEGSPNFRGAERAVEDAPQFRG |
| >ML14597a<br>MKCFTLLLIGFLI AVETLPLNSHEEDLAVDIETRKS KGGKHLVLELEERKSNKKHGLIELEERKAKPAPAPAPK KKKGLVLELEERKSKKKHGL<br>VELEERKSKKKGLVLELEERKAKPAPVPQKKGTR  |
| >ML06743a<br>MFRV FVSIHLFLHLIAARSTGQVDLEKVDKAGFFWKPKQSKRAVAEDATAPPEDDVGF FWKPKFGKRSVEIPKPNDDKKRAGFFWKPFKRSVA<br>EEATAAPEDHAGFFWKPNFGRFGKRSVVKSEPDQDGKKRAGFFWKPIQESRCRRRHRC SRPFRFFLEA                             |
| >ML06405a<br>MRKTLCIQLLVLLAIQRFTDGKA FEESENEVLSLEKRAEDLDEDFDKRETEDRENEVEIDL D   |
| >ML02212a<br>MKLFLFVLLGLVALISCETVESEVDSESESDSNAMRVKRAKFSMSNYRGHKQGNRGWTGGAMQEEE   |
| >ML01798a<br>MKLLLLTLAVLLACLTA VPVRQEEVQEEIRLERSAES SGGETARVEKRAAIDTGS DYPGFEGGKRRWYG   |
| >ML14991a<br>MSCLSNLSPCKSLLLFLGLVLLTKESVQRTLPE SGQALGMKNTIEEDATVMSDSDEEQSRMKRQFFRLKRQSF RPSRGAEWNL DGYFGNQEKS<br>EAELRDPDTQTRRFK DGRNEQLSQWRAMMNRV  |
| >ML11723a<br>MKYFMILAVLILTVGSSPF EKRAENAELASEKRSEEDPGE EYVLAKRNV DQDAVSLEKRQKYGYKRGE  |
| >ML003517a<br>MATMMGFLIVLLIAAVSGHSHSDESPQHNRPDSPPKHHIPKDVIEALQ RSGKSRGEHNAHPGAEHHPEGAHSSH LGKGNFERHPEGGRPIPP<br>KRVQRISRL   |
| >ML02736a<br>MKCFVVL FALLALSQSASLNSLESVEDVIMADNDNVELEEGALNAEEEEARVYKGYNGGNRVWYG   |
| >ML017711a<br>MKMFILIGLLITLVLNYVSAGDLARRSLEENESGINEGAAEEDDESFRGLRESEDES RKGREVADEELFRGKRDFREKRD FRGKRDFRGKREF<br>RGKREFRGKRDFRGMKSSEELVKRDL SRGQ  |
| >ML030511a<br>MALTKILFSLSLILMVSSRAFEESAGDENNAQAFGLGNKDGAVGDSLEEITQLGKVDEFKLA EAEDDQHFAVGT   |
| >ML206415a<br>MKLHLYIGTILLCLSAMFLDGI AQNDDSADDNAAGQTDQAGAENSEDDAAAAAGEEGAE TADGAETNSNDTTGAGAE GEAEEGDSKDPNGGAMS<br>NLKNSYLLLLTIPVVGRI FV  |
| >ML00992a<br>MSIMKFWLLLLLTLAITT LSAQEP AQDDSEAVNDTSPDGDAASENVADDAAPADGEAAAADGEAAAADGEAAAADGEAAPADGEDGAAAEDGAA<br>AEDGAAAEDGAAAEDGAVAAEDGAAAEDGAAAEDGAAAEDGAAAEDGAAAEEEQGEEEAEPAGSGSNVQNKICFSIFVVSILTKVLLC         |
| >ML218923a<br>MDKLMFLIIVIEVVIISGR TIISSDDTNLKSSSEDFGIKGGPWNSEEDFVGRGSGGWMSEEDFVVKGN GARMSEEDFVGRSRKGTNWEAEDLA<br>ESSEEEIYGI PGKGVWNKEDQDLLPGGAVPFSN   |
| >ML056913a<br>MFRLTSILLVVLVAIVTFTRTIEDSEEIGHGLRMDKNEEIGHGLTLDKRSADSV DTEAMADEEELVGHG IKGSHAWRK  |
| >ML030510a<br>MKFTKLIILM TLLALIASRSLEEDNNADQTI GWGRQRVAAEADFVAEEKMAGGGNMI LEMSEEEQHLGLGF  |
| >ML066512a<br>MVFYKSVLIGILALVCLTYARSLDSEFVDDNEILVLEKREEGDEEDSLDLMDTGSEIEDV VDEGGSEIMI EEKGADSDREQIQPRD GFFVFPD<br>YGRIHWP KSKRPRKQPSKSVRINSERL  |
| >ML233326a<br>MKTTFVLVLTLMICCN YQSVPM SLEEDLSDEEHRGLQKRAGTKFNKADYKSVGEGTRKWF G  |
| >ML199816a<br>MKLFLFLTASLLV LATAVTVQTEAREIVA EVAESEAVESAASEEDTFVYRKEEDSAFLFAD   |
| >ML31983a   |



MTMKIFLVTLFSLVALFAVAADTEEQAKEEFELADEAEEDSLEEGDELVEVVKRFADKKKSKKNNRMRW  
>ML065755a  
MKLAAGIFLVLACLTVVMIPEGAASLGS LDAANS DSNVLYGADHEI LESSLINRKEEAEGALYG  
>ML10665a  
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***-Not enriched in uncharacterised metacells***

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*Supplementary table 2. NeuroPID scoring for the linear neuropeptide precursors.*

| Protein Name | Extra Trees Prediction | MinEx Tree Prediction | Linear SVM Prediction | Gradient Boosting Prediction | Internal Score |
|--------------|------------------------|-----------------------|-----------------------|------------------------------|----------------|
| ML319815a    | 0,80                   | 0,86                  | 0,96                  | 1,00                         | 25,12          |
| ML14597a     | 0,83                   | 0,89                  | 0,83                  | 1,00                         | 15,38          |
