

A

<i>DmCSN6</i>	1	--MEQM---EVDVDM-----SAKPS---TSSSAAAGSSMAVDKTDQNPO	37
<i>BmCSN6</i>	1	--MSSAD---RIDFEM-----EV-----EVESASSGPPIEVNPNTSPAPT	35
<i>AgCSN6</i>	1	TMSQPTTEKMDIDNESASATSTSTASAAAMPPTASTSKAASPPAVSDMEVASGSSGKPV	60
<i>BtCSN6</i>	1	---MA---AT-----AA-----AANGTGGSSGMEVDA-----	21
<i>MmCSN6</i>	1	---MAA---AA-----AA-----GANGSGSSGMEVDA-----	22
<i>HsCSN6</i>	1	---MAAAA---AA-----AA-----ATNGTGGSSGMEVDA-----	24
<i>XlCSN6</i>	1	-----MAAAASNGNGMEVDV-----	15
<i>DrCSN6</i>	1	-----	0
<i>SmCSN6</i>	1	-----MEVDI-----	5
<i>OsCSN6</i>	1	-----MS--APSD--PA-----	8
<i>AtCSN6</i>	1	-----	0
<i>DmCSN6</i>	38	P---QGNIMAAAGTSGSVTISLHPLVIMNISEHWTRFRAQH-----	76
<i>BmCSN6</i>	36	TPGS--NKSVVVTTATAGSVTVSLHPLVIMNVSEHWTRLKAQEG-----	77
<i>AgCSN6</i>	61	PVQPEGRNVMASSATIPSVTCSLHPLVIMNIADHWTRNRQKS-----	103
<i>BtCSN6</i>	22	---A--VVPVSMASGVTGVSVALHPLVILNISDHWIRMRSEQ-----	60
<i>MmCSN6</i>	23	---A--VPSVMASGVTGVSVALHPLVILNISDHWIRMRSEQ-----	60
<i>HsCSN6</i>	25	---A--VVPVSMACGVTGVSVALHPLVILNISDHWIRMRSEQ-----	63
<i>XlCSN6</i>	16	---A--ALPSVMAQGVGTGVSVALHPLVILNISDHWIRMRSEQ-----	54
<i>DrCSN6</i>	1	---MASGVTGVSVALHPLVILNISDHWIRMRSEQ-----	33
<i>SmCSN6</i>	6	---NVDVSNVTSGTGSASVLLHPLVILNISDHWIRMRSEQ-----	43
<i>OsCSN6</i>	9	VATHPQAGAAAASSSGLTFKLHPLVIVNVSDHTRVKAQAACS-----GDGAS--SAA	61
<i>AtCSN6</i>	1	-----MAPSSSSGLTFKLHPLVILNISDHWIRMRSEQ-----	50
<i>DmCSN6</i>	77	---EPRQVYGALIGKQKGRNIEIMNSFELKTDVIGDETINKDYNNKKEQYKQVFSDDL	133
<i>BmCSN6</i>	78	---FPQTVVGALIGKQKGRNIEVMNSFELVFSMIDGDIIDRDYNNKKEQYKQVFSMD	134
<i>AgCSN6</i>	104	---SRPLIFGALIGKQKGRNIEVMNSFELKYDIVNDVAVIAMDYQVKEEQYKQVFSDDL	160
<i>BtCSN6</i>	61	---RPMQVIGALIGKQKGRNIEVMNSFELLSHTVEEKIIIDKEYYYTKEEQYKQVFSKELD	117
<i>MmCSN6</i>	61	---RPMQVIGALIGKQKGRNIEVMNSFELLSHTVEEKIIIDKEYYYTKEEQYKQVFSKELE	117
<i>HsCSN6</i>	64	---RPVQVIGALIGKQKGRNIEVMNSFELLSHTVEEKIIIDKEYYYTKEEQYKQVFSKELE	120
<i>XlCSN6</i>	55	---RPMQVIGALIGKQKGRNIEVMNSFELLSQINDEKITINKEYYYTKEEQYKQVFSKOME	111
