Additional file #1 for:

Research Article

Functional evolution of ADAMTS genes: Evidence from analyses of phylogeny and gene organization

Ainsley C. Nicholson[1,3]*, Shehre-Banoo Malik[2]*, John M. Logsdon Jr.[2] and Erwin G. Van Meir[1]§

[1]Laboratory of Molecular Neuro-Oncology, Winship Cancer Institute, 1365-C Clifton Road, Room C5078, Emory University, Atlanta GA 30322 USA. Phone: 404-778-5563, Fax: 404-778-5240.
[2]Roy J. Carver Center for Comparative Genomics, Department of Biological Sciences, 300 Old Biology Building, University of Iowa, Iowa City IA 52242-1324 USA. Phone: 319-335-1083, Fax: 319-335-1069
[3]Present address: Viral Exanthems and Herpesvirus Branch, Centers for Disease Control and Prevention, 1600 Clifton Rd, Mailstop A14, Atlanta, GA 30333 USA.

* These authors contributed equally to this work

§ Corresponding author

Email addresses:
  ACN: agn0@cdc.gov
  SBM: banoo-malik@uiowa.edu
  JML: john-logsdon@uiowa.edu
  EGVM: evanmei@emory.edu

Additional File 1 – **(NMLVadamtsalign1.pdf) Alignment used for phylogenetic analyses of human ADAMTS proteins and invertebrate homologs .** Unambiguously aligned amino acid sites, indicated by the "mask" line in the alignment, were used for phylogenetic analyses (figure 1). Intron positions in the corresponding genomic sequence are indicated, with color-coding for intron phases (table 1 and figure 3).

AC Nicholson, SB Malik, JM Logsdon Jr, E van Meir, 2004. Functional evolution of ADAMTS genes: evidence]
[from analyses of phylogeny and gene organization. Contact: john-logsdon@uiowa.edu]
[Intron phases marked 0, 1, 2]

1

```
#NEXUS
[AC Nicholson, SB Malik, JM Logsdon Jr, E van Meir, 2004. Functional evolution of ADAMTS genes:]
[evidence from analyses of phylogeny and gene organization. Contact: john-logsdon@uiowa.edu]
[Intron phases marked 0, 1, 2]
BEGIN DATA;
        DIMENSIONS  NTAX=23 NCHAR=2611;
        FORMAT DATATYPE=PROTEIN  SYMBOLS = " 1 2 3 4"  MISSING=? GAP=-  INTERLEAVE ;
MATRIX
[                   10        20        30        40        50        60]
[                    .         .         .         .         .         .]
ADAMTS6     --------------------MEILWKTL-TWILSLIMAS--------------------S  [19]
ADAMTS10    --------------------MAPACQIL-RWALALGLG--------------------L  [18]
ADAMTS18    --------MECALLLACAFPAAGSGPPRGLAGLGRVAKA------LQLCCLCCASVAAAL  [46]
ADAMTS16    -------------MKPRARGWRGLAALW-MLLAQVAEQAPACAM-GPAAAAPGSPSVPRP  [45]
ADAMTS7     --------------------MPGGPSPR-SPAPLLRPLLLLLCA-LAPG-----------  [27]
ADAMTS12    --------------------MPCAQRSW-LANLSVVAQLLNFGA-LCYG-----------  [27]
ADAMTS17    --------------------------------------------MCDGALLPPLVLP  [13]
ADAMTS19    MRLTHICCCCLLYQLGFLSNGIVSELQFAPDREEWEVVFPALWRREPVDPAGGSGGSADP  [60]
ADAMTS2     ------------MDPPAGAARRLLCPAL-LLLLLLLPPPLLPPP-PP----------PAN  [36]
ADAMTS3     ---------------------MVLLS-LWLIAAALVEVRTSA-DG-------------  [22]
ADAMTS14    -----------------------MAP-LRALLSYLLPLHCAL-CA-------------  [20]
ADAMTS13    ---------------------------------------------------------  [0]
dCG4096     -----------------------MWIR-SRWLGLLLHYWLVVV-TQGGGVRPLYGLHSD  [34]
ADAMTS4     --------------------MSQTGSHPG-RGLAGRWLWGAQPCL-LLP-----------I  [28]
ADAMTS5     ---------------MLLGWASLLLCA-FRLPLAAVGPAATPA-QDK-----------A  [31]
ADAMTS8     ----------------------------------MFPAPAAP----------------  [8]
ADAMTS1     -----------------MQRAVPEGFG-RRKLGSDMGNAERAP-GS-------------  [27]
ADAMTS15    ---------------------------------------------------------  [0]
dCG6107     -------------------------MPDGAANLHAVAHNLRSKRCANRIPHFSLSIFQ  [33]
ADAMTS9     --------------MQFVSWATLLTLL-VRDLAEMGSPDAAAA-VRKDR---------  [33]
ADAMTS20    --------------------------MRNAWELTGPVAVVA-EA-------------  [17]
mask        ---------------------------------------------------------  [0]
gon-1       --------------------------------------MRS-IGGSFHLLQPVVAAL  [18]
[Intron                            1         2                          ]

[                   70        80        90       100       110       120]
[                    .         .         .         .         .         .]
ADAMTS6     EFHSDHRLSYSSQEEFLTYLEHYQLTIPIRVDQNGAFLSFTVKN---DKHSRRRRSMDPI  [76]
ADAMTS10    MFEVTH--AFRSQDEFLSSLESYEIAFPTRVDHNGALLAFSPPP---PRRQRRG------  [67]
ADAMTS18    ASDSSSGASGLNDDYVFVTPVEVDSAGSYISHDILH--------NGRKKRS-------  [89]
ADAMTS16    PPPAERPGWMEKGEYDLVSAYEVDHRGDYVSHEIMH-----------HQRRRRAV-----  [89]
ADAMTS7     -------APGPAPGRATEGRAALDIVHPVRVDAGGSFLSYELWP---RALRKRD------  [71]
ADAMTS12    -------RQPQPGPVRFPDRRQEHFIKGLPEYHVVGPVRVDASGHFLSYGLHYPITSSRR  [80]
ADAMTS17    VLLLLVWGLDPGTAVGDAAADVEVVLPWRVRPDDVHLPPLPAAPGPRRRRRPRTPPAAPR  [73]
ADAMTS19    GWVRGVGGGGSARAQAAGSSREVRSVAPVPLEEPVEGRSESRLRPPPPPSEGEEDEELES  [120]
ADAMTS2     ARLAAAADPPG---GPLGHGAERILAVPVRTDAQGRLVSHVVSAATSRAGVRARRAAP--  [91]
ADAMTS3     QAGNEEMVQID---LPIKRYREYELVTPVSTNLEGRYLSHTLSASHKKRSARDVSSNP--  [77]
ADAMTS14    ---AAGSRTPE---LHLSGKLSDYGVTVPCSTDFRGRFLSHVVSGPAAASAGSMVVDTPP  [74]
ADAMTS13    ---------------------------------------------------------  [0]
dCG4096     ELVAGEGQLVVPRRVHPDGAFMTHQLEYAHE---------LDHRRHRQRRSLNSEHDTQA  [85]
ADAMTS4     VPLSWLVWLLLLLLASLLPSARLASPLPREEEIVFPEKLNGSV--------LPG------  [74]
ADAMTS5     GQPPTAAAAAQPRRRQGEEVQERAEPPGHPHPLAQRRRSKGLVQN-----IDQL------  [80]
ADAMTS8     RWLPFLLLLLLLLPLARGAPARPAAGGQASELVVPTRLP-------------------  [48]
ADAMTS1     RSFGPVPTLLLLAAALLAVSDALGRPSEEDEELVVPELER----------APG-----  [70]
ADAMTS15    --------MLLLGILTLAFAGRTAGGSEPEREVVVPIRLDPDINGRRYYWRGPE------  [46]
dCG6107     LEVKKRCEWWCHKYIQKMSTHWRQNACLYACCIAFLLGMLIMFHLGLRSAHKGQEELPQS  [93]
ADAMTS9     --------LHPRQVKLLETLGEYEIVSPIRVNALGEPFPTNVHFKRTRRSINSATDPWPA  [85]
ADAMTS20    ----LVRTLTSYEVVIPERVNEFGEVFPQSHHFSRQKRSS-EALEPMP-----------  [60]
mask        ---------------------------------------------------------  [0]
Ce gon-1    ILLVVCLVYALQSGSGTISEFSSDVLFSRAKYSG---VPVHHSRWRQDAGIHVIDSHHIV  [75]
[Intron                   3                   4                          ]
```

AC Nicholson, SB Malik, JM Logsdon Jr, E van Meir, 2004. Functional evolution of ADAMTS genes: evidence]
[from analyses of phylogeny and gene organization. Contact: john-logsdon@uiowa.edu]
[Intron phases marked 0, 1, 2]

```
[                    130       140       150       160       170       180]
[                      .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                 L]
ADAMTS6     ---------------------------------DPQQAVSKLFFKLSAYGKHFHLNL   [100]
ADAMTS10    --------------------------------TGATAESRLFYKVASPSTHFLLNL    [91]
ADAMTS18    --------------------------------AQNARSSLHYRFSAFGQELHLEL    [112]
ADAMTS16    --------------------------------AVSEVESLHLRLKGPRHDFHMDL    [112]
ADAMTS7     -------------------------------VSVRRDAPAFYELQYRGRELRFNL     [95]
ADAMTS12    KRD------------------------------LDGS-EDWVYYRISHEEKDLFFNL   [106]
ADAMTS17    A-RPG--------------------------------ERALLLHLPAFGRDLYLQL    [96]
ADAMTS19    QELPRGSSGAAALSPGAPASWQPPPPPQPPSPPPAQHAEPDGDEVLLRIPAFSRDLYLLL [180]
ADAMTS2     ---------------------VRTPSFPGGN--E-EEPGSHLFYNVTVFGRDLHLRL   [124]
ADAMTS3     --------------------------------------EQLFFNITAFGKDFHLRL    [95]
ADAMTS14    T-LPRHS-----------SHLRVARSPLHPGGTLWPGRVGRHSLYFNVTVFGKELHLRL  [121]
ADAMTS13    -----------------------------------------------MHQRHPRA      [8]
dCG4096     A-DLHLL-------------------------------------LPLANETLHLEL    [103]
ADAMTS4     -------------------------------SGAPAR-LLCRLQAFGETLLLEL     [96]
ADAMTS5     -------------------------------YSGGGK-VGYLVYAGGRRFLLDL    [102]
ADAMTS8     ------------------------------GSAGE-LALHLSAFGKGFVLRL     [69]
ADAMTS1     -----------------------------HGTTR----LRLHAFDQQLDLEL     [89]
ADAMTS15    -----------------------------DSGQG-LIFQITAFQEDFYLHL     [68]
dCG6107     THPLANSPPATPATLHPRRLDNDTSTDHEPPDGLDDLDEEEHSAFVMPTKVYNYSLSEAD [153]
ADAMTS9     F-ASSS-------------------------SSSTSSQAHYRLSAFGQQFLFNL     [113]
ADAMTS20    ------------------------------------FR--THYRFTAYGQLFQLNL    [78]
mask        ------------------------------------------------------------ [0]
Ce gon-1    RRDSYGR--------------------RGKRDVTSTDRRRRLQGVARDCGHACHLRL   [112]

[                    190       200       210       220       230       240]
[                      .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                   ]
ADAMTS6     TLNTDFVSKHFTVEYW-------------------------------------------  [116]
ADAMTS10    TRSSRLLAGHVSVEYW-------------------------------------------  [107]
ADAMTS18    KP-SAILSSHFIVQVL-------------------------------------------  [127]
ADAMTS16    RTSSSLVAPGFIVQTL-------------------------------------------  [128]
ADAMTS7     TANQHLLAPGFVSETR-------------------------------------------  [111]
ADAMTS12    TVNQGFLSNSYIMEKR-------------------------------------------  [122]
ADAMTS17    RRDLRFLSRGFEVEE--------------------------------------------  [111]
ADAMTS19    RRDGRFLAPRFAVEQRPNPGPGPT----------------------------------  [204]
ADAMTS2     RPNARLVAPGATMEWQG--------E--------------------------------  [142]
ADAMTS3     KPNTQLVAPGAVVEWHETSLVPGNITDPINNHQ-------------------------  [128]
ADAMTS14    RPNRRLVVPGSSVEWQE--------D--------------------------------  [139]
ADAMTS13    RCPPLCVAGILACGFLLGCW--------------------------------------   [28]
dCG4096     MAHSYFLAPNLVVERHRRDLRTRSPLTTRHL---------------------------  [134]
ADAMTS4     EQDSGVQVEGLTVQYLG-----------------------------------------  [113]
ADAMTS5     ERDGSVGIAGFVPAGGG-----------------------------------------  [119]
ADAMTS8     APDDSFLAPEFKIERLG-----------------------------------------   [86]
ADAMTS1     RPDSSFLAPGFTLQNVGRK---------------------------------------  [108]
ADAMTS15    TPDAQFLAPAFSTEHLG-V---------------------------------------   [86]
dCG6107     LIYESKRNSDINSFLKESASAFAMTGTYRNMSNEIWDPHPQYNLNVFGRQLHLVLRQDAS [213]
ADAMTS9     TANAGFIAPLFTVTLLGTPGV-------------------------------------  [134]
ADAMTS20    TADASFLAAGYTEVHLGTP---------------------------------------   [97]
mask        ------------------------------------------------------------ [0]
gon-1       RSDDAVYIVHLHRWNQIPDSHNKSVPHFSNSNFAPMVLYLDSE---------------  [155]
[Intron                        5         6                                ]
```