| ML10665a     | 0,81                   | 0,88                  | 0,96                  | 1,00                         | 15             |
| ML034332a    | 0,87                   | 0,88                  | 0,99                  | 1,00                         | 13,03          |
| ML31983a     | 0,78                   | 0,82                  | 0,91                  | 1,00                         | 11,63          |
| ML11723a     | 0,92                   | 0,90                  | 0,99                  | 1,00                         | 8,89           |
| ML06743a     | 0,88                   | 0,82                  | 0,96                  | 1,00                         | 8,63           |
| ML017711a    | 0,87                   | 0,78                  | 1,00                  | 1,00                         | 8              |
| ML06328a     | 0,81                   | 0,85                  | 0,77                  | 1,00                         | 7,14           |
| ML21545a     | 0,93                   | 0,93                  | 0,99                  | 1,00                         | 6,9            |
| ML21632a     | 0,88                   | 0,83                  | 0,96                  | 1,00                         | 6,67           |
| ML01798a     | 0,92                   | 0,90                  | 0,86                  | 1,00                         | 6,67           |
| ML040716a    | 0,83                   | 0,84                  | 0,63                  | 1,00                         | 6,25           |
| ML26664a     | 0,80                   | 0,77                  | 0,97                  | 1,00                         | 6,25           |
| ML090813a    | 0,87                   | 0,84                  | 1,00                  | 1,00                         | 5,56           |
| ML31164a     | 0,87                   | 0,92                  | 0,87                  | 1,00                         | 5,45           |
| ML233326a    | 0,84                   | 0,80                  | 0,82                  | 1,00                         | 5,41           |
| ML06405a     | 0,91                   | 0,85                  | 0,99                  | 1,00                         | 5,13           |
| ML016347a    | 0,81                   | 0,82                  | 0,91                  | 1,00                         | 4,94           |
| ML073260a    | 0,91                   | 0,93                  | 0,67                  | 1,00                         | 4,44           |
| ML07842a     | 0,97                   | 0,88                  | 0,97                  | 1,00                         | 4,29           |
| ML124215a    | 0,85                   | 0,89                  | 0,93                  | 1,00                         | 4,17           |
| ML066512a    | 0,86                   | 0,92                  | 0,32                  | 1,00                         | 4,12           |
| ML032113a    | 0,92                   | 0,90                  | 0,79                  | 1,00                         | 4,08           |
| ML065715a    | 0,71                   | 0,62                  | 0,98                  | 1,00                         | 3,93           |
| ML056913a    | 0,85                   | 0,87                  | 0,76                  | 1,00                         | 3,77           |