<i>DrCSN6</i>	34	---RAVQVYGALIGKQKGRNIEVMNSFELLSHTVEEKIIIDKEYYYTKEEQYKQVFSKEME	90
<i>SmCSN6</i>	44	---SISVTYVYGALIGKQKGRNIEVMNSFELLSHTVEEKIIIDKEYYYTKEEQYKQVFSKEME	99
<i>OsCSN6</i>	62	AGGQPPRVFGCVIGVGRGTVEIFNSFELVLDPVSG--TLDRAFLEKKQELYKKVFPDFY	119
<i>AtCSN6</i>	51	MLLQNPVRYGCVIGVGRGTVEIFNSFELVLDPVSG--TLDRSFLEKKQELYKKVFPDFY	108
<i>DmCSN6</i>	134	FIGWYTTGDNPTADDIKIQRIAAINECPIMLQNLPLRS--VDHLPLKLFESLIDLVDG	191
<i>BmCSN6</i>	135	FLGWYTTGDAPSERDIAVHRQICDINECPVMLMLNPAGRN--GDQLPVVLYESVIDVNG	192
<i>AgCSN6</i>	161	FLGWYTTDTPSEKHINIHQICEINECPMLMLLDPLNRMNVRRLPISLYESVIDIVQG	220
<i>BtCSN6</i>	118	FLGWYTTGGPPDPDSIHVHKQVCEIIESPLFLKLNPMTKH---TDLPVSVFESVIDIING	174
<i>MmCSN6</i>	118	FLGWYTTGGPPDPDSIHVHKQVCEIIESPLFLKLNPMTKH---TDLPVSVFESVIDIING	174
<i>HsCSN6</i>	121	FLGWYTTGGPPDPDSIHVHKQVCEIIESPLFLKLNPMTKH---TDLPVSVFESVIDIING	177
<i>XlCSN6</i>	112	FLGWYTTGGTPDPDSIHVHKQVCEIIESPLFLKLNPMTKH---TDLPVSVFESVIDIING	168
<i>DrCSN6</i>	91	FLGWYTTGGSPDQSDIHVHKQVCEIIESPLFLKLNPMTKH---TDLPVSVFESVIDIISG	147
<i>SmCSN6</i>	100	IVGWYTTGGAINKEDELFRQMLNLSLLIKLDPQLTC--GENLPVIGVSVVD--N	154
<i>OsCSN6</i>	120	VLGWYSTGSDVRDMDQIHKALMDINESPVYLLNPAINL--SQKDLPTVITYESELHVIDG	178
<i>AtCSN6</i>	109	VLGWYSTGSDATESDMHIKALMDINESPVYLLNPAINH--AQKDLPTVITYESELHVIDG	167
<i>DmCSN6</i>	192	EATMLFVPLTYTLATEEAERIGVDHVARMTSNESGE--KSVVAEHLVAQDSAIAKMLNTRIK	250
<i>BmCSN6</i>	193	RATMLLAPLTYTLAAEEAERIGVDHVARVSSGEAAL--NSLVAEHLTAQSAIAKMLVSRVR	251
<i>AgCSN6</i>	221	QAMMLFVPLVYTLATEEAERIGVDHVARMSNNDTDA--NSTVAEHLAQYNAIAKMLNSRVK	279
<i>BtCSN6</i>	175	EATMLFAELTYTLATEEAERIGVDHVARMTATGSGE--NSTVAEHLIAQHSIAKMLHSRVK	233
<i>MmCSN6</i>	175	EATMLFAELTYTLATEEAERIGVDHVARMTATGSGE--NSTVAEHLIAQHSIAKMLHSRVK	233
<i>HsCSN6</i>	178	EATMLFAELTYTLATEEAERIGVDHVARMTATGSGE--NSTVAEHLIAQHSIAKMLHSRVK	236
<i>XlCSN6</i>	169	EATMLLAELSYTLATEEAERIGVDHVARMTATGSGE--NSTVAEHLIAQHSIAKMLHSRVK	227
<i>DrCSN6</i>	148	EATMLFAELPYTLATEEAERIGVDHVARMTATGGE--NSTVAEHLIAQHSIAKMLHSRVK	206