3

```
[              250       260       270       280       290      300]
[            .         .         .         .         .         .]
[Modal, ≥80%, full maj.                   C    G                    G ]
ADAMTS6     ------------------GKDGPQWKH--DFLDNCHYTGYLQDQRSTT-KVALSNCVG-   [153]
ADAMTS10    ------------------TREGLAWQR--AARPHCLYAGHLQGQASSS-HVAISTCGG-   [144]
ADAMTS18    ------------------GKDGASETQ-KPEVQQCFYQGFIRNDSSSS--VAVSTCAG-   [164]
ADAMTS16    ------------------GKTGTKSVQTLPPEDFCFYQGSLRSHRNSS--VALSTCQG-   [166]
ADAMTS7     ------------------RRGGLGRAHIRAHTPACHLLGEVQDPELEGGLAAISACDG-   [151]
ADAMTS12    ------------------YGNLSHVKMMASSAPLCHLSGTVLQQGTRVGTAALSACHG-   [162]
ADAMTS17    -----------------AGAARRGRPAELCFYSGRVLGHPGSL--VSLSACGAA-       [147]
ADAMTS19    ------------------GAASAPQPPAPPDAGCFYTGAVLRHPGSL--ASFSTCG G-   [241]
ADAMTS2     -----------------KGTTRVEPLLGSCLYVGDVAGLAEASS-VALSNCDG-        [177]
ADAMTS3     -----------------PGSATYRIRKTEPLQTNCAYVGDIVDIPGTS--VAISNCDG-   [167]
ADAMTS14    -----------------FRELFRQPLRQECVYTGGVTGMPGAA--VAISNCDG-        [173]
ADAMTS13    ------------------------GPSHFQQSCLQALEPQ--------AVSS-----     [48]
dCG4096     ----------------NCHFHGKVRGQPATNVAISTCAGLVSCPNFC-VLPELITLCQ-   [175]
ADAMTS4     ----------------------QAPELLGGAEPGTYLTGTINGDPESV--ASLHWDGGA   [148]
ADAMTS5     ----------------------TSAPWRHRSHCFYRGTVDASPRSL--AVFDLCGGL     [152]
ADAMTS8     -------------------GSGRATGGERGLRGCFFSGTVNGEPESL--AAVSLCRG-    [122]
ADAMTS1     -------------------SGSETPLPETDLAHCFYSGTVNGDPSSA--AALSLCEG-    [144]
ADAMTS15    ------------------PLQGLTGGSSDLRRCFYSGDVNAEPDSF--AAVSLCGG-     [122]
dCG6107     F-VHNHSMTHIRILKEGEEHPGPETEAEAEQRHLGCFYSGYVEDDPHSM--VSVSLCGG-  [269]
ADAMTS9     -------------------NQTKFYSEE-EAELKHCFYKGYVNTNSEHT--AVISLCSG-  [171]
ADAMTS20    ------------------ERGAWESDAGPSDLRHCFYRGQVNSQEDYK--AVVSLCGG-   [135]
mask        --------------------------------1 11111 1111-------1111-----   [13]
Ce gon-1    --------------------EEVRGGMSRTDPDCIYRAHVKGVHQHSIVNLCDSEDG-    [192]
[Intron                                     7                           ]
[                                 Prodomain                          ]

[              310       320       330       340       350      360]
[            .         .         .         .         .         .]
[≥80%, full maj.G          P              H                       ]
ADAMTS6     --LHGVIATEDEEYFIEPLKN-TTEDSKHFSYENG-HPHVIYKKSALQQRHLYDHSHCGV   [209]
ADAMTS10    --LHGLIVADEEEYLIEPLHG--GPKGSR-SPEE-SGPHVVYKRSSLRHPHLDTACGVRD   [198]
ADAMTS18    --LSGLIRTRKNEFLISPLPQL-LAQEHNYSSPAGHHPHVLYKRTAEEKIQRYRGYPGSG   [221]
ADAMTS16    --LSGMIRTEEADYFLRPLPSH-LSWKLGRAAQGSSPSHVLYKRSTEPHAPGASEVLVTS   [223]
ADAMTS7     --LKGVFQLSNEDYFIEPLDS--APARPG-----HAQPHVVYKRQAPERLAQRGDSSAPS   [202]
ADAMTS12    --LTGFFQLPHGDFFIEPVKK--HPLVEG-----GYHPHIVYRQKVPETKEPTCGLKD-   [212]
ADAMTS17    GGLVGLIQLGQEQVLIQPLNN--SQGPFS-----G-REHLIRRKWSLTPSPSAEAQRPEQ   [199]
ADAMTS19    -GLMGFIQLNEDFIFIEPLND--------TMAITG-HPHRVYRQKRSMEEKVTEKSALHS   [291]
ADAMTS2     --LAGLIRMEEEEFFIEPLEK--GLAAQEAEQ--G-RVHVVYRRPPTSPPLGGPQALDTG   [230]
ADAMTS3     --LAGMIKSDNEEYFIEPLER--GKQMEEE-K--G-RIHVVYKRSAVEQAPI--------   [211]
ADAMTS14    --LAGLIRTDSTDFFIEPLER--GQQEKEA-S--G-RTHVVYRREAVQQEWAEPDGDLHN   [225]
ADAMTS13    -----------YLSPGAPLK-------------GFRPPSPGFQRQRQ-------------   [70]
dCG4096     ---VGHIRTAGNEYFIEPSKEHEPHP------VNG-HPHVVFQRSSVKPKHSLRKRNKRK   [225]
ADAMTS4     --LLGVLQYRGAELHLQPLEGGTPNSAGGP------GAHILRRKSP--------------  [186]
ADAMTS5     DGFFAVKHARYTLKPLLRGPWAEEEKGRVYGDGSARILHVYTREGFSFEALPPRASCE--  [210]
ADAMTS8     --LSGSFLLDGEEFTIQPQGA--GGSLA--------QPHRLQRWGPAGARPLPR------  [164]
ADAMTS1     --VRGAFYLLGEAYFIQPLPAASERLATAAPGEKPPAPLQFHLLRRNRQGDVGG--TCGV  [200]
ADAMTS15    --LRGAFGYRGAEYVISPLPN--ASA--PAAQRNSQGAHLLQRRGVPG-----------  [164]
dCG6107     --MTGYIKTSFGALLIQPVNR--TSSDE-------VLHRVFRKSQRNARHAVSKFEL--   [315]
ADAMTS9     --MLGTFRSHDGDYFIEPLQS--MDEQEDEEEQN--KPHIIYRRSAPQREPSTGR-----  [220]
ADAMTS20    --LTGTFKGQNGEYFLEPIMK--ADGNEYED--GHNKPHLIYRQDLNNSFLQT-------  [182]
mask        -----------11111111------------------111111111-----------   [30]
Ce gon-1    --LYGMLALPSGIHTVEPIIS--GNGTEHD----GASRHRQHLVRKFDPMHFKSF-----  [239]
[Intron          8                       9    10          11          ]
```

AC Nicholson, SB Malik, JM Logsdon Jr, E van Meir, 2004. Functional evolution of ADAMTS genes: evidence
[from analyses of phylogeny and gene organization. Contact: john-logsdon@uiowa.edu]
[Intron phases marked 0, 1, 2]

4

```
[              370       380       390       400       410       420]
[               .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                                    ]
ADAMTS6     SD-----------------------------------FTRSGKPWWLNDTSTVSYSLP  [232]
ADAMTS10    -----------------------------------EKPWKGRPWWLRTLKPPPARP  [219]
ADAMTS18    RNYPGYSPSHIPHASQSRETEYHHRRLQKQHFCGRRKKYAPKPPTEDTYLRFDEYGS---  [278]
ADAMTS16    R-------TWELAHQPLHSSDLRLGLPQKQHFCGRRKKYMPQPPKEDLFILPDEYKS---  [273]
ADAMTS7     TCGVQV-----------------------------YPELESRR----ERWEQRQQW  [225]
ADAMTS12    -----------------------------------SVNISQKQELWREKWERHNLP  [233]
ADAMTS17    LCKVLT-----E------------------------KKKPTW--------GRPSRDW  [219]
ADAMTS19    HYCGIISD-----------------------------KGRPRSRKIA----------  [309]
ADAMTS2     -----------------------------------ASLDSLDSLSRALGVLEEHAN  [251]
ADAMTS3     --DMSKDFHYRE-------------------------SDLEGLDDLGTVYGNIHQQLN  [242]
ADAMTS14    EA-----------------------------------FGLGDLPNLLGLVGDQLG---  [245]
ADAMTS13    --------------------------------------------------------  [70]
dCG4096     RGGKSGSGAEVSNCGTREPRRRMETRLEWQARGKVKVQGGRQIRRHHHHHHHHHHKHKYR  [285]
ADAMTS4     -----------------------------ASGQGPMCN----VKAP----LGSPS--P  [205]
ADAMTS5     -TPAS-TPEAHEHAPAHSNP-------SGRAALASQL-----LDQSALSPAGGSGP-QTW  [255]
ADAMTS8     -----GP-EWEVETGEGQRQER-------GDHQEDSEEE----SQEEEAEGASEPPPPLG  [207]
ADAMTS1     VDDEPRP-TGKAETEDEDEGTE--------GEDEGPQWS-----PQDPALQGVGQPTG-L  [245]
ADAMTS15    -----GP-SGDPTSRCGVASGW--------NPAILRALD-----PYKPRRAGFGESRSRR  [205]
dCG6107     ---GLDDFMSKLEQVQEEEQKSKSRKLN------------------------------  [340]
ADAMTS9     ------------------------------HACDTSEHKNRHSKDKKKTRARKWGERI  [248]
ADAMTS20    ------------------------------LKYCSVSESQIKETSLPFHTYSNMNEDLN  [211]
mask        --------------------------------------------------------  [30]
Ce gon-1    -----------DHLNSTSVNETETTVATWQDQWEDVIERKA------------------  [269]
[Intron                                         12               13]


[              430       440       450       460       470       480]
[               .         .         .         .         .         .]
[Modal, ≥80%, full maj.                   R   R          E L   D]
ADAMTS6     INNTHI--HH-----------------------RQKR-----SVSIERFVETLVVAD  [259]
ADAMTS10    LGNETE--RGQP---------------------GLKR------SVSRERYVETLVVAD  [248]
ADAMTS18    -SG------------------------------RPRRSAG---KSQKGLNVETLVVAD  [302]
ADAMTS16    -CL------------------------------RHKRSLLRS-HRNEELNVETLVVVD  [299]
ADAMTS7     RRP------------------------------RLRRLHQR--SVSKEKWVETLVVAD  [251]
ADAMTS12    SRS------------------------------LSRR------SISKERWVETLVVAD  [255]
ADAMTS17    ---------------------------------RERRNAI---RLTSEHTVETLVVAD  [241]
ADAMTS19    ------------------------------ESGRGKRYSY---KLPQEYNIETVVVAD  [334]
ADAMTS2     SS-------------------------------RRRARRH---AADDDYNIEVLLGVD  [275]
ADAMTS3     ETM------------------------------RRRRH-----AGENDYNIEVLLGVD  [265]
ADAMTS14    DTE------------------------------RKRRH-----AKPGSYSIEVLLVVD  [268]
ADAMTS13    ---------------------------------RQRR------AAGGILHLELLVAVG  [89]
dCG4096     HHQQKISRVPHTKFKYETQFQTE-----PDHAEIPRRRR------SISSPRHVETLIVAD  [334]
ADAMTS4     RPR------------------------------RAKR------FASLSRFVETLVVAD  [227]
ADAMTS5     WR-------------------------------RRRR------SISRARQVELLLVAD  [276]
ADAMTS8     ATS------------------------------RTKR------FVSEARFVETLLVAD  [229]
ADAMTS1     GSI------------------------------RKKR------FVSSHRYVETMLVAD  [267]
ADAMTS15    RSG------------------------------RAKR------FVSIPRYVETLVVAD  [227]
dCG6107     ---------------------------------RKKR--HYADVDNQVYTLEVLIAVD  [363]
ADAMTS9     NLAGDVAALNSGLATEAFSAYGNKTDNTREKRTHRRTKR------FLSYPRFVEVLVVAD  [302]
ADAMTS20    VMKERVLGHTSKNV-----------PLKDERRHSRKKR------LISYPRYIEIMVTAD  [253]
mask        ---------------------------------1111-----111111111111111  [49]
Ce gon-1    ---------------------------------RSRR-----AANSWDHYVEVLVVAD  [289]
[Intron                                          ▲ 14                          ]
[                             furin prodomain cleavage motif                   ]
```

```
[                    490       500       510       520       530       540]
[              .         .         .         .         .         .]
[≥80%, full maj. HG      Y LT          S                             ]
ADAMTS6    KMMVGYHGRKDIEHYILSVMNIVAKLYRDSSLGNVVNIIVARLIVLTEDQPNLE-INH-H [317]
ADAMTS10   KMMVAYHGRRDVEQYVLAIMNIVAKLFQDSSLGSTVNILVTRLILLTEDQPTLE-ITH-H [306]
ADAMTS18   KKMVEKHGKGNVTTYILTVMNMVSGLFKDGTIGSDINVVVVSLILLEQEPGGLL-INH-H [360]
ADAMTS16   KKMMQNHGHENITTYVLTILNMVSALFKDGTIGGNINIAIVGLILLEDEQPGLV-ISH-H [357]
ADAMTS7    AKMVEYHGQPQVESYVLTIMNMVAGLFHDPSIGNPIHITIVRLVLLEDEEEDLK-ITH-H [309]
ADAMTS12   TKMIEYHGSENVESYVLTIMNMVTGLFHNPSIGNAIHIVVVRLILLEEEEQGLK-IVH-H [313]
ADAMTS17   ADMVQYHGAEAAQRFILTVMNMVYNMFQHQSLGIKINIQVTKLVLLRQRPAKLS-IGH-H [299]
ADAMTS19   PAMVSYHGADAARRFILTILNMVFNLFQHKSLGVQVNLRVIKLILLHETPPELY-IGH-H [392]
ADAMTS2    DSVVQFHGKEHVQKYLLTLMNIVNEIYHDESLGAHINVVLVRIILLSYGKSMSL-IEIGN [334]
ADAMTS3    DSVVRFHGKEHVQNYLLTLMNIVNEIYHDESLGVHINVVLVRMIMLGYAKSISL-IERGN [324]
ADAMTS14   DSVVRFHGKEHVQNYVLTLMNIVDEIYHDESLGVHINIALVRLIMVGYRQSLSL-IERGN [327]
ADAMTS13   PDVFQAHQE-DTERYVLTNLNIGAELLRDPSLGAQFRVHLVKMVILTEPEGAPN-ITA-N [146]
dCG4096    ATMSAFHR--DLNGYLLTIMNMVSALYKDPSIGNSIEIVVVRIIQLDEEESQLQLNLTQN [392]
ADAMTS4    DKMAAFHGA-GLKRYLLTVMAAAAKAFKHPSIRNPVSLVVTRLVILGSGEEGPQ-VGP-S [284]
ADAMTS5    ASMARLYGR-GLQHYLLTLASIANRLYSHASIENHIRLAVVKVVVLGDKDKSLE-VSK-N [333]
ADAMTS8    ASMAAFYGA-DLQNHILTLMSVAARIYKHPSIKNSINLMVVKVLIVEDEKWGPE-VSD-N [286]
ADAMTS1    QSMAEFHGS-GLKHYLLTLFSVAARLYKHPSIRNSVSLVVVKILVIHDEQKGPE-VTS-N [324]
ADAMTS15   ESMVKFHGA-DLEHYLLTLLATAARLYRHPSILNPINIVVVKVLLLRDRDSGPK-VTG-N [284]
dCG6107    NSMKQFHGE-DLQPYILILMSIVSSIFADASIGNSIRILLVRLISLPNIN-----DQTHS [417]
ADAMTS9    NRMVSYHGE-NLQHYILTLMSIVASIYKDPSIGNLINIVIVNLIVIHNEQDGPS-ISF-N [359]
ADAMTS20   AKVVSAHGS-NLQNYILTLMSIVATIYKDPSIGNLIHIVVVKLVMIHREEEGPV-INF-D [310]
mask       11111111--111111111111111111111111111111111111-----------1 [96]
Ce gon-1   TKMYEYHGR-SLEDYVLTLFSTVASIYRHQSLRASINVVVVKLIVLKTENAGPR-ITQ-N [346]
[Intron              15        16                          17          ]


[                    550       560       570       580       590       600]
[              .         .         .         .         .         .]
[≥80%, full maj.L    C W                   D A    TR D               ]
ADAMTS6    ADKSLDSFCKWQKSILSHQSDGNTIPENG----IAHHDNAVLITRYDICTYKNKP-CGTL [372]
ADAMTS10   AGKSLDSFCKWQKSIVNHSGHGNAIPENG----VANHDTAVLITRYDICIYKNKP-CGTL [361]
ADAMTS18   ADQSLNSFCQWQSALIGKNG--------------KRHDHAILLTGFDICSWKNEP-CDTL [405]
ADAMTS16   ADHTLSSFCQWQSGLMGKDG--------------TRHDHAILLTGLDICSWKNEP-CDTL [402]
ADAMTS7    ADNTLKSFCKWQKSINMKGDAHP-----------LHHDTAILLTRKDLCAAMNRP-CETL [357]
ADAMTS12   AEKTLSSFCKWQKSINPKSDLNP-----------VHHDVAVLLTRKDICAGFNRP-CETL [361]
ADAMTS17   GERSLESFCHWQNEEYGGARYLGNNQVPGGKDDPPLVDAAVFVTRTDFCVHKDEP-CDTV [358]
ADAMTS19   GEKMLESFCKWQHEEFGKKNDIHLEMSTNWGEDMTSVDAAILITRKDFCVHKDEP-CDTV [451]
ADAMTS2    PSQSLENVCRWAYLQQKPDTGHD-----------EYHDHAIFLTRQDFGP------SGMQ [377]
ADAMTS3    PSRSLENVCRWASQQQRSDLNHS-----------EHHDHAIFLTRQDFGP------AGMQ [367]
ADAMTS14   PSRSLEQVCRWAHSQQRQDPSHA-----------EHHDHVVFLTRQDFGP------SGMQ [370]
ADAMTS13   LTSSLLSVCGWSQTINPEDDTDP-----------GHADLVLYITRFDLELPDGN--RQVR [193]
dCG4096    AQKNLDRFCSWQHKLNKGSEKDP-----------HHHDVAILITRKNICANN----CMTL [437]
ADAMTS4    AAQTLRSFCAWQRGLNTPEDSDP-----------DHFDTAILFTRQDLC-GVST--CDTL [330]
ADAMTS5    AATTLKNFCKWQHQHNQLGDDHE-----------EHYDAAILFTREDLC-GHHS--CDTL [379]
ADAMTS8    GGLTLRNFCNWQRRFNQPSDRHP-----------EHYDTAILLTRQNFC-GQEGL-CDTL [333]
ADAMTS1    AALTLRNFCNWQKQHNPPSDRDA-----------EHYDTAILFTRQDLC-GSQT--CDTL [370]
ADAMTS15   AALTLRNFCAWQKKLNKVSDKHP-----------EYWDTAILFTRQDLC-GATT--CDTL [330]
dCG6107    SNEMLKHFCQFINQ----------------SGYERDTAMLITREPICGSVPGKICHML [459]
ADAMTS9    AQTTLKNLCQWQHSKNSPGGI-------------HHDTAVLLTRQDIC-RAHDK-CDTL [403]
ADAMTS20   GATTLKNFCSWQQTQNDLDDVHP-----------SHHDTAVLITREDIC-SSKEK-CNML [357]
mask       11111111111111--------------------111111111111111------1111 [128]
Ce gon-1   AQQTLQDFCRWQQYYNDPDDSSV-----------QHHDVAILLTRKDIC-RSQGK-CDTL [393]
[Intron              18                          19,20        21       ]
```