| ML040029a    | 0,75                   | 0,81                  | 0,33                  | 1,00                         | 3,73           |
| ML08268a     | 0,81                   | 0,77                  | 0,81                  | 1,00                         | 3,66           |
| ML154515a    | 0,85                   | 0,94                  | 0,43                  | 1,00                         | 3,17           |
| ML14991a     | 0,93                   | 0,89                  | 0,90                  | 1,00                         | 2,97           |
| ML46396a     | 0,80                   | 0,77                  | 0,95                  | 1,00                         | 2,94           |
| ML199816a    | 0,83                   | 0,78                  | 0,93                  | 1,00                         | 2,86           |
| ML1541126a   | 0,84                   | 0,93                  | 0,68                  | 1,00                         | 2,76           |
| ML005019a    | 0,88                   | 0,88                  | 0,75                  | 1,00                         | 2,56           |
| ML065755a    | 0,72                   | 0,83                  | 0,84                  | 1,00                         | 2,5            |
| ML039810a    | 0,73                   | 0,79                  | 0,90                  | 1,00                         | 2,47           |
| ML051421a    | 0,87                   | 0,85                  | 0,83                  | 1,00                         | 2,41           |
| ML174759a    | 0,89                   | 0,90                  | 0,96                  | 1,00                         | 2,38           |
| ML02212a     | 0,83                   | 0,89                  | 0,95                  | 1,00                         | 2,33           |
| ML215411a    | 0,76                   | 0,84                  | 0,76                  | 1,00                         | 2,22           |
| ML093052a    | 0,85                   | 0,85                  | 0,85                  | 1,00                         | 2              |
| ML33461a     | 0,79                   | 0,77                  | 0,84                  | 1,00                         | 1,89           |

|           |      |      |      |      |      |
|-----------|------|------|------|------|------|
| ML216920a | 0,86 | 0,88 | 0,87 | 1,00 | 1,45 |
| ML003517a | 0,88 | 0,88 | 0,88 | 1,00 | 1,27 |
| ML01134a  | 0,84 | 0,78 | 0,91 | 1,00 | 1,11 |
| ML218923a | 0,81 | 0,85 | 0,89 | 0,99 | 0,98 |
| ML07361a  | 0,81 | 0,85 | 0,97 | 1,00 | 0    |
| ML07012a  | 0,80 | 0,85 | 0,95 | 1,00 | 0    |
| ML030512a | 0,85 | 0,85 | 0,90 | 1,00 | 0    |
| ML02736a  | 0,82 | 0,85 | 0,82 | 1,00 | 0    |
| ML043317a | 0,83 | 0,81 | 0,93 | 1,00 | 0    |
| ML00497a  | 0,79 | 0,81 | 0,85 | 1,00 | 0    |
| ML053619a | 0,77 | 0,81 | 0,89 | 1,00 | 0    |
| ML053618a | 0,77 | 0,81 | 0,89 | 1,00 | 0    |
| ML258215a | 0,80 | 0,80 | 0,98 | 1,00 | 0    |
| ML100012a | 0,80 | 0,77 | 0,99 | 1,00 | 0    |
| ML090812a | 0,83 | 0,78 | 0,96 | 1,00 | 0    |
| ML05859a  | 0,76 | 0,85 | 0,87 | 1,00 | 0    |
| ML030510a | 0,81 | 0,79 | 0,90 | 1,00 | 0    |
| ML05367a  | 0,76 | 0,80 | 0,85 | 1,00 | 0    |
| ML11691a  | 0,77 | 0,71 | 0,93 | 1,00 | 0    |
