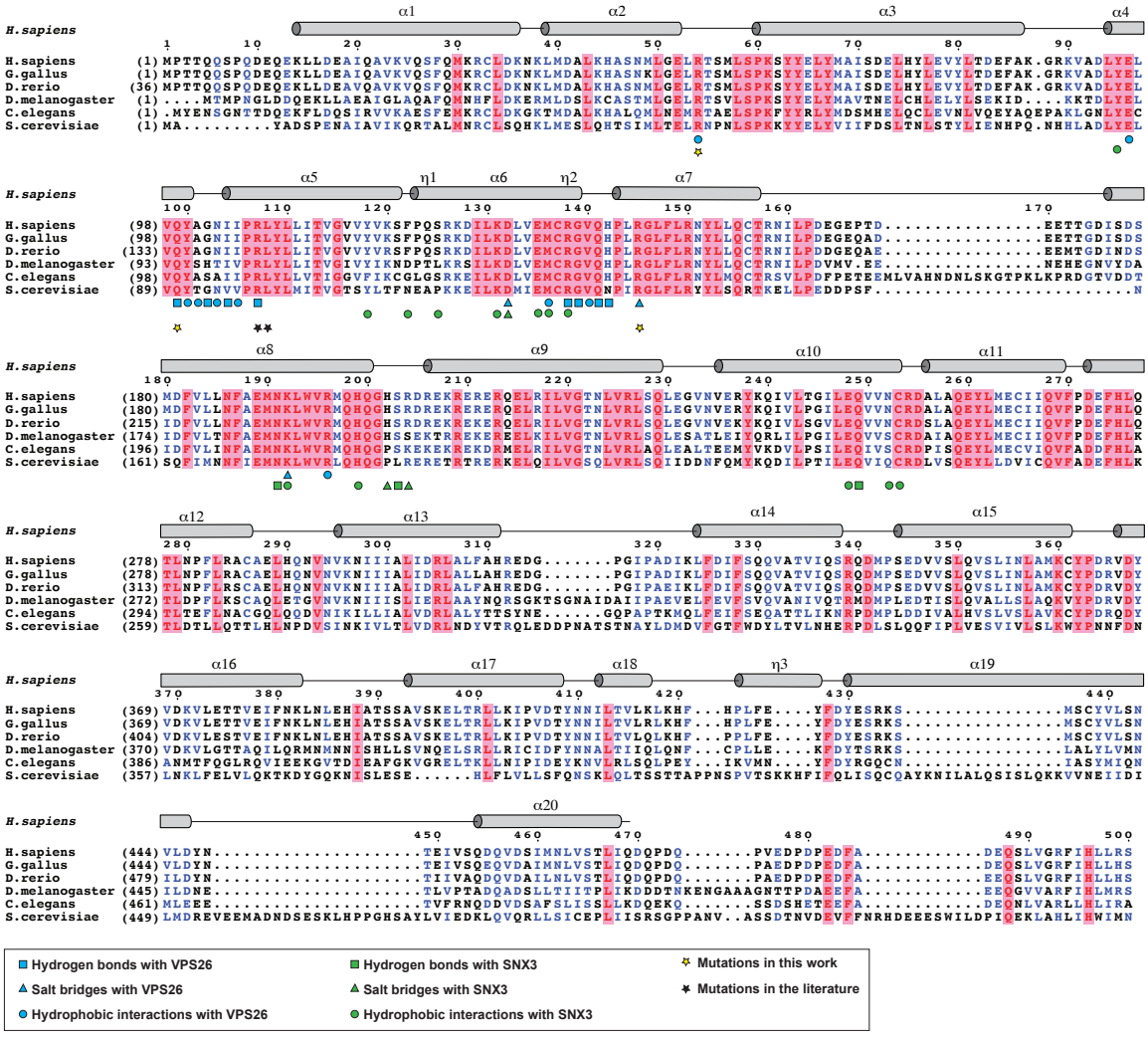
A
VPS35
H.sapiens
H.sapiens (1) MPTTQQSPQDEQEKLLDEAIQAVKVQSFQMKRCLDKNKLMDALKHASNMLGELRTSMLSPKSYYELYMAISDELHYLEVYLTDEFAK.GRKVADLYEL
G.gallus (1) MPTTQQSPQDEQEKLLDEAIQAVKVQSFQMKRCLDKNKLMDALKHASNKLGELRTSMLSPKSYYELYMAISDELHYLEVYLTDEFAK.GRKVADLYEL
D.rerio (36) MPTTQQSPQDEQEKLLDEAVQAVKVQSFQMKRCLDKNKLMDALKHASNMLGELRTSMLSPKSYYELYMAISDELHYLEVYLTDEFAK.GRKVADLYEL
D.melanogaster (1) ....MTMPNGLDDQEKLLAEAIGLAQAFQMNHFLDKERMLDSLKCASTMLGELRTSVLSPKSYYELYMAVTNELCHLELYLSEKID....KKTDLYEL
C.elegans (1) .MYENSGNTTDQEKFLDQSIRVVKAESFEMKRCLDKGKTNDALKHALQMLNEMRTAELSPKFYYRLYMDSMHELQCLEVNLVQEYAQEPAKLGNLYEC
S.cerevisiae (1) MA.....YADSPENAIAVIKQRTALMNRCLSQHKLMESLQHTSIMLTELRNPNLSPKKYYELYVIIFDSLTNLSTYLIENHPQ.NHHLADLYEL
α1
α2
α3
α4
H.sapiens
H.sapiens (98) VQYAGNIIPRLYLLITVGVVYVKSFPQSRKDILKDLVEMCRGVQHPLRGLFLRNYLLQCTRNILPDEGEPTD.....EETTGDISDS
G.gallus (98) VQYAGNIIPRLYLLITVGVVYVKSFPQSRKDILKDLVEMCRGVQHPLRGLFLRNYLLQCTRNILPDEGEQAD.....EETTGDISDS
D.rerio (133) VQYAGNIIPRLYLLITVGVVYVRSFPQSRKDILKDLVEMCRGVQHPLRGLFLRNYLLQCTRNILPDDGEQAE.....EEMTGDINDS
D.melanogaster (93) VQYSHTIVPRLYLLITVGIVYIKNDPTLKRSILKDLVEMCRGVQHPLRGLFLRNYLLQCTRNILPDVMV.EE.....NEHEGNVYDA
C.elegans (98) VQYASAIIPRLYLLVTIGGVFIKCGLGSRKELILKDLVEMCRGVQHPLRGLFLRNYLMQCTRSVLPDFPETEEMLVAHNDNLSKGTPKLKPRDGTVDDT
S.cerevisiae (89) VQYTGNVVPRLYLLMITVGTSYLTFNEAPKKELILKDMIEMCRGVQNPIRGLFLRYYLSQRTKELLPEDDPSF.....N
α5
η1
α6
η2
α7
H.sapiens
H.sapiens (180) MDFVLLNFAEMNKLWVRMQHQGHSRDREKRERERQELRILVGTNLVRLSQLEGVNVERYKQIVLTGILEQVVNCRDALAQEYLMECIIQVFPDEFHLQ
G.gallus (180) MDFVLLNFAEMNKLWVRMQHQGHSRDREKRERERQELRILVGTNLVRLSQLEGVNVERYKQIVLPGILEQVVNCRDALAQEYLMECIIQVFPDEFHLQ
D.rerio (215) IDFVLLNFAEMNKLWVRMQHQGHSRDREKRERERQELRILVGTNLVRLSQLEGVNVEKYKQIVLSGVLEQVVNCRDSLAQEYLMECIIQVFPDEFHLQ