AC Nicholson, SB Malik, JM Logsdon Jr, E van Meir, 2004. Functional evolution of ADAMTS genes: evidence]
[from analyses of phylogeny and gene organization. Contact: john-logsdon@uiowa.edu]
[Intron phases marked 0, 1, 2]

```
[                 610       620       630       640       650       660]
[                  .         .         .         .         .         .]
[≥80%,maj.  G      C    SC       G    AFT AHE GH       HD      C         ]
ADAMTS6    GLASVAGMCEPERSCSINEDIGLGSAFTIAHEIGHNFGMNHDGIGNS-C-GTKG------   [424]
ADAMTS10   GLAPVGGMCERERSCSVNEDIGLPQAFTIAHEIGHTFGMNHDGVGNS-C-GARG------   [413]
ADAMTS18   GFAPISGMCSKYRSCTINEDTGLGLAFTIAHESGHNFGMIHDGEGNP-CRKAEG------   [458]
ADAMTS16   GFAPISGMCSKYRSCTINEDTGLGLAFTIAHESGHNFGMIHDGEGNM-CKKSEG------   [455]
ADAMTS7    GLSHVAGMCQPHRSCSINEDTGLPLAFTVAHELGHSFGIQHDGSGND-C-EPVG------   [409]
ADAMTS12   GLSHLSGMCQPHRSCNINEDSGLPLAFTIAHESKFGIQHDGKEND-C-EPVG------   [413]
ADAMTS17   GTAYLGGVCSAKRKCVLAEDNGLNLAFTIAHELGHNLGMNHDDDHSS-C----------   [406]
ADAMTS19   GIAYLSGMCSEKRKCIIAEDNGLNLAFTIAHEMGHNMGINHDNDHPS-C----------   [499]
ADAMTS2    GYAPVTGMCHPVRSCTLNHEDGFSSAFVVAHETGHVLGMEHDGQGNR-C-----GD-----   [427]
ADAMTS3    GYAPVTGMCHPVRSCTLNHEDGFSSAFVVAHETGHVLGMEHDGQGNR-C-----GD-----   [417]
ADAMTS14   GYAPVTGMCHPLRSCALNHEDGFSSAFVIAHETGHVLGMEHDGQGNG-C-----D-----   [419]
ADAMTS13   GVTQLGGACSPTWSCLITEDTGFDLGVTIAHEIGHSFGLEHDGAPGSGC-----------   [242]
dCG4096    GLANVGGMCKPKQSCSVNEDNGIMLSHTITHELGHNFGMFHDTAKIG-CHPRVGPIV---   [493]
ADAMTS4    GMADVGTVCDPARSCAIVEDDGLQSAFTAAHELGHVFNMLHDNSKP--CISLNGP-----   [383]
ADAMTS5    GMADVGTICSPERSCAVIEDDGLHAAFTVAHEIGHLLGLSHDDSKF--CEETFG------   [431]
ADAMTS8    GVADIGTICDPNKSCSVIEDEGLQAAHTLAHELGHVLSMPHDDSKP--CTRLFG------   [385]
ADAMTS1    GMADVGTVCDPSRSCSVIEDDGLQAAFTTAHELGHVFNMPHDDAKQ--CASLNG------   [422]
ADAMTS15   GMADVGTMCDPKRSCSVIEDDGLPSAFTTAHELGHVFNMPHDNVKV--CEEVFG------   [382]
dCG6107    GLAELGTVCS-SSSCSIVQDTGLPTAFTMAHELGHILNMNHDDDDK--CMPYVTRQN---   [513]
ADAMTS9    GIAELGTICDPYRSCSISEDSGLSTAFTIAHELGHVFNMPHDDNNK--C-KEEG------   [454]
ADAMTS20   GLSYLGTICDPLQSCFINEEKGLISAFTIAHELGHTLGVQHDDNPR--C-KEM-------   [407]
mask       111111111111111111111111111111111111111111111111----1----------   [175]
Ce gon-1   GLAELGTMCDMQKSCAIIEDNGLSAAFTIAHELGHVFSIPHDDERK--CSTYMPVNKVCK   [451]
[Intron    22                                23,24                       ]
[                                      catalytic Zn++ binding motif      ]


[                 670       680       690       700       710       720]
[                  .         .         .         .         .         .]
[Modal, ≥80%, full maj.  M          WS CS       L        CL    P]
ADAMTS6    ----------HEAAKLMAAHITA--NTNPFSWSACSRDYITSFLDSGRGT--CLDNE-P   [468]
ADAMTS10   ----------QDPAKLMAAHITM--KTNPFVWSSCNRDYITSFLDSGLGL--CLNNR-P   [457]
ADAMTS18   ---------------NIMSPTLTG--NNGVFSWSSCSRQYLKKFLSTPQAG--CLVDE-P   [498]
ADAMTS16   ---------------NIMSPTLAG--RNGVFSWSPCSRQYLHKFLSTAQAI--CLADQ-P   [495]
ADAMTS7    ------------KRPFIMSPQLLY--DAAPLTWSRCSRQYITRFLDRGWGL--CLDDP-P   [452]
ADAMTS12   ------------RHPYIMSRQLQY--DPTPLTWSKCSEEYITRFLDRGWGF--CLDDI-P   [456]
ADAMTS17   ----------AGRSHIMSGEWVKGRNPSDLSWSSCSRDDLENFLKSKVST--CLLVTDP   [453]
ADAMTS19   ----------ADGLHIMSGEWIKGQNLGDVSWSRCSKEDLERFLRSKASN--CLLQTNP   [546]
ADAMTS2    ---------EVRLGSIMAPLVQA--AFHRFHWSRCSQQELSRYLHS--YD--CLLDD-P   [470]
ADAMTS3    ---------ETAMGSVMAPLVQA--AFHRYHWSRCSGQELKRYIHS--YD--CLLDD-P   [460]
ADAMTS14   ---------ETSLGSVMAPLVQA--AFHRFHWSRCSKLELSRYLPS--YD--CLLDD-P   [462]
ADAMTS13   -----------GPSGHVMASDGAA--PRAGLAWSPCSRRQLLSLLSAGFRAR--CVWDP-P   [286]
dCG4096    ---------------HIMTPTFGA--DTLQVCWSNCSRKYITHFLDQGLGE--CLDDP-P   [533]
ADAMTS4    ---------LSTSRHVMAPVMAH--VDPEEPWSPCSARFITDFLDNGYGH--CLLDK-P   [428]
ADAMTS5    ---------STEDKRLMSSILTS--IDASKPWSKCTSATITEFLDDGHGN--CLLDL-P   [476]
ADAMTS8    ---------PMGKHHVMAPLFVH--LNQTLPWSPCSAMYLTELLDGGHGD--CLLDA-P   [430]
ADAMTS1    ---------VNQDSHMMASMLSN--LDHSQPWSPCSAYMITSFLDNGHGE--CLMDK-P   [467]
ADAMTS15   ---------KLRANHMMSPTLIQ--IDRANPWSACSAAIITDFLDSGHGD--CLLDQ-P   [427]
dCG6107    ---------NNKVLHIMSSVMGI--HMHPWSWSKCSRHFVSEFLEKTDKS--CLETS-V   [558]
ADAMTS9    ---------VKSPQHVMAPTLNF--YTNPWMWSKCSRKYITEFLDTGYGE--CLLNE-P   [499]
ADAMTS20   ---------KVTKYHVMAPALSF--HMSPWSWSNCSRKYVTEFLDTGYGE--CLLDK-P   [452]
mask       ---------------1111111----------11111111111111---11--1111--1   [203]
Ce gon-1   FQSTKFDKTQFQNNFHIMAPTLEY--NTHPWSWSPCSAGMLERFLENNRGQTQCLFDQ-P   [508]
[Intron                25                         26,27,28              ]
```

```
[                 730       740       750       760       770       780]
[                   .         .         .         .         .         .]
[Modal, ≥80%, full maj.  PG    Y    QC    G      C        C  LWC      ]
ADAMTS6      ---PKRDFLYPAVAPG--QVYDADEQCRFQYGATSRQCKYG-----EVCRELWCLSK--S   [516]
ADAMTS10     ---PRQDFVYPTVAPG--QAYDADEQCRFQHGVKSRQCKYG-----EVCSELWCLSK--S   [505]
ADAMTS18     --KQAGQYKYPDKLPG--QIYDADTQCKWQFGAKAKLCSLG--FVKDICKSLWCHRV--G   [550]
ADAMTS16     --KPVKEYKYPEKLPG--ELYDANTQCKWQFGEKAKLCMLD-FKKADICKALWCHRI--G   [548]
ADAMTS7      ---AKDIIDFPSVPPG--VLYDVSHQCRLQYGAYSAFCEDM----DNVCHTLWCSV---G   [500]
ADAMTS12     ---KKKGLKSKVIAPG--VIYDVHHQCQLQYGPNATFCQEVE----NVCQTLWCSV---K   [504]
ADAMTS17     --RSQHTVRLPHKLPG--MHYSANEQCQILFGMNATFCRNME---HLMCAGLWCLVE--G   [504]
ADAMTS19     --QSVNSVMVPSKLPG--MTYTADEQCQILFGPLASFCQEMQ---HVICTGLWCKVE--G   [597]
ADAMTS2      --FAHDWPALP-QLPG--LHYSMNEQCRFDFGLGYMMCTA--FRTFDPCKQLWCSHPD-N   [522]
ADAMTS3      --FDHDWPKLP-ELPG--INYSMDEQCRFDFGVGYKMCTA--FRTFDPCKQLWCSHPD-N   [512]
ADAMTS14     --FDPAWPQPP-ELPG--INYSMDEQCRFDFGSGYQTCLA--FRTFEPCKQLWCSHPD-N   [514]
ADAMTS13     RPQPGSAGHPPDAQPG--LYYSANEQCRVAFGPKAVACTFA-REHLDMCQALSCHTDPLD   [343]
dCG4096      T--PLDEYNYTGELPG--MRYNARGQCRLQFNLTTDSEVGACSAPHEFCSTLWCKVNGE-   [588]
ADAMTS4      ----EAPLHLPVTFPG--KDYDADRQCQLTFGPDSRHCPQL----PPPCAALWCSGHLNG   [478]
ADAMTS5      ----RKQILGPEELPG--QTYDATQQCNLTFGPEYSVCPGM----DVCARLWCAVVRQG   [525]
ADAMTS8      ----GAALPLPTGLPGRMALYQLDQQCRQIFGPDFRHCPNT--SAQDVCAQLWCHTDGAE   [484]
ADAMTS1      ----HNPIQLPGDLPG--TSYDANRQCQFTFGEDSKHCPDA----ASTCSTLWCTGTSGG   [517]
ADAMTS15     ----SKPISLPEDLPG--ASYTLSQQCELAFGVGSKPCPYM-----QYCTKLWCTGKAKG   [476]
dCG6107      ---GAHIPYGTERLPG--EIYSLDAQCQLSFGNDFGYCPTD-----EECKRLWCNRTSGN   [608]
ADAMTS9      ---ESRPYPLPVQLPG--ILYNVNKQCELIFGPGSQVCPY-----MMQCRRLWCNNVNGV   [549]
ADAMTS20     ---DEEIYNLPSELPG--SRYDGNKQCELAFGPGSQMCPHI----ENICMHLWCTSTEKL   [503]
mask         ----1111111-1111--11111111111111111111111----111111111----   [246]
Ce gon-1     VERRYYEDVFVRDEPG--KKYDAHQQCKFVFGPASELCPYM-----PTCRRLWCATFYGS   [561]
[Intron                                               29,30,31            ]


[                 790       800       810       820       830       840]
[                   .         .         .         .         .         .]
[≥80%, full maj.C      P   GT C      C  G  C         G  W   W        ]
ADAMTS6      NR--CVTNS--IPAAEGTLCQTGNIEKGWCYQGDCVPFGTW-PQSI--DGGWGPWSLWGE   [569]
ADAMTS10     NR--CITNS--IPAAEGTLCQTHTIDKGWCYKRVCVPFGSR-PEGV--DGAWGPWTPWGD   [558]
ADAMTS18     HR--CETKF--MPAAEGTVCGL----SMWCRQGQCVKFGELGPRPI--HGQWSAWSKWSE   [600]
ADAMTS16     RK--CETKF--MPAAEGTICGH----DMWCRGGQCVKYGDEGPKPT--HGHWSDWSSWSP   [598]
ADAMTS7      TT--CHSKL--DAAVDGTRCGE----NKWCLSGECVPVGFR-PEAV--DGGWSGWSAWSI   [549]
ADAMTS12     GF--CRSKL--DAAADGTQCGE----KKWCMAGKCITVGKH-PESI--PGGWGRWSPWSH   [553]
ADAMTS17     DTS-CKTKL--DPPLDGTECGA----DKWCRAGECVSKTPI-PEHV--DGDWSPWGAWSM   [554]
ADAMTS19     EKE-CRTKL--DPPMDGTDCDL----GKWCKAGECTSRTSA------PEHLAGEWSLWSP   [644]
ADAMTS2      PYF-CKTKK--GPPLDGTMCAP----GKHCFKGHCIWLT---PDILKRDGSWGAWSPFGS   [572]
ADAMTS3      PYF-CKTKK--GPPLDGTECAA----GKWCYKGHCMWK---NANQQKQDGNWGSWTKFGS   [562]
ADAMTS14     PYF-CKTKK--GPPLDGTECAP----GKWCFKGHCIWKS--PEQTYGQDGGWSSWTKFGS   [565]
ADAMTS13     QSS-CSRLL--VPLLDGTECGV----EKWCSKGRCRSLVELTP-IAAVHGRWSSWGPRSP   [395]
dCG4096      ----CVTHM--RPTAPGTLCGR----NKWCQNGKCVRREELAAV----NGGWGDWSEWSE   [634]
ADAMTS4      HAM-CQTKH--SPWADGTPCGP----AQACMGGRCLHMDQLQDFNIPQAGGWGPWGPWGD   [531]
ADAMTS5      QMV-CLTKK--LPAVEGTPCGK----GRICLQGKCVDKTKKKYYSTSSHGNWGSWGSWGQ   [578]
ADAMTS8      PL--CHTKNGSLPWADGTPCGP----GHLCSEGSCLPEEEVERPKPVVDGGWAPWGPWGE   [538]
ADAMTS1      VLV-CQTKH--FPWADGTSCGE----GKWCINGKCVNKTDRKHFDTPFHGNWGMWGPWGD   [570]
ADAMTS15     QMV-CQTRH--FPWADGTSCGE----GKLCLKGACVERHNLNKHRV--DGSWAKWDPYGP   [527]
dCG6107      SNEQCASSN--LPWADGTPCGSS---GHWCQRGKCVSNKHGY--GRQVNGGWGPWTPFTP   [661]
ADAMTS9      HKG-CRTQH--TPWADGTECEP----GKHCKYGFCVPKEMDVPV-T--DGSWGSWSPFGT   [599]
ADAMTS20     HKG-CFTQH--VPPADGTDCGP----GMVHCRHGLCVNKETE---TRPVNGEWGPWEPYSS   [554]
mask         ----11111--1111111111-----1111111111-----------11111111111   [285]
Ce gon-1     QMG-CRTQH--MPWADGTPCDESR--SMFCHHGACVRLAPESL--TKIDGQWGDWRSWGE   [614]
[Intron                            32          33           ▲             ]
[                                                   Thrombospondin➔    ]
```

```
[                850       860       870       880       890       900]
[                 .    .    .    .    .    .    .    .    .    .    .]
[≥80%, maj. CSR CG G      R  C  P  P  GG  C  G        C    C        FR  QC  ]
ADAMTS6    CSRTCGGGVSSSLRHCDSPAPSGGGKYCLGERKRYRSCNTDPCPL---GSRDFREKQCAD  [626]
ADAMTS10   CSRTCGGGVSSSSRHCDSPRPTIGGKYCLGERRHRSCNTDDCPP---GSQDFREVQCSE  [615]
ADAMTS18   CSRTCGGGVKFQERHCNNPKPQYGGLFCPGSSRIYQLCNINPCNE---NSLDFRAQQCAE  [657]
ADAMTS16   CSRTCGGGVSHRSRLCTNPKPSHGGKFCEGSTRTLKLCNSQKCPR---DSVDFRAAQCAE  [655]
ADAMTS7    CSRSCGMGVQSAERQCTQPTPKYKGRYCVGERKRFRLCNLQACPA---GRPSFRHVQCSH  [606]
ADAMTS12   CSRTCGAGVQSAERLCNNPEPKFGGKYCVGERKRYRLCNVHPCRS--EAPTFRQMQCSE  [610]
ADAMTS17   CSRTCGTGARFRQRKCDNPPPGPGGTHCPGASVEHAVCENLPCPK---GLPSFRDQQCQA  [611]
ADAMTS19   CSRTCSAGISSRERKC--PGLDSEARDCNGPRKQYRICENPPCPA---GLPGFRDWQCQA  [699]
ADAMTS2    CSRTCGTGVKFRTRQCDNPHPANGGRTCSGLAYDFQLCSRQDCPD---SLADFREEQCRQ  [629]
ADAMTS3    CSRTCGTGVRFRTRQCNNPMPINGGQDCPGVNFEYQLCNTEECQK---HFEDFRAQQCQQ  [619]
ADAMTS14   CSRSCGGGVRSRSRSCNNPSPAYGGRLCLGPMFEYQVCNSEECPG---TYEDFRAQQCAK  [622]
ADAMTS13   CSRSCGGGVVTRRRQCNNPRPAFGGRACVGADLQAEMCNTQACEK---TQLEFMSQQCAR  [452]
dCG4096    CSRSCGGGVSTQQRECDNPVPANGGVFCIGERKRYKICRKRPCPA---EEPSFRAQQCAR  [691]
ADAMTS4    CSRTCGGGVQFSSRDCTRPVPRNGGKYCEGRRTRFRSCNTEDCPT--GSALTFREEQCAA  [589]
ADAMTS5    CSRSCGGGVQFAYRHCNNPAPRNNGRYCTGKRAIYRSCSLMPCPP---NGKSFRHEQCEA  [635]
ADAMTS8    CSRTCGGGVQFSHRECKDPEPQNGGRYCLGRRAKYQSCHTEECPP---DGKSFREQQCEK  [595]
ADAMTS1    CSRTCGGGVQYTMRECDNPVPKNGGKYCEGKRVRYRSCNLEDCPD--NNGKTFREEQCEA  [628]
ADAMTS15   CSRTCGGGVQLARRQCTNPTPANGGKYCEGVRVKYRSCNLEPCPSS-ASGKSFREEQCEA  [586]
dCG6107    CSLTCGGGVQESRRECNQPVPENGGKYCTGSRKKYRSCNTHQCPP---GSMDPREQQCYA  [718]
ADAMTS9    CSRTCGGGIKTAIRECNRPEPKNGGKYCVGRRMKFKSCNTEPCLK---QKRDFRDEQCAH  [656]
ADAMTS20   CSRTCGGGIESATRRCNRPEPRNGGNYCVGRRMKFRSCNTDSCPK---GTQDFREKQCSD  [611]
mask       111111111111111111111111111111111111111111111111111---111111111111  [341]
Ce gon-1   CSRTCGGGVQKGLRDCDSPKPRNGGKYCVGQRERYRSCNTQECPW---DTQPYREVQCSE  [671]
[Intron                    34                  35    36,37,38             ]


[                910       920       930       940       950       960]
[                 .    .    .    .    .    .    .    .    .    .    .]
[Modal, ≥80%, full maj.    W            C  L  C           V  DGT  C  ]
ADAMTS6    FDNM--PFRGKYY---NWKPYTGG---G-VKPCALNCLAEGYNFYTERAPAVIDGTQCNA  [677]
ADAMTS10   FDSI--PFRGKFY---KWKTYRGG---G-VKACSLTSLAEGFNFYTERAAAVVDGTPCRP  [666]
ADAMTS18   YNSK--PFRGWFY---QWKPYTKVEE-F--DRCKLYCKAENFEFFFAMSGKVKDGTPCSP  [709]
ADAMTS16   HNSR--RFRGRHY---KWKPYTQVED-Q--DLCKLYCIAEGFDFFFSLSNKVKDGTPCSE  [707]
ADAMTS7    FDAM--LYKGQLH---TWVPVVND-----VNPCELHCRPANEYFAKKLRDAVVDGTPCYQ  [656]
ADAMTS12   FDTV--PYKNELY---HWFPIFNP-----AHPCELYCRPIDGQFSEKMLDAVIDGTPCFE  [660]
ADAMTS17   HDR---LSPKKKG---LLTAVVVDD--K---PCELYCSPLLVADRVLDGTPCGP  [660]
ADAMTS19   YSVR-TSSPKHIL---QWQAVLDEE--K--PCALFCSPVGKEQPILLSEKVMDGTSCGY  [750]
ADAMTS2    WDLY-FEHGDAQH---HWLPHEHRDA-K--ERCHLYCESRETGEVVSMKRMVHDGTRCSY  [682]
ADAMTS3    RNSH-FEYQNTKH---HWLPYEHPDP-K--KRCHLYCQSKETGDVAYMKQLVHDGTHCSY  [672]
ADAMTS14   RNSY-YVHQNAKH---SWVPYEPDDD-A--QKCELICQSADTGDVVFMNQVVHDGTRCSY  [675]
ADAMTS13   TDGQPLRSSPGGASFYHWGAAVPHSQGD--ALCRHMCRAIGESFIMKRGDSFLDGTRCMP  [510]
dCG4096    FDNV--SYQGATYK---WLPFFDKN--N---PCKLFCSDVDDTIIANWGATVLDGTPCTL  [741]
ADAMTS4    YNHR-TDLFKSFPGPMDWVPRYTGVA-P-QDQCKLTCQARALGYYYVLEPRVVDGTPCSP  [646]
ADAMTS5    KNGY-QSDAKGVKTFVEWVPKYAGVL-P-ADVCKLTCRAKGTGYYVVFSPKVTDGTECRP  [692]
ADAMTS8    YNAY-NYTDMDGN-LLQWVPKYAGVS-P-RDRCKLFCRARGRSEFKVFEAKVIDGTLCGP  [651]
ADAMTS1    HNEF-SKASFGSGPAVEWIPKYAGVS-P-KDRCKLICQAKGIGYFFVLQPKVVDGTPCSP  [685]
ADAMTS15   FNGY-NHSTNRLTLAVAWVPKYSGVS-P-RDKCKLICRANGTGYFYVLAPKVVDGTLCSP  [643]
dCG6107    MNGRN-MNIPGVNPDTKWVPKYEK---D---ACKLFCRMDMKVTYFMLKSMVTDGTSCAV  [771]
ADAMTS9    FDGK-HFNINGLLPNVRWVPKYSGI--L-MKDRCKLFCRVAGNTAYYQLRDRVIDGTPCGQ  [713]
ADAMTS20   FNGK-HLDISGIPSNVRWLPRYSGI--G-TKDRCKLYCQVAGTNYFYLLKDMVEDGTPCGT  [668]
mask       11-------------11111111-------111111111111111111111111111111  [380]
Ce gon-1   FNNKDIGIQGVASTNTHWVPKYANVAPN--ERCKLYCRLSGSAAFYLLRDKVVDGTPCDR  [729]
[Intron                     39                    40                     ]
```