| ML083811a | 0,59 | 0,60 | 0,87 | 1,00 | 0    |
| ML218823a | 0,76 | 0,78 | 0,91 | 1,00 | 0    |
| ML00992a  | 0,71 | 0,79 | 0,96 | 1,00 | 0    |
| ML206415a | 0,76 | 0,80 | 0,87 | 1,00 | 0    |
| ML030511a | 0,76 | 0,78 | 0,84 | 1,00 | 0    |
| ML067017a | 0,65 | 0,73 | 0,87 | 1,00 | 0    |



**Supplementary table 3. Neuropeptide homologs uncovered in other ctenophore species**

|           |   |
|-----------|---|
| ML01798a  | <p>&gt;Pukia_falcata_sb 13085131 <br/>         &gt;Pukia_falcata_sb 13047163 <br/>         &gt;Dryodora_glandiformis_sb 284310 <br/>         &gt;GHXS01075231.1 TSA: Hormiphora californensis isolate 20161213-T1 tx_DN13442_c0_g3_i1, transcribed RNA sequence<br/>         &gt;GGLO01069197.1 TSA: Hormiphora californensis TR28038_c0_g1_i2 transcribed RNA sequence</p>   |
| ML02212a  | <p>&gt;Pleur_sb 12660472 <br/>         &gt;Pukia_falcata_sb 13062132 <br/>         &gt;Dryodora_glandiformis_sb 292161 <br/>         &gt;Bolinopsis_infundibulum_sb 12215413 <br/>         &gt;Bolinopsis_ashleyi_sb 12973892 <br/>         &gt;GHXS01044202.1 TSA: Hormiphora californensis isolate 20161213-T1 tx_DN17776_c0_g1_i1, transcribed RNA sequence<br/>         &gt;GHXY01365093.1 TSA: Beroe forskalii isolate Bf201507 CTE_B_forskalii.D785-D11.30471c0g1i3, transcribed RNA sequence</p>   |
| ML02736a  | <p>&gt;Pleur_sb 12672458 <br/>         &gt;Pukia_falcata_sb 13054685 <br/>         &gt;Euplokamis_dunlapae_sb 10633353 <br/>         &gt;Bolinopsis_infundibulum_sb 12166874 <br/>         &gt;Bolinopsis_ashleyi_sb 12966060 <br/>         &gt;GGLO01055400.1 TSA: Hormiphora californensis TR22397_c1_g1_i1 transcribed RNA sequence<br/>         &gt;GHXY01172047.1 TSA: Beroe forskalii isolate Bf201507 CTE_B_forskalii.D785-D11.25303c0g5i3, transcribed RNA sequence<br/>         &gt;GHXY01128478.1 TSA: Beroe forskalii isolate Bf201507 CTE_B_forskalii.D785-D11.35947c8g1i4, transcribed RNA sequence<br/>         &gt;GHXY01128479.1 TSA: Beroe forskalii isolate Bf201507 CTE_B_forskalii.D785-D11.35947c8g1i5, transcribed RNA sequence<br/>         &gt;GHXY01128476.1 TSA: Beroe forskalii isolate Bf201507 CTE_B_forskalii.D785-D11.35947c8g1i8, transcribed RNA sequence<br/>         &gt;GGLO01055401.1 TSA: Hormiphora californensis TR22397_c1_g1_i2 transcribed RNA sequence<br/>         &gt;Beroe_abyssicola_sb 12131309 <br/>         &gt;Beroe_sp_pink_sb 12859312 </p> |
| ML07842a  | <p>&gt;Pukia_falcata_sb 13030337 <br/>         &gt;Bolinopsis_infundibulum_sb 12232314 <br/>         &gt;Bolinopsis_ashleyi_sb 12925108 </p>  |
| ML017711a | <p>&gt;Pukia_falcata_sb 13023494 <br/>         &gt;Bolinopsis_infundibulum_sb 12232315 <br/>         &gt;Bolinopsis_ashleyi_sb 12948034 <br/>         &gt;GHXY01131763.1_3 TSA: Beroe forskalii isolate Bf201507 CTE_B_forskalii.D785-D11.29326c5g3i1, transcribed RNA sequence<br/>         &gt;GGLO01068950.1_2 TSA: Hormiphora californensis TR27976_c4_g1_i2 transcribed RNA sequence<br/>         &gt;GHXS01104377.1_3 TSA: Hormiphora californensis isolate 20161213-T1 tx_DN17364_c0_g3_i4, transcribed RNA sequence<br/>         &gt;GGLO01068949.1_2 TSA: Hormiphora californensis TR27976_c4_g1_i1 transcribed RNA sequence</p>   |
| ML06743a  | <p>&gt;Pleur_sb 12652162 <br/>         &gt;Pukia_falcata_sb 13031051 <br/>         &gt;Euplokamis_dunlapae_sb 10678971 </p>   |