<i>SmCSN6</i>	155	DGRVHFROVLYTLATEEAERIGVDYVARISMSSTDQTSMTAEHLLGNYQAIQMLSSRLQ	214
<i>OsCSN6</i>	179	SPQLIFVRANYTITVEAERISVDHVAHLKPSDGGSAATQLAAHLTGHSIAKMLNSRVK	238
<i>AtCSN6</i>	168	IPQSIFVHTSYTITVEAERISVDHVAHLKPSDGGSAATQLAAHLTGHSIAKMLNSRVK	227
<i>DmCSN6</i>	251	IVLQYIRDVEAGKLRANQEILREAYALCHRLPVMQVPA--FQEEFYTQCNDVGLISYLG	308
<i>BmCSN6</i>	252	AVLATVRAIRDGKLQPRPALLREARALANRLPLTSSQ--FRTHFYQCNDVALMTYLG	309
<i>AgCSN6</i>	280	IILAYIKAVENDQKPNQEIILRMAYSLSRRLPIVQNPS--FKEEFYTQSNQNDVGLITYLGA	337
<i>BtCSN6</i>	234	LILEYVKASEAGEVPPFNHEILREAYALCHCLPVLSTDK--FKTDFYDQCNDVGLMAYLGT	291
<i>MmCSN6</i>	234	LILEYVKASEAGEVPPFNHEILREAYALCHCLPVLSTDK--FKTDFYDQCNDVGLMAYLGT	291
<i>HsCSN6</i>	237	LILEYVKASEAGEVPPFNHEILREAYALCHCLPVLSTDK--FKTDFYDQCNDVGLMAYLGT	294
<i>XlCSN6</i>	228	LILEYVRAAEGGEVPPFNHEILREASALCHCLPVLSTDK--FKTDFYDQCNDVGLMAYLGT	285
<i>DrCSN6</i>	207	VILEYVKAQAGEVPPFNHEILREANALCHRLPVLNTLK--FKTDFYDQCNDVGLMAYLGT	264
<i>SmCSN6</i>	215	LIRSYVAVAAGELPPNARLREINLVKRIPFMPSSAAEQNDNLRYQANDVCLTALLAS	274
<i>OsCSN6</i>	239	VIHQYLVSMQKGDMPDNLNLLRQVSSLVRLPAMESEK--FQDDFLMEYNDTLLMTYLAM	296
<i>AtCSN6</i>	228	VLYQHIVAMQKGDMPDNLNLLRQVSSLVRLPAMESEK--FQDDFLMEYNDKLLMSYLAM	285
<i>DmCSN6</i>	309	LTGKCNMDMHFVNKFNMLYDRQGSARRMRGLFY-----	341
<i>BmCSN6</i>	310	ITKGCNAINQLVNRFNVLVYDRQGMGRMRGLFF-----	342
<i>AgCSN6</i>	338	LTQVANDMNLVNFVNLVYDRQAMGRRLRGLFF-----	370
<i>BtCSN6</i>	292	ITKTCNTMNQFVNKFNVLVYDRQIGRRMRGLFF-----	324
<i>MmCSN6</i>	292	ITKTCNTMNQFVNKFNVLVYDRQIGRRMRGLFF-----	324
<i>HsCSN6</i>	295	ITKTCNTMNQFVNKFNVLVYDRQIGRRMRGLFF-----	327
<i>XlCSN6</i>	286	ITKTCNTMNQFVNKFNVLVYDRQIGRRMRGLFF-----	318
<i>DrCSN6</i>	265	ITKTCNSMNQFVNKFNVLVYDRQIGRRMRGLFF-----	297
<i>SmCSN6</i>	275	ITQGLHTLYGCMVKTSHVIDRRSIPLSVSGSMDSGSSRFKVSMSMGNSN	325
<i>OsCSN6</i>	297	FTNCSSTMNELVEKFNATYERSTARRGGGAFM-----	329
<i>AtCSN6</i>	286	ITNCTNSNMNEVVDFKFNATYDKH--SRGGRTAFM-----	317