[Intron phases marked 0, 1, 2]

```
[                    970        980       990       1000      1010      1020]
[                     .    .    .    .    .    .    .    .    .    .    .]
[≥80%, full maj.       C  G C   GCD    S     D C VC G    C    G         ]
ADAMTS6     ------DSLDICINGECKHVGCDNILGSDAREDRCRVCGGDGSTCDAIEGFFNDSLPR--   [729]
ADAMTS10    ------DTVDICVSGECKHVGCDRVLGSDLREDKCRVCGGDGSACETIEGVFSPASPG--   [718]
ADAMTS18    ------NKNDVCIDGVCELVGCDHELGSKAVSDACGVCKGDNSTCKFYKGLYLNQHKA--   [761]
ADAMTS16    ------DSRNVCIDGICERVGCDNVLGSDAVEDVCGVCNGNNSACTIHRGLYTKHHHT--   [759]
ADAMTS7     VR----ASRDLCINGICKNVGCDFEIDSGAMEDRCGVCHGNGSTCHTVSGTFEEAE-G--   [709]
ADAMTS12    GG----NSRNVCINGICKMVGCDYEIDSNATEDRCGVCLGDGSSCQTVRKMFKQKE-G--   [713]
ADAMTS17    ------YETDLCVHGKCQKIGCDGIIGSAAKEDRCGVCSGDGKTCHLVKGDFSHAR-G--   [711]
ADAMTS19    ------QGLDICANGRCQKVGCDGLLGSLAREDHCGVCNGNGKSCKIIKGDFNHTR-G--   [801]
ADAMTS2     K-----DAFSLCVRGDCKVGCDGVIGSSKQEDKCGVCGGDNSHCKVVKGTFTRSPKK--   [735]
ADAMTS3     K-----DPYSICVRGECKVGCDKEIGSNKVEDKCGVCGGDNSHCRTVKGTFTRTPRK--   [725]
ADAMTS14    R-----DPYSVCARGECVPVGCDKEVGSMKADDKCGVCGGDNSHCRTVKGTLGKASKQ--   [728]
ADAMTS13    SGPREDGTLSLCVSGSCRTFGCDGRMDSQQVWDRCQVCGGDNSTCSPRKGSFTAGRA---   [567]
dCG4096     ------GTNNMCIDGICKVGCDWIVDSEVQDDRCGVCGGSGDQCQPVRETYTDPFAA--   [793]
ADAMTS4     ------DSSSVCVQGRCIHAGCDRIIGSKKKFDKCMVCGGDGSGCSKQSGSFRKFR----   [696]
ADAMTS5     ------YSNSVCVRGKCVRTGCDGIIGSKLQYDKCGVCGGDNSSCTKIVGTFNKKS----   [742]
ADAMTS8     ------ETLAICVRGQCVKAGCDHVVDSPRKLDKCGVCGGKGNSCRKVSGSLTPTN----   [701]
ADAMTS1     ------DSTSVCVQGQCVKAGCDRIIDSKKKFDKCGVCGGNGSTCKKISGSVTSAK----   [735]
ADAMTS15    ------DSTSVCVQGKCIKAGCDGNLGSKKRFDKCGVCGGDNKSCKKVTGLFTKPM----   [693]
dCG6107     ------DSFDKCVNGICRPAGCDNELNSIAKLDRCGVCEGRNDTCHEVTGNLLVSNLLGL   [825]
ADAMTS9     ------DTNDICVQGLCRQVGCDHVLNSKARRDKCGVCGGDNSSCKTVAGTFNTVH----   [763]
ADAMTS20    ------ETHDICVQGQCMAAGCDHVLNSSAKIDKCGVCGGDNSSCKTITGVFNSSH----   [718]
mask        -------1111111111111111111111111111111111111111111111-----   [428]
Ce gon-1    ------NGDDICVAGACMPAGCDHQLHSTLRRDKCGVCGGDDSSCKVVKGTFNEQG-T--   [780]
[Intron                      41,42        43                            ]


[                    1030       1040      1050      1060      1070      1080]
[                     .    .    .    .    .    .    .    .    .    .    .]
[≥80%, full maj.       Y      IP G                              N       ]
ADAMTS6     -------GGYMEVVQIPRGSVHIEVREVAMSKN-----YIALKSE--GDDYYINGAWTID   [775]
ADAMTS10    -------AGYEDVVWIPKGSVHIFIQDLNLSLS-----HLALKGD--QESLLLEGLPGTP   [764]
ADAMTS18    -------NEYYPVVLIPAGARSIEIQELQVSSS-----YLAVRSL--SQKYYLTGGWSID   [807]
ADAMTS16    -------NQYHMVTIPSGARSIRIYEMNVSTS-----YISVRNA--LRRYYLNGHWTVD   [805]
ADAMTS7     -------LGYVDVGLIPAGAREIRIQEVAEAAN-----FLALRSED-PEKYFLNGGWTIQ   [756]
ADAMTS12    -------SGYVDIGLIPKGARDIRVMEIEGAGN-----FLAIRSED-PEKYYLNGGFIIQ   [760]
ADAMTS17    -------TGYIEAAVIPAGARRIRVVEDKPAHS-----FLALKDS---GKGSINSDWKIE   [756]
ADAMTS19    -------AGYVEVLVIPAGARRIKVVEEKPAHS-----YLALRDA--GKQSINSDWKIE   [846]
ADAMTS2     -------HGYIKMFEIPAGARHLLIQEVDATSH-----HLAVKNLE-TGKFILNEENDVD   [782]
ADAMTS3     -------LGYLKMFDIPPGARHVLIQEDEASPH-----ILATKNQA-TGHYILNGKG-EE   [771]
ADAMTS14    -------AGALKLVQIPAGARHIQIEALEKSPH-----RIVVKNQV-TGSFILNPKG-KE   [774]
ADAMTS13    -------REYVTFLTVTPNLTSVYIANHRPLFT-----HLAVRI---GGRYVVAGKMSIS   [612]
dCG4096     -----KDGAYVEIVTIPARARHILIRELANSPH-----FLAIATGDGSGDYRFYLNGDSLIS   [843]
ADAMTS4     -------YGYNNVVTIPAGATHILVRQQGNPGHRS--IYLALKLP--DGSYALNGEYTLM   [745]
ADAMTS5     -------KGYTDVVRIPEGATHIKVRQFKAKDQTRFTAYLALKKK--NGEYLINGKYMIS   [793]
ADAMTS8     -------YGYNDIVTIPAGATNIDVKQRSHPGVQNDGNYLALKTA--DGQYLLNGNLAIS   [752]
ADAMTS1     -------PGYHDIITIPTGATNIEVKQRNQRGSRNNGSFLAIKAA--DGTYILNGDYTLS   [786]
ADAMTS15    -------HGYNFVVAIPAGASSIDIRQRGYKGLIGDDNYLALKNS--QGKYLLNGHFVVS   [744]
dCG6107     NDGNEPNKTLYYVTRIPKGASNIIITQRGYPDQ-----NFIVLTDDR-DNELLNGKFLKT   [879]
ADAMTS9     -------YGYNTVVRIPAGATNIDVRQHSFSGETDDDNYLATSSS--KGEFLLNGNFVVT   [814]
ADAMTS20    -------YGYNVVVKIPAGATNVDIRQYSYSGQPDDS-YLALSDA--EGNFLFNGNFLLS   [768]
mask        -------11111111111111111111111111111-----111111----1111111111-11   [471]
Ce gon-1    -------FGYNEVMKIPAGSANIDIRQKGYNNMKEDDNYLSTRAA--NGEFLLNGHFQVS   [831]
[Intron               44,45        46                47                  ]
```

```
[                     1090      1100      1110      1120      1130      1140]
[                     .         .         .         .         .         .]
[≥80%, full maj.      G         Y         E                                ]
ADAMTS6     WPRK---FDVAG--TAFHYKRPTDEPESLE-----ALGPTSENLIVMVLLQ---------   [816]
ADAMTS10    QPHR---LPLAG--TTFQLRQGPDQVQSLE-----ALGPINASLIVMVLAR---------   [805]
ADAMTS18    WPGE---FPFAG--TTFEYQRSFNRPERLY-----APGPTNETLVFEILMQ---------   [848]
ADAMTS16    WPGR---YKFSG--TTFDYRRSYNEPENLI-----ATGPTNETLIVELLFQ---------   [846]
ADAMTS7     WNGD---YQVAG--TTFTYARR-GNWENLT-----SPGPTKEPVWIQLLFQ---------   [796]
ADAMTS12    WNGN---YKLAG--TVFQYDRK-GDLEKLM-----ATGPTNESVWIQLLFQ---------   [800]
ADAMTS17    LPGE---FQIAG--TTVRYVRR-GLWEKIS-----AKGPTKLPLHLMVLLFH--------   [797]
ADAMTS19    HSGA---FNLAG--TTVHYVRR-GLWEKIS-----AKGPTTAPLHLLVLLFQ--------   [887]
ADAMTS2     ASSK--TFIAMG--VEWEYRDE-DGRETLQ-----TMGPLHGTITVLVIPVG--------   [824]
ADAMTS3     AKSR--TFIDLG--VEWDYNIE-DDIESLH-----TDGPLHDPVIVLIIPQEN-------   [814]
ADAMTS14    ATSR--TFTAMG--LEWEDAVE-DAKESLK-----TSGPLPEAIAILALPPTEG------   [818]
ADAMTS13    PNTTYPSLLEDG--RVEYRVALTEDRLPRLEEIRIWGPLQEDADIQVYRRYGEEYGN--   [667]
dCG4096     MPGE---FEIAG--AESLYDRV-DEQETIT-----IPQPIQHSISLYAIVRGN-------   [885]
ADAMTS4     PSPT--DVVLPGA-VSLRYSGATAASETLS-----GHGPLAQPLTLQVLVAGN-------   [790]
ADAMTS5     TSET--IIDING--TVMNYSGWSHRDDFLHGM---GYSATKEILIVQILATDP-------   [839]
ADAMTS8     AIEQ--DILVKG--TILKYSGSIATLERLQ-----SFRPLPEPLTVQLLTVPGE------   [797]
ADAMTS1     TLEQ--DIMYKG--VVLRYSGSSAALERIR-----SFSPLKEPLTIQVLTVGN-------   [830]
ADAMTS15    AVER--DLVVKG--SLLRYSGTGTAVESLQ-----ASRPILEPLTVEVLSVGK-------   [788]
dCG6107     YPLK---FVYAG--VTMQYTGSSSVVEQVN---TTYSWKLSRDLIVQIISLDV-------   [931]
ADAMTS9     MAKR--E-IRIG--NAVVEYSGSETAVERIN-----STDRIEQELLLQVLSVGK------   [858]
ADAMTS20    TSKK--EINVQGTRTVIEYSGSNNAVERIN-----STNRQEKELILQVLCVGN-------   [814]
mask        1111-----111----1111111-1111111-----11111111111111----------   [505]
Ce gon-1    LARQ---QIAFQD-TVLEYSGSDAIIERIN-----GTGPIRSDIYVHVLSVG-------   [874]
[Intron                                                    48              ]


[                     1150      1160      1170      1180      1190      1200]
[                     .         .         .         .         .         .]
[Modal, ≥80%, full maj.               Y                                    ]
ADAMTS6     -----------------EQNLGIRYKFNVPITRTGSGDNEVGFT---------------   [843]
ADAMTS10    -----------------TELPALRYRFNAPIARDSLPPYS------------------   [828]
ADAMTS18    -----------------GKNPGIAWKYALPKVMNGTPPATKRPAYT-------------   [877]
ADAMTS16    -----------------GRNPGVAWEYSMPRLGTEKQPPAQPSYT-------------   [874]
ADAMTS7     -----------------ESNPGVHYEYTIHREAGGHDEVPPPVFS-------------   [824]
ADAMTS12    -----------------VTNPGIKYEYTIQKDGLDNDVEQMYF--------------   [826]
ADAMTS17    -----------------DQDYGIHYEYTVPVNRTAENQSEPEKPQDSLFI---------   [830]
ADAMTS19    -----------------DQNYGLHYEYTIPSDPLPENQSSKAPEPLFM----------   [918]
ADAMTS2     ----------------DTRVSLTYKYMIHEDSLN-VDDNNVLEEDSVVYE--------   [857]
ADAMTS3     -----------------DTRSSLTYKYIIHEDSVPTINSNNVIQEELDTFE--------   [848]
ADAMTS14    -----------------GPRSSLAYKYVIHEDLLPLIGSNNVLLEEMDTYE--------   [852]
ADAMTS13    -----------------LTRPDITFTYFQPKPRQAWV--------------------   [687]
dCG4096     -----------------ESNAGIFYEFTLPALNVTAGRQFQ----------------   [909]
ADAMTS4     -----------------PQDTRLRYSFFVPRPTPSTPRPTPQDWLHRRAQILEILRRRP   [832]
ADAMTS5     -----------------TKPLDVRYSFFVPKKSTPKVNS-VTSHGSNKVGSHTSQPQ--   [878]
ADAMTS8     -----------------VFPPKVKYTFFVPNDVDFSMQS-SKERATTNIIQPLLH-AQ-   [836]
ADAMTS1     -----------------ALRPKIKYTYFVKKKKESFNAIPTFSA--------------   [857]
ADAMTS15    -----------------MTPPRVRYSFYLPKEPREDKSSHPKDPRGPSVLHNSVLSLSN   [830]
dCG6107     -------------SPSKRQDTVLLSYSYTIDKPPDYEAEVEIYR---------------   [975]
ADAMTS9     -----------------LYNPDVRYSFNIPIEDKPQQFY------------------   [880]
ADAMTS20    -----------------LYNPDVHYSFNIPLEERSDMFT------------------   [836]
mask        -----------------1111111111111111111----------------------   [523]
Ce gon-1    -----------------SHPPDISYEYMTAAVPNAVIRPISSALYL------------   [903]
```

```
[                   1210      1220      1230      1240      1250      1260]
[                    .         .         .         .         .         .]
[≥80%, full maj.        W          C    C  G         C                  C      P]

ADAMTS6     ------------WNHQP-WSECSATCAGGVQRQEVVCKRLDDNSIVQNNY--CDPDSK-P   [887]
ADAMTS10    ------------WHYAP-WTKCSAQCAGGSQVQAVECRNQLDSSAVAPHY--CSAHSK-L   [872]
ADAMTS18    ------------WSIVQ--SECSVSCGGGYINVKAICLRDQNTQVNSSF---CSAKTK-P   [919]
ADAMTS16    ------------WAIVR--SECSVSCGGGQMTVREGCYRDLKFQVNMSF---CNPKTR-P   [916]
ADAMTS7     ------------WHYGP-WTKCTVTCGRGVQRQNVYCLERQAGPVDEEH---CDPLGR-P   [867]
ADAMTS12    ------------WQYGH-WTECSVTCGTGTRRQTAHCIKKGRGMVKATF---CDPETQ-P   [869]
ADAMTS17    ------------WTHSG-WEGCSVQCGGGERRTIVSCTRIVNKTTTLVNDSDCPQASR-P   [876]
ADAMTS19    ------------WTHTS-WEDCDATCGGGFRKTTVSCTKIMSKNISIVDNEKCKYLTK-P   [964]
ADAMTS2     ------------WALKK-WSPCSKPCGGGSQFTKYGCRRRLDHKMVHRGF--CAALSK-P   [901]
ADAMTS3     ------------WALKS-WSQVSKPCGGGFQYTKYGCRRKSDNKMVHRSF--CEANKK-P   [892]
ADAMTS14    ------------WALKS-WAPCSKACGGGIQFTKYGCRRRRDHHMVQRHL--CDHKKR-P   [896]
ADAMTS13    ------------WAAVR--GPCSVSCGAGLRWVNYSCLDQARKELVETVQ--CQGSQQ-P   [730]
dCG4096     ------------WRLSN-WTACSASCGGGVQHREPICQENGKGESNEPFQ--RIVSIK-R   [953]
ADAMTS4     ------------WAGRK-------------------------------------------   [837]
ADAMTS5     ------------WVTGP-WLACSRTCDTGWHTRTVQCQDGNRKLAKG-----CPLSQR-P   [919]
ADAMTS8     ------------WVLGD-WSECSSTCGAGWQRRTVECRDPSGQASAT-----CNKALK-P   [877]
ADAMTS1     ------------WVIEE-WGECSKSCELGWQRRLVECRDINGQPASE-----CAKEVK-P   [898]
ADAMTS15    QVEQPDDRPPARWVAGS-WGPCSASCGSGLQKRAVDCRGSAGQRTVPA----CDAAHR-P   [884]
dCG6107     ------------WEMQA-PSNCDSLCE-GRSHRLPACISTTQGVKVAPQF--CDKSAM-P   [1018]
ADAMTS9     ------------WNSHGPWQACSKPCQ-GPRKRKLVCTRESDQLTVSDQR--CDRLPQ-P   [924]
ADAMTS20    ------------WDPYGPWEGCTKMCQ-GLQRRNITCIHKSDHSVVSDKE--CDHLPL-P   [880]
mask        ------------11111------------------------------------------   [528]
Ce gon-1    ------------WRVTDTWTECDRACR-GQQSQKLMCLDMSTHRQSHDRN--CQNVLK-P   [947]
[Intron                                 49                                    ]