| ML21545a  | <p>&gt;Dryodora_glandiformis_sb 290240 </p>   |

|           |  |
|-----------|--|
|           | <p>&gt;Bolinopsis_infundibulum_sb 12203994 </p> <p>&gt;Bolinopsis_infundibulum_sb 12284934 </p> <p>&gt;Beroe_abyssicola_sb 12126456 </p> <p>&gt;Beroe_sp_pink_sb 12870588 </p>   |
| ML030510a | <p>&gt;Bolinopsis_ashleyi_sb 12953705 </p> <p>&gt;Bolinopsis_infundibulum_sb 12247816 </p> <p>&gt;Bolinopsis_infundibulum_sb 12202816 </p>   |
| ML31983a  | <p>&gt;Bolinopsis_ashleyi_sb 12936299 </p>   |
| ML043317  | <p>&gt;P-bachei_GeneM_sb 11611576 </p> <p>&gt;Bolinopsis_infundibulum_sb 12203929</p> <p>&gt;GHXY01322137.1_1 TSA: Beroe forskalii isolate Bf201507<br/>CTE_B_forskalii.D785-D11.36135c9gli2 transcribed RNA sequence</p> <p>&gt;Beroe_sp_pink_sb 12908207 </p>  |
| ML056913a | <p>&gt;Pleur_sb 12812941 </p> <p>&gt;Pukia_falcata_sb 13012837 </p> <p>&gt;Dryodora_glandiformis_sb 290245 </p> <p>&gt;Bolinopsis_ashleyi_sb 12952707 </p> <p>&gt;GGLO01074549.1_2 TSA: Hormiphora californensis TR29740_c0_g1_i2<br/>transcribed RNA sequence</p> <p>&gt;GHXS01080954.1_1 TSA: Hormiphora californensis isolate<br/>20161213-T1 tx_DN13025_c0_g1_i1 transcribed RNA sequence</p> <p>&gt;GHXY01201788.1_2 TSA: Beroe forskalii isolate Bf201507<br/>CTE_B_forskalii.D785-D11.35563c0gli1 transcribed RNA sequence</p> <p>&gt;Beroe_abyssicola_sb 12126338 </p> <p>&gt;Beroe_sp_pink_sb 12885168 </p> |
| ML065755a | <p>&gt;Pleur_sb 12752694 </p> <p>&gt;Pukia_falcata_sb 13044247 </p> <p>&gt;Bolinopsis_infundibulum_sb 12202363 </p> <p>&gt;GHXY01305395.1 TSA: Beroe forskalii isolate Bf201507<br/>CTE_B_forskalii.D785-D11.26122c4gli3 transcribed RNA sequence</p> <p>&gt;GHXS01080165.1 TSA: Hormiphora californensis isolate 20161213-<br/>T1 tx_DN12392_c1_g1_i2 transcribed RNA sequence</p> <p>&gt;Beroe_sp_pink_sb 12842138 </p>  |
| ML066512a | <p>&gt;Bolinopsis_ashleyi_sb 12949501 </p>   |
| ML199816a | <p>&gt;Pleur_sb 12660689 </p> <p>&gt;Pukia_falcata_sb 13058854 </p> <p>&gt;Euplokamis_dunlapae_sb 10617555 </p> <p>&gt;Bolinopsis_infundibulum_sb 12214463 </p> <p>&gt;Bolinopsis_ashleyi_sb 12935571 </p> <p>&gt;GGLO01031268.1 TSA: Hormiphora californensis TR13199_c3_g1_i1<br/>transcribed RNA sequence</p> <p>&gt;Beroe_abyssicola_sb 12118498 </p> <p>&gt;Beroe_sp_pink_sb 12869105 </p>  |
| ML233326a | <p>&gt;Pleur_sb 12660472 </p> <p>&gt;Pukia_falcata_sb 13042259 </p> <p>&gt;Bolinopsis_infundibulum_sb 12225922 </p> <p>&gt;Bolinopsis_ashleyi_sb 12973892 </p> <p>&gt;GHXS01067440.1 TSA: Hormiphora californensis isolate 20161213-<br/>T1 tx_DN14248_c0_g1_i1 transcribed RNA sequence</p> <p>&gt;GHXY01353421.1 TSA: Beroe forskalii isolate Bf201507<br/>CTE_B_forskalii.D785-D11.23317c0gli1 transcribed RNA sequence</p> <p>&gt;Beroe_sp_pink_sb 12857913 </p>   |
| ML218923a | <p>&gt;P-bachei_GeneM_sb 11609489 </p> <p>&gt;Pukia_falcata_sb 13091370 </p> <p>&gt;GHXS01041156.1 TSA: Hormiphora californensis isolate 20161213-<br/>T1 tx_DN18013_c2_g5_i1 transcribed RNA sequence</p>   |

**Supplementary table 4. Summary of neuropeptide expression patterns and metacell annotation.**

The first match between a neuropeptide expression site and a metacell is highlighted in red; such matches correspond to specific expression in particular metacells and were key for the annotation of other metacells.