D.melanogaster (174) IDFVLTNFAEMNKLWVRMQHQGHSSEKTRREKERELKILVGTNLVRLSQLESATLEIYQRLILPGILEQVVSCRDAIAQEYLMECIIQVFPDEFHLK
C.elegans (196) IDFVLINFAEMNKLWVRMQHQGPSKEKERKERDRMELRILVGTNLVRLAQLEALTEEMYVKDVLPSILEQVVSCRDPISQEYLMECVIQVFADDFHLA
S.cerevisiae (161) SQFIMNNFIEMNKLWVRLQHQGPLRERETRTRERKELQILVGSQLVRLSQIIDDNFQMYKQDILPTILEQVIQCRDLVSQEYLLDVICQVFADEFHLK
α8
α9
α10
α11
H.sapiens
H.sapiens (278) TLNPFLLRACAELHQNVNVKNIIIALIDRLALFAHREDG.....PGIPADIKLFDIFSQQVATVIQSRQDMPSEDVVSLQVSLINLAMKCYPDRVDY
G.gallus (278) TLNPFLLRACAELHQNVNVKNIIIALIDRLALLAHREDG.....PGIPADIKLFDIFSQQVATVIQSRQDMPSEDVVSLQVSLINLAMKCYPDRVDY
D.rerio (313) TLNPFLRSCAELHQNVNVKNIIIALIDRLALFAHREDG.....PGIPAEIKLFDIFSQQVATVIQSRQDMPSEDVVSLQVSLINLAMKCYPDRVDY
D.melanogaster (272) TLDPFLKSCAQLETGVNVKNIISLIERLAAYHQRSGKTSGNAIDAIPAEVELFEVFSVQVANIVQTRMDMPLEDTISLQVALLSLAQKVYPDRVDY
C.elegans (294) TLTEFLNACGQLQQDVNIKILLIALVDRLALYTTSYNE.....GQPAPTKMQLFEIFSEQATTLIKNRPDMPLDDIVALHVSLVSLAVKCYPDRQDY
S.cerevisiae (259) TLDTLLQTTLHLNPDVSINKIVLTLVDRLNDYVTRQLEDDPNATSTNAYLDMDVFGTFWDYLTVLNHERPDLSLQQFIPLVESVIVLSLKWYPNNFDN
α12
α13
α14
α15
H.sapiens
H.sapiens (369) VDKVLETTVEIFNKLNLEHIATSSAVSKELTRLLKIPVDTYNNILTVLKLKHF...HPLFE....YFDYESRKS.....MSCYVLSN
G.gallus (369) VDKVLETTVEIFNKLNLEHIATSSAVSKELTRLLKIPVDTYNNILTVLRLKHF...HPLFE....YFDYESRKS.....MSCYVLSN
D.rerio (404) VDKVLESTVEIFNKLNLEHIATSSAVSKELTRLLKIPVDTYNNILTVLQLKHF...PPLFE....YFDYESRKS.....MSCYVLSN
D.melanogaster (370) VDKVLGTTAQILQRMNMNNISHLLSVNQELSRLLRICIDFYNNALTIIQLQNF...CPLLE....KFDYTSRKS.....LALYLVMN
C.elegans (386) ANMTFQGLRQVIEEKGVTDIEAFGKVGRELTKLLNIPIDEYKNVLRLSQLPEY....IKVMN....YFDYRGQCN.....IASYMIQN
S.cerevisiae (357) LNKLFELVLQKTKDYGQKNISLESE.....HLFLVLLSFQNSKLQLTSSTTAPPNSPVTSKKHFIFQLISQCQAYKNILALQSISLQKKVVNEIIDI