[                   1270      1280      1290      1300      1310      1320]
[                    .         .         .         .         .         .]
[≥80%, full maj.  C       C                                                 ]
ADAMTS6     PENQRACNTEPCPPE-WFIGDWLECSKTCDGGMRTRAVL-CIRKIGPSEEETLDYSG-CL   [944]
ADAMTS10    PKRQRACNTEPCPPD-WVVGNWSLCSRSCDAGVRSRSVV-CQRRVSAAEEKALDDSA-CP   [929]
ADAMTS18    VTEPKICNAFSCPAY-WMPGEWSTCSKACAGGQQSRKIQ-CVQKKPFQKEEAVLHSL-CP   [976]
ADAMTS16    VTGLVPCKVSACPPS-WSVGNWSACSRTCGGGAQSRPVQ-C-TRRVHYDSEPVPASL-CP   [972]
ADAMTS7     DDQQRKCSEQPCPAR-WWAGEWQLCSSSCGPGGLSRRAVLCIRSVGLDEQSALEPPA-CE   [925]
ADAMTS12    NGRQKKCHEKACPPR-WWAGEWEACSATCGPHGEKKRTVLCIQTMVSDEQ-ALPPTD-CQ   [926]
ADAMTS17    EPQVRRCNLHPCQSR-WVAGPWSPCSATCEKGFQHREVT-CVYQLQNGTHVATRPLY-CP   [933]
ADAMTS19    EPQIRKCNEQPCQTR-WMMTEWTPCSRTCGKGMQSRQVA-CTQQLSNGTLIRARERD-CI   [1021]
ADAMTS2     KAIRRACNPQECSQPVWVTGEWEPCSQTCGRTGMQVRSVRCIQPLHDNTTRSVHAKH-CN   [960]
ADAMTS3     KPIRRMCNIQECTHPLWVAEEWEHCTKTCGSSGYQLRTVRCLQPLLDGTNRSVHSKY-CM   [951]
ADAMTS14    KPIRRRCNQHPCSQPVWVTEEWGACSRSCGKLGVQTRGIQCLLPLSNGTHKVMPAKA-CA   [955]
ADAMTS13    PAWPEACVLEPCPPY-WAVGDFGPCSASCGGGLRERPV-RCVEAQGSLLKTLPPAR--CR   [786]
dCG4096     NLLIALGDTLPC----WTHAKN-KR-PARQSRG-------------------------   [980]
ADAMTS4     -----------------------------------------------------------   [837]
ADAMTS5     SAFKQ-CLLKKC-----------------------------------------------   [930]
ADAMTS8     EDAKP-CESQLCPL---------------------------------------------   [890]
ADAMTS1     ASTRP-CADHPCPQ--WQLGEWSSCSKTCGKGYKKRSLK-CLSHDGGVLSHES-----CD   [949]
ADAMTS15    VETQA-CGEP-CPT--WELSAWSPCSKSCGRGFQRRSLK-CVGHGGRLLARDQ-----CN   [934]
dCG6107     KIDDRACNTD-CRLN-LTVTSISECSAACGELGTREKTYACVQTFTNMQRSNIVDMSYCK  [1076]
ADAMTS9     GHITEPCGTD-CDLR-WHVASRSECSAQCGLGYRTLDIY-CAKYSRLDGKTEKVDDGFCS  [981]
ADAMTS20    SFVTQSCNTD-CELR-WHVIGKSECSSQCGQGYRTLDIH-CMKYSIHEGQTVQVDDHYCG  [937]
mask        -----------------------------------------------------------   [528]
Ce gon-1    KQATRMCNID-CSTR-WITEDVSSCSAKCGSGQKRQRVS-CVKMEGDRQTPASEHL--CD  [1002]
[Intron                      50                                             ]
```

```
[                1330      1340      1350      1360      1370      1380]
[                  .         .         .         .         .         .]
[≥80%, full maj.      C         C                                     ]
ADAMTS6     THRPVEKEP---CNNQS-CPPQ-WVALDWSECTPKCGP-GFKHRIVLCKSSDLSKTFPAA    [998]
ADAMTS10    QPRPPVLEA---CHGPT-CPPE-WAALDWSECTPSCGP-GLRHRVVLCKSADHRATLPPA    [983]
ADAMTS18    VSTPTQVQA---CNSHA-CPPQ-WSLGPWSQCSKTCGR-GVRKRELLCKGSAAETLPESQ    [1030]
ADAMTS16    QPAPSSRQA---CNSQS-CPPA-WSAGPWAECSHTCGK-GWRKRAVACKSTNPSARAQLL    [1026]
ADAMTS7     HLPRPPTETP--CNRHVPCPAT-WAVGNWSQCSVTCGE-GTQRRNVLCTNDTGVP-----    [976]
ADAMTS12    HLLKPKTLLS--CNRDILCPSD-WTVGNWSECSVSCGG-GVRIRSVTCAKNHDEP-----    [977]
ADAMTS17    GPRPAAVQS---CEGQD-CLSI-WEASEWSQCSASCGK-GVWKRTVACTNSQGK------    [981]
ADAMTS19    GPKPASAQR---CEGQD-CMTV-WEAGVWSECSVKCGK-GIRHRTVRCTNPRKK------    [1069]
ADAMTS2     DARPESRRA---CSREL-CPGR-WRAGPWSQCSVTCGN-GTQERPVPCRTADDSFGI---    [1011]
ADAMTS3     GDRPESRRP---CNRVP-CPAQ-WKTGPWSECSVTCGE-GTEVRQVLCRAGDH-------    [1005]
ADAMTS14    GDRPEARRP---CLRVP-CPAQ-WRLGAWSQCSATCGE-GIQQRQVVCRTNANSLGH---    [1006]
ADAMTS13    AGAQQPAVALETCNPQP-CPAR-WEVSEPSSCTSAGGA-GLALENETCVPGADGLEAPVT    [843]
dCG4096     ------------CGDQP-CPAH-WWPGPWQFCPVTCRPVGFVAPPQRRRSVVCLDEHDVV    [1026]
ADAMTS4     -----------------------------------------------------------    [837]
ADAMTS5     -----------------------------------------------------------    [930]
ADAMTS8     -----------------------------------------------------------    [890]
ADAMTS1     PLKKPKHFIDF-CTMAE-CS----------------------------------------    [967]
ADAMTS15    LHRKPQELDF--CVLRP-C-----------------------------------------    [950]
dCG6107     LKFDVAYHEE--CREG--C----WVLSEWSTCSKSCGT-GSQQREAHCYLHNSRVSDDL-    [1126]
ADAMTS9     SHPKPSNREK--CSGE--CNTGGWRYSAWTECSKSCDG-GTQRRRAICVNTRNDVLDDSK    [1036]
ADAMTS20    DQLKPPTQEL--CHGN--CVFTRWHYSEWSQCSRSCGG-GERSRESYCMNNFGHRLADNE    [992]
mask        -----------------------------------------------------------    [528]
Ce gon-1    RNSKPSDIAS--CYID--CSGRKWNYGEWTSCSETCGSNGKMHRKSYCVDDSNRRVDESL    [1058]
[Intron                          51        52                         ]
```

```
[                1390      1400      1410      1420      1430      1440]
[                  .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                         ]
ADAMTS6     Q----CPEESKPPVRIR---CSLGR--CPPPR----------------------WVTGD    [1026]
ADAMTS10    H----CSPAAKPPATMR---CNLRR--CPPAR----------------------WVAGE    [1011]
ADAMTS18    -----CTSLPRPELQEG---CVLGR--CPKNSRLQ-------------------WVASS    [1060]
ADAMTS16    PDAV-CTSEPKPRMHEA---CLLQR--CHKPKKLQ-------------------WLVSA    [1060]
ADAMTS7     -----CDEAQQPASEVT---CSLPL--CR------------------------WPLGT    [1000]
ADAMTS12    -----CDVTRKPNSRAL---CGLQQ--CP------------------------SS       [998]
ADAMTS17    -----CDASTRPRAEEA---CEDYSG-CYE-----------------------WKTGD    [1007]
ADAMTS19    -----CVLSTRPREAED---CEDYSK-CYV-----------------------WRMGD    [1095]
ADAMTS2     -----CQEERPETART-CRLGPCPRNISDPSKKSYVV----------------QWLSRP    [1048]
ADAMTS3     -----CDGEKPESVRA-CQLPPCNDEP- --------------------------       [1027]
ADAMTS14    -----CEGDRPDTVQV-CSLPACGGNHQNSTVRADVWELVTPEG---------QWVPQS    [1041]
ADAMTS13    EGPG-SVDEKLPAPEP----CVGMS--CPPGWGHTDATSAGEKAPSPWGSIRTGAQAAHV    [896]
dCG4096     VADAECGHLQKPAEME---PCESSLPICRTK-----------------------------    [1054]
ADAMTS4     -----------------------------------------------------------    [837]
ADAMTS5     -----------------------------------------------------------    [930]
ADAMTS8     -----------------------------------------------------------    [890]
ADAMTS1     -----------------------------------------------------------    [967]
ADAMTS15    -----------------------------------------------------------    [950]
dCG6107     -----CNPRTKPHLNTLIGICNTES--CPTYTKSPNALAVSN-------------WVIGE    [1166]
ADAMTS9     -----CTHQEKVTIQR----CSEFP--CPQ-----------------------WKSGD    [1060]
ADAMTS20    -----CQELSRVTREN----CNEFS--CPS-----------------------WAASE    [1016]
mask        -----------------------------------------------------------    [528]
Ce gon-1    -----CGREQKEATERE---CNRIP--CPR-----------------------WVYGH    [1083]
[Intron                          53        54,55                      ]
```

```
[                  1450      1460      1470      1480      1490      1500]
[                    .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                                    ]
ADAMTS6     WGQ----CSAQCGLGQQMRTVQCLSYTGQASSD-------CLETVRPPSMQQ--CESK-C    [1072]
ADAMTS10    WGE----CSAQCGVGQRQRSVRCTSHTGQASHE-------CTEALRPPTTQQ--CEAK-C    [1057]
ADAMTS18    WSE----CSATCGLGVRKREMKCSEKGFQGKLITFPERR-CRNIKKPNLDLEETCNRRAC    [1115]
ADAMTS16    WSQ----CSVTCERGTQKRFLKCAEKYVSGKYRELASKK-CSHLPKPSLELERACAPLPC    [1115]
ADAMTS7     LGPEGSGSGSSSHELFNEADFIPHHLAPRPSPASSPKPG-TMGNAIEEEAPELDLPGPVF    [1059]
ADAMTS12    RRVLKPNKGTISNGKNPPTLKPVPPPTSRPRMLTTPTGP--------ESMSTSTPAISSP    [1050]
ADAMTS17    WST----CSSTCGKGLQSRVVQCMHKVTGRHGSE------CPALSKPAPYRQ--CYQEVC    [1055]
ADAMTS19    WSK----CSITCGKGMQSRVIQCMHKITGRHGNE------CFSSEKPAAYRP--CHLQPC    [1143]
ADAMTS2     ---------DPDSPIRKISSKGHCQGDKSIFCRMEVLSRYCSIPGYNKLS----CKS--C    [1093]
ADAMTS3     ----- ----------------CLGDKSIFCQMEVLARYCSIPGYNKLC----CES--C    [1027]
ADAMTS14    ----------PLHPIYKISSTEPCTGDRSVFCQMEVLDRYCSIPGYHRL-----CCVS-C    [1095]
ADAMTS13    WTPAAGSCSVSCGRGMMELRFLCMDSALRVPVQEEL----CGLASKPGSRREV-CQAVPC    [951]
dCG4096     -----------------------------------------------------------    [1054]
ADAMTS4     -----------------------------------------------------------    [837]
ADAMTS5     -----------------------------------------------------------    [930]
ADAMTS8     -----------------------------------------------------------    [890]
ADAMTS1     -----------------------------------------------------------    [967]
ADAMTS15    -----------------------------------------------------------    [950]
dCG6107     WGE----CNEWCEKTRSVS---CSHPYGIG----------CGSRKPKDVRK---CCHIKY    [1206]
ADAMTS9     WSE----CLVTCGKGHKHRQVWCQFGEDRLNDRM------CDPETKPTSMQT--CQQPEC    [1108]
ADAMTS20    WSE----CLVTCGKGTKQRQVWCQLNVDHLSDGF------CNSSTKPESLSP--CELHTC    [1064]
mask        -----------------------------------------------------------    [528]
Ce gon-1    WSE----CSRSCDGGVKMRHAQCLDAADRETHTSR-----CGPAQTQEH-----CNEHAC    [1129]
[Intron           56       57       58                                      ]


[                  1510      1520      1530      1540      1550      1560]
[                    .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                                    ]
ADAMTS6     D--------S-TPISNTEECKDVNKVAYCPLVLKFKFCSRAYFRQMCCKTCQGH------    [1117]
ADAMTS10    D--------SPTPGDGPEECKDVNKVAYCPLVLKFQFCSRAYFRQMCCKTCQGH------    [1103]
ADAMTS18    PAHPVYNMVAG----WYSLPWQQCTVTCGGGVQTRSVHCVQQGRPSSS--------CLLH    [1163]
ADAMTS16    PRHPPFAAAGPSRGSWFASPWSQCTASCGGGVQTRSVQCLAGGRPASG--------CLLH    [1167]
ADAMTS7     VDDFYYDYNFINFHEDLSYGPSEEPDLDLAGTGDRTPPPHSRPAAPSTGSPVPATEPPAA    [1119]
ADAMTS12    SPTTASKEGDLGGKQWQDSSTQPELSSRYLISTGSTSQPILTSQSLSIQPSEENVSSSDT    [1110]
ADAMTS17    NDRINANTITSPRLAALTYKCTRDQWTVYCRVIREKNLCQDMRWYQRCCQTCRDFYANKM    [1115]
ADAMTS19    NEKINVNTITSPRLAALTFKCLGDQWPVYCRVIREKNLCQDMRWYQRCCETCRDFYAQKL    [1150]
ADAMTS2     NLYNNLTNVEGRIEPPPGKHNDIDVF---------------------------------    [1119]
ADAMTS3     SKRSSTLPPPYLLEAAETHDDVISNP---------------------------------    [1076]
ADAMTS14    IKKASGPNPGPDPGPTSLPP---------------------------------------    [1115]
ADAMTS13    PA-------------RWQYKLAACSVSCGRGVVRRILYCARAHGEDDGEEILLDTQCQGL    [998]
dCG4096     -----------------------------------------------------------    [1054]
ADAMTS4     -----------------------------------------------------------    [837]
ADAMTS5     -----------------------------------------------------------    [930]
ADAMTS8     -----------------------------------------------------------    [890]
ADAMTS1     -----------------------------------------------------------    [967]
ADAMTS15    -----------------------------------------------------------    [950]
dCG6107     TSD----------------WTDCSVQCGEGVKRKKQSCTRVYKPDVPGTR---KRRVYD    [1246]
ADAMTS9     AS------------WQAGPWGQCSVTCGQGYQLRAVKCIIGTYMSVVDDND----CNAA    [1151]
ADAMTS20    AS------------WQVGPWGPCTTTCGHGYQMRDVKCVNELASAVLEDTE----CHEA    [1107]
mask        -----------------------------------------------------------    [528]
Ce gon-1    TW------------WQFGVWSDCSAKCGDGVQYRDANCTDRHRSVLPEHR-----CLKM    [1171]
[Intron           59,60,61,62                               63              ]
```