| Probe      | Localisation                          | Metacell                     |
|------------|---------------------------------------|------------------------------|
| ML065755a  | AO                                    | C29, C30                     |
| ML206415a  | AO                                    | C29, C30                     |
| ML14991a   | AO                                    | C28, C29, C32, C36, (C39)    |
| ML003517a  | AO                                    | C32, C36                     |
|            | AO rim                                | C27                          |
| ML07842a   | Pharyngeal neural net                 | C34                          |
|            | AO                                    | C40                          |
| ML43317a   | Sensory neurons gut/mouth             | C35                          |
| ML030510a, | Sensory neurons gut/mouth             | C35                          |
| ML030511a  | AO rim                                | C27                          |
| ML233326a  | Tentacles                             | C55                          |
| ML01798a   | Tentacles                             | C55                          |
| ML02212a   | Epithelial neural net                 | C33                          |
|            | Pharyngeal neural net                 | C34                          |
|            | Sensory neurons gut/mouth             | C35                          |
|            | AO                                    | C30                          |
|            | Tentacle bulb                         | C33                          |
| ML02736a   | Epithelial neural net                 | C33                          |
|            | Pharyngeal neural net                 | C34                          |
|            | Sensory neurons gut/mouth             | C35                          |
|            | AO                                    | C33, C40                     |
|            | Tentacle bulb                         | C33                          |
|            | Tentacles                             | ?                            |
| ML199816a  | Epithelial neural net                 | C33                          |
|            | Pharyngeal neural net                 | C34                          |
|            | Sensory neurons gut/mouth             | C35                          |
|            | Tentacle bulb                         | C33                          |
|            | Mesogleal neurons inside the tentacle | ?                            |
|            | AO                                    | C33, C28, C32, C36, C40      |
| ML056913a  | Epithelial neural net                 | C33                          |
|            | Pharyngeal neural net                 | C34                          |
|            | Sensory neurons gut/mouth             | C35                          |
|            | Tentacles                             | C55                          |
|            | AO                                    | C28, C29, C32, C36           |
| ML21545a   | Sensory neurons gut/mouth             | C35                          |
|            | AO                                    | C31                          |
| ML17711a   | AO                                    | C28, C29, C31, C32, C36, C40 |
|            | Epithelial neural net                 | C33                          |
|            | Pharyngeal neural net                 | C34                          |