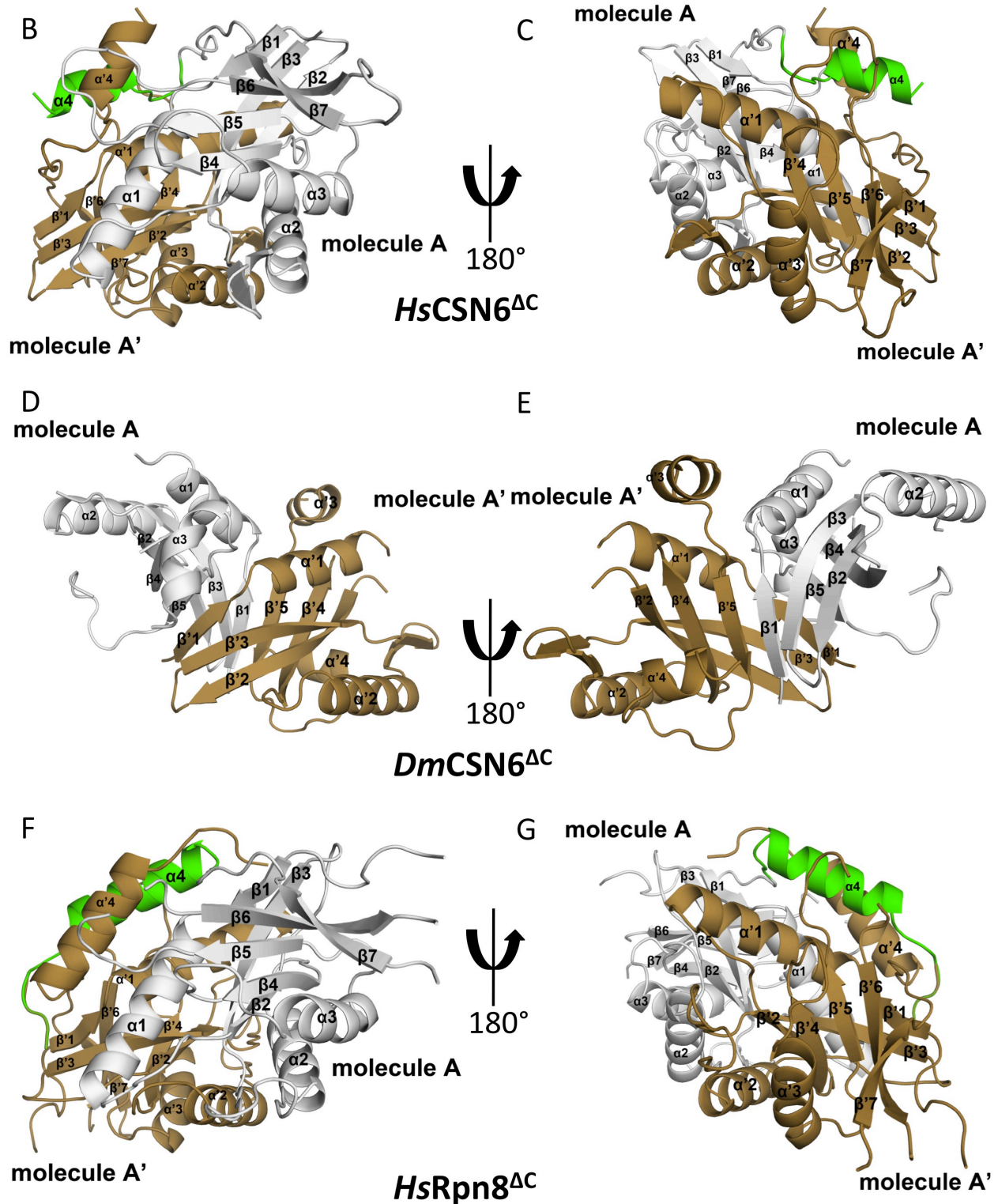


Figure S4. CSN6 sequences and MPN domain structure. (A) Sequence alignment of human CSN6 and CSN6 sequences from 10 diverse representative organisms. To obtain this sequence alignment, CSN6 sequences were retrieved with a Blastp step using human CSN6 as the search and 10 diverse sequences from representative organisms were selected in addition to the human one. A multiple sequence alignment using these eleven sequences was done with the Clustal Omega server (default parameters). This procedure was entirely carried out on the Uniprot website (www.uniprot.org). *Dm*: *Drosophila*

melanogaster (Uniprot entry: Q9VCY3); *Bm: Bombyx mori* (Uniprot entry: Q2F614); *Ag: Anopheles gambiae* (Uniprot entry: Q7Q421); *Bt: Bos taurus* (Uniprot entry: A6QQ21); *Mm: Mus musculus* (Uniprot entry: Q3UIT2); *Hs: Homo sapiens* (Uniprot entry: Q7L5N1); *Xl: Xenopus laevis* (Uniprot entry: Q6NUC2); *Dr: Danio rerio* (Uniprot entry: Q567F8); *Sm: Schistosoma mansoni* (Uniprot entry: G4V7G0); *Os: Oryza sativa* (Uniprot entry: Q6ZKM2); *At: Arabidopsis thaliana* (Uniprot entry: Q8W1P0). A “*” sign indicates a residue strictly conserved among the eleven selected sequences. The residues H44 and V115 discussed in the text are highlighted with an orange box and CSN6 residues involved in the CSN5ΔC/CSN6ΔC complex that we propose in this study are boxed in blue. **(B-G) Illustration of (B,C) human CSN6^{ΔC}, (D,E) DmCSN6 fragment (residues 51-187) and (F,G) human Rpn8^{ΔC} (residues 1-186) homodimers. Two orientations (0; 180°) are displayed for each protein.** The protomers in dimer are represented in brown ribbons. In human CSN6^{ΔC} and in Rpn8^{ΔC}, the C-terminal helical portion (green) of molecule A is engaged in a helix swap with the molecule A'. Defined secondary structure elements are labelled. Human CSN6^{ΔC} and Rpn8^{ΔC} contain seven β-strands and four α-helices. *DmCSN6^{ΔC}* structure contains five β-strands and two to three α-helices, depending on the considered monomer. Structural comparison of the monomeric form of *HsCSN6^{ΔC}* with *HsRpn8^{ΔC}* and *DmCSN6^{ΔC}* using LSQMAN program (2) gave rmsd values of 1.64 Å for 153 Cα pairs and 1.35 Å for 84 Cα pairs, respectively.

Reference.

2. Kleywegt, G. J. (1999) Experimental assessment of differences between related protein crystal structures. *Acta Crystallogr D Biol Crystallogr* **55**, 1878-1884