[Intron phases marked 0, 1, 2]

14

```
[                       1570      1580      1590      1600      1610      1620]
[                        .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                       ]
ADAMTS6     ------------------------------------------------------------  [1117]
ADAMTS10    ------------------------------------------------------------  [1103]
ADAMTS18    QKPPVLRACNTNFCP---------------------------------------------  [1178]
ADAMTS16    QKPSASLACNTHFCP---------------------------------------------  [1182]
ADAMTS7     KEEGVLGPWSPSPWPSQAGRSPPPPSEQTPGNPLINFLPEEDTPIGAPDLGLPSLSWPRV  [1179]
ADAMTS12    GPTSEGGLVATTTSGSGLSSSRNPITWPVTPFYNTLTKGPEMEIHSGSGEEREQPEDKDE  [1170]
ADAMTS17    RQPPPSS-----------------------------------------------------  [1122]
ADAMTS19    QQKS--------------------------------------------------------  [1150]
ADAMTS2     ------------------------------------------------------------  [1119]
ADAMTS3     SDLPRSLVMPTSLVPYHSETPAKKMSLSSISSVGGPNAYAAFRPNSKPDGANLRQRSAQQ  [1136]
ADAMTS14    ------------------------------------------------------------  [1115]
ADAMTS13    PRPEPQEACSLEPCPPRWKVMSLGPCSASCGLGTARRSVACVQLDQGQDVEVDEAACAAL  [1058]
dCG4096     ------------------------------------------------------------  [1054]
ADAMTS4     ------------------------------------------------------------  [837]
ADAMTS5     ------------------------------------------------------------  [930]
ADAMTS8     ------------------------------------------------------------  [890]
ADAMTS1     ------------------------------------------------------------  [967]
ADAMTS15    ------------------------------------------------------------  [950]
dCG6107     QLQVECLGLEALSC----------------------------------------------  [1260]
ADAMTS9     TRPTDTQ----------------CSATCGKGTRMRYVSCRDENGSVADESAC-ATLPR    [1192]
ADAMTS20    SRPSDRQ----------------CSVSCGRGTQARYVSCRDALDRIADESYC-AHLPR    [1148]
mask        ------------------------------------------------------------  [528]
Ce gon-1    EKIIT-KPCHRESCPKYKLGEWSQ-CSVSCEDGWSSRRVSCVSGNGTEVDMSLC-GTASD  [1228]
[Intron                    64        65                                      ]

[                       1630      1640      1650      1660      1670      1680]
[                        .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                       ]
ADAMTS6     ------------------------------------------------------------  [1117]
ADAMTS10    ------------------------------------------------------------  [1103]
ADAMTS18    ------------------------------------------------------------  [1178]
ADAMTS16    ------------------------------------------------------------  [1182]
ADAMTS7     STDGLQTPATPESQNDFPVGKDSQSQLPPPWRDRTNEVFKDDEEPKGRGAPHLPPRPSST  [1239]
ADAMTS12    SNPVIWTKIRVPGNDAPVESTEMPLAPPLTPDLSRESWWPPFSTVMEGLLPSQRPTTSET  [1230]
ADAMTS17    ------------------------------------------------------------  [1122]
ADAMTS19    ------------------------------------------------------------  [1150]
ADAMTS2     -MPTLPVPTVAMEVRPSPSTPLEVPLNASSTNATEDHPETNAVDEPYKIHGLEDEVQPPN  [1178]
ADAMTS3     AGSKTVRLVTVPSSPPTKRVHLSSASQMAAASFFAASDSIGASSQARTSKKDGKIIDNRR  [1196]
ADAMTS14    ------------------------------------------------------------  [1115]
ADAMTS13    VRPEASVPCLIADCTYRWHVGTWMECSVSCGDGIQRRRDTCLGPQAQAPVPADFCQHLPK  [1118]
dCG4096     ------------------------------------------------------------  [1054]
ADAMTS4     ------------------------------------------------------------  [837]
ADAMTS5     ------------------------------------------------------------  [930]
ADAMTS8     ------------------------------------------------------------  [890]
ADAMTS1     ------------------------------------------------------------  [967]
ADAMTS15    ------------------------------------------------------------  [950]
dCG6107     ------------------------------------------------------------  [1260]
ADAMTS9     PVAKEE-CSVTPCGQ--WKALDWSSCSVTCGQGRATRQVMCVNYSDHVIDRSECDQDYIP  [1249]
ADAMTS20    PAEIWD-CFTP-CGE--WQAGDWSPCSASCGHGKTTRQVLCMNYHQPIDENY-CDPEVRP  [1203]
mask        ------------------------------------------------------------  [528]
Ce gon-1    RPASHQTCNLGTCPF--WRNTDWSACSVSCGIGHRERTTECIYREQSVDASF-CGDTKMP  [1285]
[Intron                              66                                      ]
```

```
[                         1690      1700      1710      1720      1730      1740]
[                           .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                                    ]
ADAMTS6    ----------------------------------------------------------- [1117]
ADAMTS10   ----------------------------------------------------------- [1103]
ADAMTS18   ----------------------------------------------------------- [1178]
ADAMTS16   ----------------------------------------------------------- [1182]
ADAMTS7    LPPLSPVGSTHSSPSPDVAELWTGGTVAWEPALEGGLGPVDSELWPTVGVASLLPPPIAP [1299]
ADAMTS12   GTPRVEGMVTEKPANTLLPLGGDHQPEPSGKTANRNHLKLPNNMNQTKSSEPVLTEEDAT [1290]
ADAMTS17   ----------------------------------------------------------- [1122]
ADAMTS19   ----------------------------------------------------------- [1150]
ADAMTS2    LIPRRPSPYEKTRNQRIQELIDEMRKKEMLGKF-------------------------- [1211]
ADAMTS3    PTRSSTLER-------------------------------------------------- [1205]
ADAMTS14   ----------------------------------------------------------- [1115]
ADAMTS13   PVTVRGCWAGPCVGQGTPSLVPHEEAAAPGRTTATPAGASLEWSQARGLLFSPAPQPRRL [1178]
dCG4096    ----------------------------------------------------------- [1054]
ADAMTS4    ----------------------------------------------------------- [837]
ADAMTS5    ----------------------------------------------------------- [930]
ADAMTS8    ----------------------------------------------------------- [890]
ADAMTS1    ----------------------------------------------------------- [967]
ADAMTS15   ----------------------------------------------------------- [950]
dCG6107    ----------------------------------------------------------- [1260]
ADAMTS9    ETDQDCSMSPCPQRTPDSGLAQHPFQNEDYRPRSAS--------PSRTHVLGGNQWRTGP [1301]
ADAMTS20   LMEQECSLAACPPAHSHFPSSPVQPSYYLSTNLPLTQKLEDNENQVVHPSVRGNQWRTGP [1263]
mask       ----------------------------------------------------------- [528]
Ce gon-1   ETSQTCHLLPCTS-------------------------------------WKPSH      [1303]
[Intron                                                                                    ]

[                         1750      1760      1770      1780      1790      1800]
[                           .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                                    ]
ADAMTS6    ----------------------------------------------------------- [1117]
ADAMTS10   ----------------------------------------------------------- [1103]
ADAMTS18   ----------------------------------------------------------- [1178]
ADAMTS16   ----------------------------------------------------------- [1182]
ADAMTS7    LPEMKVRDSSLEPGTPSFPAPGPGSWDLQTVAVWGTFLPTTLTGLGHMPEPALNPGPKGQ [1359]
ADAMTS12   SLITEGFLLNASNYKQLTNGHGSAHWIVGNWSECSTTCGLGAYWKRVECTTQMDSDCAAI [1350]
ADAMTS17   ----------------------------------------------------------- [1122]
ADAMTS19   ----------------------------------------------------------- [1150]
ADAMTS2    ----------------------------------------------------------- [1211]
ADAMTS3    ----------------------------------------------------------- [1205]
ADAMTS14   ----------------------------------------------------------- [1115]
ADAMTS13   LPGPQENSVQSSACGRQHLEPTGTIDMRGPGQADCAVAIGRPLGEVVTLRVLESSLNCSA [1238]
dCG4096    ----------------------------------------------------------- [1054]
ADAMTS4    ----------------------------------------------------------- [837]
ADAMTS5    ----------------------------------------------------------- [930]
ADAMTS8    ----------------------------------------------------------- [890]
ADAMTS1    ----------------------------------------------------------- [967]
ADAMTS15   ----------------------------------------------------------- [950]
dCG6107    ----------------------------------------------------------- [1260]
ADAMTS9    WGACSSTCAGGSQRRVVVCQDENGYTAND---CVERIKPDEQRACESGPCPQ-------- [1350]
ADAMTS20   WGSCSSSCSGGLQHRAVVCQDENGQSASY---CDAASKPPELQQCGPGPCPQ-------- [1312]
mask       ----------------------------------------------------------- [528]
Ce gon-1   WSPCSVTCGSGIQTRSVSCTRGSEGTIVDEYFCDRNTRPRLKKTCEKDTCDGPRVLQKLQ [1363]
[Intron            67        68                      69                                     ]
```

```
[                      1810      1820      1830      1840      1850      1860]
[                        .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                                    ]
 ADAMTS6     ------------------------------------------------------------     [1117]
 ADAMTS10    ------------------------------------------------------------     [1103]
 ADAMTS18    ------------------------------------------------------------     [1178]
 ADAMTS16    ------------------------------------------------------------     [1182]
 ADAMTS7     PESLSPEVPLSSRLLSTPAWDSPANSHRVPETQPLAPSLAEAGPPADPLVVRNASWQAGN     [1419]
 ADAMTS12    QRPDPAKRCHLRPCAGWKVGNWSKCSRNCSGGFKIREIQCVDSRDHRNLRPFHCQFLAGI     [1410]
 ADAMTS17    ------------------------------------------------------------     [1122]
 ADAMTS19    ------------------------------------------------------------     [1150]
 ADAMTS2     ------------------------------------------------------------     [1211]
 ADAMTS3     ------------------------------------------------------------     [1205]
 ADAMTS14    ------------------------------------------------------------     [1115]
 ADAMTS13    GDMLLLWGRLTWRKMCRKLLDMTFSSKTNTLVVRQRCGRPGGGVLLRYGSQLAPETFYRE     [1298]
 dCG4096     ------------------------------------------------------------     [1054]
 ADAMTS4     ------------------------------------------------------------     [837]
 ADAMTS5     ------------------------------------------------------------     [930]
 ADAMTS8     ------------------------------------------------------------     [890]
 ADAMTS1     ------------------------------------------------------------     [967]
 ADAMTS15    ------------------------------------------------------------     [950]
 dCG6107     ------------------------------------------------------------     [1260]
 ADAMTS9     -------WAYGNWGECTKLCGGGIRTRLVVCQRSNGERFPDLSCEILDKPPDREQCNTHA     [1403]
 ADAMTS20    -------WNYGNWGECSQTCGGGIKSRLVICQFPNGQILEDHNCEIVNKPPSVIQCHMHA     [1365]
 mask        ------------------------------------------------------------     [528]
 Ce gon-1    ADVPPIRWATGPWTACSATCGNGTQRRLLKCRDHVRDLPDEY-CNHLDKEVSTRNCRLRD     [1422]
[Intron       70               71                                               ]

[                      1870      1880      1890      1900      1910      1920]
[                        .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                                    ]
 ADAMTS6     ------------------------------------------------------------     [1117]
 ADAMTS10    ------------------------------------------------------------     [1103]
 ADAMTS18    ------------------------------------------------------------     [1178]
 ADAMTS16    ------------------------------------------------------------     [1182]
 ADAMTS7     WSECSTTCGLGAVWRPVRCSSGRDEDCAPAGRPQPARRCHLRPCAT--------------     [1465]
 ADAMTS12    PPPLSMSCNPEPCEAWQVEPWSQCSRSCGGGVQERGVFCPGGLCDWTKRPTSTMSCNEHL     [1470]
 ADAMTS17    ------------------------------------------------------------     [1122]
 ADAMTS19    ------------------------------------------------------------     [1150]
 ADAMTS2     ------------------------------------------------------------     [1211]
 ADAMTS3     ------------------------------------------------------------     [1205]
 ADAMTS14    ------------------------------------------------------------     [1115]
 ADAMTS13    CDMQLFGPWGEIVSPSLSPATSNAGGCRLFINVAPHARIAIHALATNMGAGTEGANASYI     [1358]
 dCG4096     ------------------------------------------------------------     [1054]
 ADAMTS4     ------------------------------------------------------------     [837]
 ADAMTS5     ------------------------------------------------------------     [930]
 ADAMTS8     ------------------------------------------------------------     [890]
 ADAMTS1     ------------------------------------------------------------     [967]
 ADAMTS15    ------------------------------------------------------------     [950]
 dCG6107     ------------------------------------------------------------     [1260]
 ADAMTS9     CPHDAAWSTGPWSSCSVSCGRGHKQRNVY-CMAKDGSHLESDY---CKHLAKPHGHRKCR     [1459]
 ADAMTS20    CPADVSWHQEPWTSCSASCGKGRKYREVF-CIDQFQRKLEDTN---CSQVQKPPTHKACR     [1421]
 mask        ------------------------------------------------------------     [528]
 Ce gon-1    CSY---WKMAEWEECPATCGTHVQQSRNVTCVSAEDGGRTILKDVDCDVQKRPTSARNCR     [1479]
[Intron       72                                                                ]
```

```
[                     1930      1940      1950      1960      1970      1980]
[                       .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                      ]
ADAMTS6     ------------------------------------------------------------  [1117]
ADAMTS10    ------------------------------------------------------------  [1103]
ADAMTS18    ------------------------------------------------------------  [1178]
ADAMTS16    ------------------------------------------------------------  [1182]
ADAMTS7     ------------WHSGNWSKCSRSCGGGSSVRDVQCVDTRDLRPLRPFHCQPGPAKPPA  [1512]
ADAMTS12    CCH----------WATGNWDLCSTSCGGGFQKRIVQCVPSEGNKTEDQDQCLCDHKPRPP  [1520]
ADAMTS17    ------------------------------------------------------------  [1122]
ADAMTS19    ------------------------------------------------------------  [1150]
ADAMTS2     ------------------------------------------------------------  [1211]
ADAMTS3     ------------------------------------------------------------  [1205]
ADAMTS14    ------------------------------------------------------------  [1115]
ADAMTS13    LLRDTHSLRTTAFHGQQVLYWESESSQAEMEFSEGFLKAQASLRGQYWTLQSWVPEMQDP  [1418]
dCG4096     ------------------------------------------------------------  [1054]
ADAMTS4     ------------------------------------------------------------   [837]
ADAMTS5     ------------------------------------------------------------   [930]
ADAMTS8     ------------------------------------------------------------   [890]
ADAMTS1     ------------------------------------------------------------   [967]
ADAMTS15    ------------------------------------------------------------   [950]
dCG6107     ------------------------------------------------------------  [1260]
ADAMTS9     GGRCPK-------WKAGAWSQCSVSCGRGVQQRHVGCQIGTHKIARETECNPYTRPESER  [1512]
ADAMTS20    SVRCPS-------WKANSWNECSVTCGSGVQQRDVYCRLKGVGQVVEEMCDQSTRPCSQR  [1474]
mask        ------------------------------------------------------------   [528]
Ce gon-1    LEPCPKGEEHIGSWIIGDWSKCSASCGGGWRRRSVSCTSSSCDETRKPKMFDKCNEELCP  [1539]
[Intron        73                    74                                   ]
[                     1990      2000      2010      2020      2030      2040]
[                       .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                      ]
ADAMTS6     ------------------------------------------------------------  [1117]
ADAMTS10    ------------------------------------------------------------  [1103]
ADAMTS18    ------------------------------------------------------------  [1178]
ADAMTS16    ------------------------------------------------------------  [1182]
ADAMTS7     HRPCGAQPCLSWYTSSWRECSEACGGGEQQRLVTCPEPGL-------CEEALRPNTTRPC  [1565]
ADAMTS12    EFKKCNQQACKKSADLLCTKDKLSASFCQTLKAMKKCSVPTVRAECCFSCPQTHITHTQR  [1580]
ADAMTS17    ------------------------------------------------------------  [1122]
ADAMTS19    ------------------------------------------------------------  [1150]
ADAMTS2     ------------------------------------------------------------  [1211]
ADAMTS3     ------------------------------------------------------------  [1205]
ADAMTS14    ------------------------------------------------------------  [1115]
ADAMTS13    QSWKGKEGT---------------------------------------------------  [1427]
dCG4096     ------------------------------------------------------------  [1054]
ADAMTS4     ------------------------------------------------------------   [837]
ADAMTS5     ------------------------------------------------------------   [930]
ADAMTS8     ------------------------------------------------------------   [890]
ADAMTS1     ------------------------------------------------------------   [967]
ADAMTS15    ------------------------------------------------------------   [950]
dCG6107     ------------------------------------------------------------  [1260]
ADAMTS9     DCQGPRCPLYTWRAEEWQECTKTCGEGSRYRKVVCVDDNKNEVHGARCDVSKRPVDRESC  [1572]
ADAMTS20    RC--------WSQDCVQHKGMERGRLNCANNCGFSYRQRITYCTEIPSTKKHKLHRLRP  [1525]
mask        ------------------------------------------------------------   [528]
Ce gon-1    PLTNNS-----WQISPWTHCSVSCGGGVQRRKIWCEDVLSGRKQDDIECSEIKPREQRDC  [1594]
[Intron                          75                                         ]
```