|            | Sensory neurons gut/mouth             | C35                          |

**Supplementary table 5. ISH probes.**

| Gene      | Sequence  |
|-----------|---|
| ML00218a  | atgaagcttatcgtggtggttgcgtggtctctctggccctggccggaagtaagctgaagaagc<br>tgaagaacgagatggcagatctagaagacaagtttgctactgtgatgaatgacactagcagctc<br>tcttgaggaactccaagcagatgtggatggactcattaccgctttaaagcagtaaaaagaagct<br>caagctaagaaagacatcgacaaccagtggaagctctgcacatggcagctgctgctgctgca<br>gaggaagcaccaccacaaggaggcaagggaccctgggtccaactcggctcgttccctaaagaaaacgg<br>agtgaaatgcatgaccagtgacagccgtaacgacgacggaaggacactctgcaaggccgaggtc<br>tctctgaccgggtaccctgggaaagccacctctacacagagcgagtcggacacttctacaact<br>acgagtgtagcggaggtggaacgcccacatcactcacaacgaggttgccggtgaggaggacgc<br>tattcaggttactgggtactgcttactacaggttctgctggt   |
| ML016347a | tttgaatctcagggttacagctgtggttcttttgaattctacttgccggggtttgcccctgca<br>gcccgatatacagctactcaagaaaacgtagcttctctgaaaccgggagaagaaaaaggagagc<br>tggatattgaggcaccgaaaacgcaaaacttcgatattttaccaaaaacgatcagaagaagg<br>caaagatgaggaccctaaacttcaatatttctacaaaatcagatcactagaggacaaagagaag<br>aaaccctaaacttcgatacttctacaaaagcgagaagagaataaagatacgaaccctaaacttc<br>gacacttctacaaaagcgagaagagaataaagatacgaaccctaaacttcgatacttcttcca<br>aaaacgtgaagagaacaaagatacgaaccctaaacttcgatacttctacaaagagcgagaagat<br>aacaagatacgaaccctaaacttcgatacttcttcaaaaacgtgaagagaacaaagatacga<br>aaccctaaacttcgaaacttctaccgaaaacgaggagaaaact   |
| ML07842a  | gatgaaactaacggtagtttgctcctctctcgtagtttgctggtaggggctgaatgcccgggt<br>ggtgaaagacacgaggagcagctgtttgatgcccgaagatgaacagcccatttcagagctgggt<br>tagagaataaagaactcgagaaaagaagtcctaaactttagatttggatcaaaaaggctcagctga<br>agatgctccaaatctaagaggaaagaggtcaaacgaagatacccccaatttttagaggaaactaaa<br>agatctgcccaggatagcccccaatttttagaggagcaaaaagatccgcagtggaagcccccaatt<br>tttagaggagccccaaaatcagaagaagatgctcctcatttttagaggagctaaaagatttgctga<br>ggatgcccccatttaagaggagtaaaagagatccaccgtagatgcccccaatttttagaggagca<br>gaaagattagaagaagatgtccctaattttaagaggagcagaaagatccgaagaaggttccccca<br>attttagaggagcagaaagagcagttgaagatg  |
| ML21545a  | taagccgggatttaaccgaaggatgctcgaagttcctatttcttactttgctggtgggccc<br>cgctcgggctgcaagcttcgcttcggactctgacaacactcttgacagctcagacgagtg<br>tagaactggatacaacatgagatacagatctggagtgtaggagaaggagggcagccagggc<br>ggcagccaggttacagctccaggaggatggagagactgaaggaggggaggagctgactaa<br>gagatcggccgagagcagaaactggaattacagcgcgaagacgagaccgcgcaaaagatc<br>gaacaacgaggagcaggactttagtggttataggcgtggaagtggacaaaaaggctctgc<br>tgaagaggacgattacgacatttcaaaaagaggggaatcagaagagcaagactactccgg<br>ttatagaggaaagggggcgaggagagtagagataacaacaataaatttcttaactacacgt<br>gctgggatctcatcttaactacacgtgctggatgctgctctctagctacacgtactgga<br>tctcatcgctagctacacgtgctggatgctcatcgctaactacaagtgctgggatgctcat<br>cgctaactacacagtacacgtgct                                 |
| ML017711a | aacatttcaagactcacataacctcataaaagatgaagatgtttatattgattggattgct<br>tgatcacactgggttctcaactacgtatcagccggagatcttgctagaagatcgcttgagg<br>aggaaaacgagctctggaataaatgaaggagctgctgaggaagatgatgagctcttcaggg<br>gcctccgagaaaagcagggatgagagtaggggtaaaaggaggtcgcagatgaagagctgt<br>tcaggggcaagcagatctcagggaaaagagagatttcagaggaaaaagggacttcagag<br>gcaagagggaattttagaggcaagagagagttcaggggcaagagagatctccgaggaatga<br>agagcagtgagaagaattagtaaaagagagatctgagtagaggacagtagtaaggatagt<br>attagaagttgaagtgagattatcaggatacatgagctcatttaaagctcgacggttgaa<br>gttttataatgagatactggtaggacctgataatgtcctgagtagatgacataattttg<br>atattcaacagcttttttacttatttttagttatagttgggtgcagctccgtgcttttcc<br>gggatgtacatcatcgactcgtgatggcaacaaggccacacacttttgagagaggca |
| ML02212a  | ctatcaagctctccaaatctcaacatgaaactcttctgcttcttcttcttctgctggtggccct<br>gatcagctgcaaaactgtggagctggaagtgacagcgaacttagcgagagtgaaagattctaac<br>gcatgaggggtgaagcagagtaagttcagcatgagcaactacagaggacacaagcagggaaaca<br>gaggctggactggaggtgccatgcaggaggaggtaggttttatgaaggagcagccacctggg<br>gacgtcatggttacgtcacttagtgacgtcatcgttacgtcacctgaccggcgggaaggagga<br>ctctttacgaaggagcatgtcttaagtttttaacttattgttaggctaccctgggttgattgctg<br>tcttagctggacagattttatcaagctcttactctctcaagatgatttttagggattgtcaata<br>ctttattgcaataatctggacaaatttccaatctagctaattaacatccttcattataaatcca<br>tcacaaaatgtcttcagatt  |

|           |   |
|-----------|---|
| ML02736a  | <p>taagagacagaaagttccagtaactttccgagacgaacgaagagaaaaccatgaagtgttctggt<br/> gtgtgtgttggccctcctcgcctatctcagtcagcctcactcaactccctagaatcagtagaag<br/> atgtgataatggctgataacgacaacggttgaactggaagaaggtgccctgaacgctgaggagga<br/> agcccgagtttacaaggctacaacgggaggttaaccgagctcggtagcgaataagaagacagacaa<br/> ccaacaaggacaagactcaccatgacaacaatcactatggcaacgctcaccatggtaacgctcacc<br/> atggcaacgctcaccatggtgacctcatcatggtgccgtgaaatcttgtcgacatggcatcacct<br/> tggttacatcttctgtcttcccatcaccacctcagcagcagatactgcactcgtgagcttgtccat<br/> tttgtcaccggtgttttgtgatttaagaacccggacagtttccacggttacatgatgagttaatc<br/> cattttgaatcttgttacogttaaactgtttctgtaattatattacaattaatttaaggat<br/> tgtgtcactgttattctcgaataataagacaagaaggtg</p> |
| ML056913a | <p>tccatcctccttgtcctcgtcctcgcctcgtgactttcaccagaacaattgaagattctgaag<br/> aaatcggacatggactaaggatggataagaacgaggagattggacacggtctgactttagacaa<br/> acgaagtgcagacagcgtggacacggaggcaatggctgacgaagaagaactggttggctcaccgga<br/> atcaaaggatcccatgctggtggaggaagtaaggactgttacggttggtagcgtcacccaacatca<br/> ccatgacgctcactgggtgttggccatgctggttggcgtggtaacgcatgtcctgcaaccttacc<br/> attgactttaacaacacgggtcttaaaaagtatgtttggcagcagctgaggatcgttatttaga<br/> ttgacaattcttagcaaattttaattagtttagcactcagatgttcatatttggaggggtctttgc<br/> agagaggataatatttattggatgctgattcctaagttcaaaatacagttaagattgggtatgctctt<br/> a</p>  |
| ML199816a | <p>tttatagtttgacattcgtatcogatattaattogaacaacaacaaaatgaagctgttctcttt<br/> ctgaccgctctctgctcgtgctcgtactgttactgtccagacagaggctagagaaatagtcg<br/> cggaggtagccgagtcggaagcagtgaggctcggcagcaagtgaagaagacactttcgtgtacag<br/> aaaagaggaggactccgctttctgtttgctgacttaattctcacatctgctagagcaacgctcag<br/> gttccactgagagagagacgacgagacagagagataggtctctatttgagacaagcctcttttt<br/> gggacaagcctctttttgagacaagcctctttttgagggcaggtctctttttgagattaagtctc<br/> gctatgaaagccggtactggaaaggactgtgtgcttgcacttttcatttaatcgcattgggcag<br/> tcaattcgcattgaaatgatacagatacttt</p>   |
| ML233326a | <p>aggagctttacagctacacacacaatgaagacccttcttgttctgaccttatgattat<br/> ctgctgtaactacgtgcagctctgtaccaatgagcttgaagaggatctcagcagatgaagagcac<br/> cgtggtctacagaagcagcgggacccaagtttaacaaggctgactacaaatcagtcggagaag<br/> gcaocaggaaatgggtcggataatctgcctacctcaoctcttttatcagcctcggcgtcagc<br/> gtcagaataacctaaactttaaaacagaaatgaagagcagctttaggactacgcttttaaaa<br/> aagacaaaactgtatcatttttaagttcgtgttgatccatgtggcttgctatttaaatttttac<br/> gaaatattgaaaatcgcctcgttcaaatgactatttttaagtaattaacagcaaaaatacttgg<br/> tacgtcttcaagaagt</p>   |
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| ML01798a  | <p>atgaagctcctactcctaaccctggcagttctcctggcctgcttgactgcagtgctcagac<br/> aagaggaggtcccacaagaagagatccgattagaaagatcagctgagagttccggaggagagac<br/> agcagaggtggaaaaaagagccgcaatcgatactggttctgattatcccggattcaggggcgga<br/> aaacggaggtggtagcgttaagaagttctgttcttcttcttagtgacgtcctttcctaaagagtg<br/> ccaacgacctcaccgctgatcttctcgaagtatcctcagatcctcgtgattggagcgcaga<br/> cttgggtgaaatcagactttattgttcaaatgataatcaggcgtcttttatagttgtttatctt<br/> ccatttgcaattgggtggctctataatagttattgcaaacatacaattctgattgaaatcttatg<br/> catatgttaaaaatacccgatgttgcctaactaccttaatcagatttaaggagcatctttgatc<br/> taagattc</p>   |
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*Supplementary tables 6-9. Provided as separate Excel sheets.*