18

```
[                      2050      2060      2070      2080      2090      2100]
[                       .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                      ]
 ADAMTS6     ------------------------------------------------------------    [1117]
 ADAMTS10    ------------------------------------------------------------    [1103]
 ADAMTS18    ------------------------------------------------------------    [1178]
 ADAMTS16    ------------------------------------------------------------    [1182]
 ADAMTS7     NTHPCTQ-WVVGPWGQCSAPCGGGVQRRLVKCVNTQTGLPEEDSDQCGHEAWPESSRPCG    [1624]
 ADAMTS12    QRRQRLLQKSKEL-----------------------------------------------    [1593]
 ADAMTS17    ------------------------------------------------------------    [1122]
 ADAMTS19    ------------------------------------------------------------    [1150]
 ADAMTS2     ------------------------------------------------------------    [1211]
 ADAMTS3     ------------------------------------------------------------    [1205]
 ADAMTS14    ------------------------------------------------------------    [1115]
 ADAMTS13    ------------------------------------------------------------    [1427]
 dCG4096     ------------------------------------------------------------    [1054]
 ADAMTS4     ------------------------------------------------------------    [837]
 ADAMTS5     ------------------------------------------------------------    [930]
 ADAMTS8     ------------------------------------------------------------    [890]
 ADAMTS1     ------------------------------------------------------------    [967]
 ADAMTS15    ------------------------------------------------------------    [950]
 dCG6107     ------------------------------------------------------------    [1260]
 ADAMTS9     SLHPCEYVWITGEWSECSVTCGKGYKQRLVSCSEIYTGKENYEYSSQTTINCPGTQPPSV    [1632]
 ADAMTS20    IVYQECPVVPSSQVYQCINSCLHLATWKVGKWSKCSVTCGIGIMKRQVKCITKHGLSSDL    [1585]
 mask        ------------------------------------------------------------    [528]
 Ce gon-1    EMPPCRSHYHNKTSSASMTSLSSSNSNTTSSASASSLPILPPVVSWQTSAWSACSAKCGR    [1654]
[Intron                                  76                                  ]

[                      2110      2120      2130      2140      2150      2160]
[                       .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                      ]
 ADAMTS6     ------------------------------------------------------------    [1117]
 ADAMTS10    ------------------------------------------------------------    [1103]
 ADAMTS18    --------------------------------------------------APEKREDPS    [1187]
 ADAMTS16    --------------------------------------------------IAEKKDAF-    [1190]
 ADAMTS7     TEDCEPVEPPRCERDRLSFGFCETLRLLGRCQLPTIRTQCCRSCSPPSHGAPSRGHQRVA    [1684]
 ADAMTS12    ------------------------------------------------------------    [1593]
 ADAMTS17    ------------------------------------------------------------    [1122]
 ADAMTS19    ------------------------------------------------------------    [1162]
 ADAMTS2     ------------------------------------------------------------    [1211]
 ADAMTS3     ------------------------------------------------------------    [1205]
 ADAMTS14    ------------------------------------------------------------    [1115]
 ADAMTS13    ------------------------------------------------------------    [1427]
 dCG4096     ------------------------------------------------------------    [1054]
 ADAMTS4     ------------------------------------------------------------    [837]
 ADAMTS5     ------------------------------------------------------------    [930]
 ADAMTS8     ------------------------------------------------------------    [890]
 ADAMTS1     ------------------------------------------------------------    [967]
 ADAMTS15    ------------------------------------------------------------    [950]
 dCG6107     ------------------------------------------------------------    [1260]
 ADAMTS9     HPCYLRDCPVSATWRVGNWGSCSVSCGVGVMQRSVQCLNNAVQPSHLCRSDLKPEERKTC    [1692]
 ADAMTS20    CLNHLKPGAQKKCYANDCKS----------------------------FTTCKEIQV     [1614]
 mask        ------------------------------------------------------------    [528]
 Ce gon-1    GTKRRVVECVNPSLNVTVASTECDQTKKPVEEVRCRTKHCPRWKTTTWSSCSVTCGRGIR    [1714]
[Intron                            77   78                          79        ]
```

19

```
[                     2170      2180      2190      2200      2210      2220]
[                       .         .         .         .         .        .]
[Modal, ≥80%, full maj.                                                    ]
ADAMTS6    ------------------------------------------------------------  [1117]
ADAMTS10   ------------------------------------------------------------  [1103]
ADAMTS18   CVDFFNWCHLVPQHGVCNHKFYGKQCCKSCTRKI--------------------------  [1221]
ADAMTS16   CKDYFHWCYLVPQHGMCSHKFYGKQCCKTCSKSNL--------------------------  [1225]
ADAMTS7    RR----------------------------------------------------------  [1686]
ADAMTS12   ------------------------------------------------------------  [1593]
ADAMTS17   ------------------------------------------------------------  [1122]
ADAMTS19   ------------------------------------------------------------  [1207]
ADAMTS2    ------------------------------------------------------------  [1211]
ADAMTS3    ------------------------------------------------------------  [1205]
ADAMTS14   ------------------------------------------------------------  [1115]
ADAMTS13   ------------------------------------------------------------  [1427]
dCG4096    ------------------------------------------------------------  [1054]
ADAMTS4    ------------------------------------------------------------  [837]
ADAMTS5    ------------------------------------------------------------  [930]
ADAMTS8    ------------------------------------------------------------  [890]
ADAMTS1    ------------------------------------------------------------  [967]
ADAMTS15   ------------------------------------------------------------  [950]
dCG6107    ------------------------------------------------------------  [1260]
ADAMTS9    RNVYN-------------------------------------------------------  [1697]
ADAMTS20   KN-HIRKDGDYYLNIKGRIIKVL-------------------------------------  [1636]
mask       ------------------------------------------------------------  [528]
Ce gon-1   RREVQCYRGRKNLVSDSECNPKTKLNSVANCFPVACPAYRWNVTPWSKCKDECARGQKQT  [1774]

[                     2230      2240      2250      2260      2270      2280]
[                       .         .         .         .         .        .]
[Modal, ≥80%, full maj.                                                    ]
ADAMTS6    ------------------------------------------------------------  [1117]
ADAMTS10   ------------------------------------------------------------  [1103]
ADAMTS18   ------------------------------------------------------------  [1221]
ADAMTS16   ------------------------------------------------------------  [1225]
ADAMTS7    ------------------------------------------------------------  [1686]
ADAMTS12   ------------------------------------------------------------  [1593]
ADAMTS17   ------------------------------------------------------------  [1122]
ADAMTS19   ------------------------------------------------------------  [1207]
ADAMTS2    ------------------------------------------------------------  [1211]
ADAMTS3    ------------------------------------------------------------  [1205]
ADAMTS14   ------------------------------------------------------------  [1115]
ADAMTS13   ------------------------------------------------------------  [1427]
dCG4096    ------------------------------------------------------------  [1054]
ADAMTS4    ------------------------------------------------------------  [837]
ADAMTS5    ------------------------------------------------------------  [930]
ADAMTS8    ------------------------------------------------------------  [890]
ADAMTS1    ------------------------------------------------------------  [967]
ADAMTS15   ------------------------------------------------------------  [950]
dCG6107    ------------------------------------------------------------  [1260]
ADAMTS9    ------------------------------------------------------------  [1697]
ADAMTS20   ------------------------------------------------------------  [1636]
mask       ------------------------------------------------------------  [528]
Ce gon-1   RRVHCISTSGKRAAPRMCELARAPTSIRECDTSNCPYEWVPGDWQTCSKSCGEGVQTREV  [1834]
```

```
[                     2290      2300      2310      2320      2330      2340]
[                       .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                    ]
ADAMTS6      ------------------------------------------------------------ [1117]
ADAMTS10     ------------------------------------------------------------ [1103]
ADAMTS18     ------------------------------------------------------------ [1221]
ADAMTS16     ------------------------------------------------------------ [1225]
ADAMTS7      ------------------------------------------------------------ [1686]
ADAMTS12     ------------------------------------------------------------ [1593]
ADAMTS17     ------------------------------------------------------------ [1122]
ADAMTS19     ------------------------------------------------------------ [1207]
ADAMTS2      ------------------------------------------------------------ [1211]
ADAMTS3      ------------------------------------------------------------ [1205]
ADAMTS14     ------------------------------------------------------------ [1115]
ADAMTS13     ------------------------------------------------------------ [1427]
dCG4096      ------------------------------------------------------------ [1054]
ADAMTS4      ------------------------------------------------------------ [837]
ADAMTS5      ------------------------------------------------------------ [930]
ADAMTS8      ------------------------------------------------------------ [890]
ADAMTS1      ------------------------------------------------------------ [967]
ADAMTS15     ------------------------------------------------------------ [950]
dCG6107      ------------------------------------------------------------ [1260]
ADAMTS9      ------------------------------------------------------------ [1697]
ADAMTS20     ------------------------------------------------------------ [1636]
mask         ------------------------------------------------------------ [528]
Ce gon-1     RCRRKINFNSTIPIIFMLEDEPAVPKEKCELFPKPNESQTCELNPCDSEFKWSFGPWGEC [1894]

[                     2350      2360      2370      2380      2390      2400]
[                       .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                    ]
ADAMTS6      ------------------------------------------------------------ [1117]
ADAMTS10     ------------------------------------------------------------ [1103]
ADAMTS18     ------------------------------------------------------------ [1221]
ADAMTS16     ------------------------------------------------------------ [1225]
ADAMTS7      ------------------------------------------------------------ [1686]
ADAMTS12     ------------------------------------------------------------ [1593]
ADAMTS17     ------------------------------------------------------------ [1122]
ADAMTS19     ------------------------------------------------------------ [1207]
ADAMTS2      ------------------------------------------------------------ [1211]
ADAMTS3      ------------------------------------------------------------ [1205]
ADAMTS14     ------------------------------------------------------------ [1115]
ADAMTS13     ------------------------------------------------------------ [1427]
dCG4096      ------------------------------------------------------------ [1054]
ADAMTS4      ------------------------------------------------------------ [837]
ADAMTS5      ------------------------------------------------------------ [930]
ADAMTS8      ------------------------------------------------------------ [890]
ADAMTS1      ------------------------------------------------------------ [967]
ADAMTS15     ------------------------------------------------------------ [950]
dCG6107      ------------------------------------------------------------ [1260]
ADAMTS9      ------------------------------------------------------------ [1697]
ADAMTS20     ------------------------------------------------------------ [1636]
mask         ------------------------------------------------------------ [528]
Ce gon-1     SKNCGQGIRRRRVKCVANDGRRVERVKCTTKKPRRTQYCFERNCLPSTCQELKSQNVKAK [1954]
```

```
[                    2410      2420      2430      2440      2450      2460]
[                      .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                                    ]
ADAMTS6      ------------------------------------------------------------ [1117]
ADAMTS10     ------------------------------------------------------------ [1103]
ADAMTS18     ------------------------------------------------------------ [1221]
ADAMTS16     ------------------------------------------------------------ [1225]
ADAMTS7      ------------------------------------------------------------ [1686]
ADAMTS12     ------------------------------------------------------------ [1593]
ADAMTS17     ------------------------------------------------------------ [1122]
ADAMTS19     ------------------------------------------------------------ [1207]
ADAMTS2      ------------------------------------------------------------ [1211]
ADAMTS3      ------------------------------------------------------------ [1205]
ADAMTS14     ------------------------------------------------------------ [1115]
ADAMTS13     ------------------------------------------------------------ [1427]
dCG4096      ------------------------------------------------------------ [1054]
ADAMTS4      ------------------------------------------------------------ [837]
ADAMTS5      ------------------------------------------------------------ [930]
ADAMTS8      ------------------------------------------------------------ [890]
ADAMTS1      ------------------------------------------------------------ [967]
ADAMTS15     ------------------------------------------------------------ [950]
dCG6107      ------------------------------------------------------------ [1260]
ADAMTS9      ------------------------------------------------------------ [1697]
ADAMTS20     ------------------------------------------------------------ [1636]
mask         ------------------------------------------------------------ [528]
Ce gon-1     DGNYTILLDGFTIEIYCHRMNSTIPKAYLNVPRTNFAEVYGKKLIYPHTCPFNGDRNDS [2014]

[                    2470      2480      2490      2500      2510      2520]
[                      .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                                    ]
ADAMTS6      ------------------------------------------------------------ [1117]
ADAMTS10     ------------------------------------------------------------ [1103]
ADAMTS18     ------------------------------------------------------------ [1221]
ADAMTS16     ------------------------------------------------------------ [1225]
ADAMTS7      ------------------------------------------------------------ [1686]
ADAMTS12     ------------------------------------------------------------ [1593]
ADAMTS17     ------------------------------------------------------------ [1122]
ADAMTS19     ------------------------------------------------------------ [1207]
ADAMTS2      ------------------------------------------------------------ [1211]
ADAMTS3      ------------------------------------------------------------ [1205]
ADAMTS14     ------------------------------------------------------------ [1115]
ADAMTS13     ------------------------------------------------------------ [1427]
dCG4096      ------------------------------------------------------------ [1054]
ADAMTS4      ------------------------------------------------------------ [837]
ADAMTS5      ------------------------------------------------------------ [930]
ADAMTS8      ------------------------------------------------------------ [890]
ADAMTS1      ------------------------------------------------------------ [967]
ADAMTS15     ------------------------------------------------------------ [950]
dCG6107      ------------------------------------------------------------ [1260]
ADAMTS9      ------------------------------------------------------------ [1697]
ADAMTS20     ------------------------------------------------------------ [1636]
mask         ------------------------------------------------------------ [528]
Ce gon-1     CHCSEDGDASAGLTRFNKVRIDLLNRKFHLADYTFAKREYGVHVPYGTAGDCYSMKDCPQ [2074]
```

```
[                       2530      2540      2550      2560      2570      2580]
[                         .         .         .         .         .         .]
[Modal, ≥80%, full maj.                                                      ]
ADAMTS6     --------------------------------------------------------    [1117]
ADAMTS10    --------------------------------------------------------    [1103]
ADAMTS18    --------------------------------------------------------    [1221]
ADAMTS16    --------------------------------------------------------    [1225]
ADAMTS7     --------------------------------------------------------    [1686]
ADAMTS12    --------------------------------------------------------    [1593]
ADAMTS17    --------------------------------------------------------    [1122]
ADAMTS19    --------------------------------------------------------    [1207]
ADAMTS2     --------------------------------------------------------    [1211]
ADAMTS3     --------------------------------------------------------    [1205]
ADAMTS14    --------------------------------------------------------    [1115]
ADAMTS13    --------------------------------------------------------    [1427]
dCG4096     --------------------------------------------------------    [1054]
ADAMTS4     --------------------------------------------------------    [837]
ADAMTS5     --------------------------------------------------------    [930]
ADAMTS8     --------------------------------------------------------    [890]
ADAMTS1     --------------------------------------------------------    [967]
ADAMTS15    --------------------------------------------------------    [950]
dCG6107     --------------------------------------------------------    [1260]
ADAMTS9     --------------------------------------------------------    [1697]
ADAMTS20    --------------------------------------------------------    [1636]
mask        --------------------------------------------------------    [528]
Ce gon-1    GIFSIDLKSAGLKLVDDLNWEDQGHRTSSRIDRFYNNAKVIGHCGGFCGKCSPERYKGLI [2134]

[                       2590      2600      2610]
[                         .         .         . ]
[Modal, ≥80%, full maj.                         ]
ADAMTS6     ----------------------------    [1117]
ADAMTS10    ----------------------------    [1103]
ADAMTS18    ----------------------------    [1221]
ADAMTS16    ----------------------------    [1225]
ADAMTS7     ----------------------------    [1686]
ADAMTS12    ----------------------------    [1593]
ADAMTS17    ----------------------------    [1122]
ADAMTS19    ----------------------------    [1207]
ADAMTS2     ----------------------------    [1211]
ADAMTS3     ----------------------------    [1205]
ADAMTS14    ----------------------------    [1115]
ADAMTS13    ----------------------------    [1427]
dCG4096     ----------------------------    [1054]
ADAMTS4     ----------------------------    [837]
ADAMTS5     ----------------------------    [930]
ADAMTS8     ----------------------------    [890]
ADAMTS1     ----------------------------    [967]
ADAMTS15    ----------------------------    [950]
dCG6107     ----------------------------    [1260]
ADAMTS9     ----------------------------    [1697]
ADAMTS20    ----------------------------    [1636]
mask        ----------------------------    [528]
Ce gon-1    FEVNTKLLNHVKNGGHIDDELDDDGFSGDMD [2165]
;
END;
```