α16
α17
α18
η3
α19
H.sapiens
H.sapiens (444) VLDYN.....TEIVSQDQVDSIMNLVSTLIQDQPDQ.....PVEDPDPEDFA.....DEQSLVGRFIHLLRS
G.gallus (444) VLDYN.....TEIVSQEQVDAIMNLVSTLIQDQPDQ.....PAEDPDPEDFA.....DEQSLVGRFIHLLHS
D.rerio (479) VLDYN.....TIIVAQDQVDAILNLVSTLIQDQPDQ.....PAEDPDPEDFA.....EEQSLVGRFIHLLHS
D.melanogaster (445) ILDNE.....TLVPTADQADSLLTIITPLIKDDDTNKENGAAAGNTTPDAEEFA.....EEQGVVARFIHLMRS
C.elegans (445) MLEEE.....TVFRNQDDVDSAFSLISSLLKDQEKQ.....SSDSHETEEFA.....DEQNLVARLLHLIRA
S.cerevisiae (449) LMDREVEEMADNDSESKLHPPGHSAYLVIEDKLQVQRLLSICEPLIISRSGPPANV..ASSDTNVDEVFFNRHDEEESWILDPIQEKLAHLIHWIMN
α20
H.sapiens
Hydrogen bonds with VPS26
Salt bridges with VPS26
Hydrophobic interactions with VPS26
Hydrogen bonds with SNX3
Salt bridges with SNX3
Hydrophobic interactions with SNX3
Mutations in this work
Mutations in the literature
B
VPS26
H.sapiens
H.sapiens (1) MSFLGGFFGPICELDIVLNDGETRKMAEMKTEDGK.....VEKHYLFYDGESVSGKVNLAFKQPGKRLEHQGIRIEFVGQI..EL.....
G.gallus (1) MSFLGGFFGPVCELDIVLNDAETRKTAEMKTEDGK.....VEKHFLFYDGESVSGKVNVS.KQQGKRLEHQGIRIEFVGQI..EL.....
D.rerio (1) MSFLGGLFGPACELDIVLNDAESRKTAELKTEEGK.....LEKHYLFYDGESVSGKVNINVKQTSKRLEHQGIRIEFVGQI..EL.....
D.melanogaster (1) MNFLG..FGQSADIEIVF.DGAEHKTAEVKGEDGK.....VEKMLLFYDGETVSGKVNVTLKKPGSKLEHQGIKIEFIGQI..EL.....
C.elegans (1) MAMLFG.FGQSAEIQIRLSNEDTRKIVKARGDDGN.....MDHFLYYDGESVTGTVHVNLKKANHKFEHQGIRIEFIGQIVSEV.....
S.cerevisiae (1) ...MSIFFKPPIDIEILFDNEESRKHVDIATRSSNSSYKSMKESLPVYEDGESLGGIVTLRVR.DSKKVDHLGIKVSVIGSIDMLKSHG(20)
η1
β6
β6´
β7
β8
β9
H.sapiens
H.sapiens (79)..FNDKSNTHEFVNLVKELALPGELTQSRSYDFEFMQVEKPYESYIGANVRLRYFLKVTIVRRLTDLVKEYDLIVH.....QLATYPDV
G.gallus (78)..FNDKSNTHEFVNLVKELALPGELTQSRSYDFEFMQVEKPYESYIGANVRLRYFLKVTIVRRLSDLVKEYDLIVH.....QLATYPDV
D.rerio (79)..FSDKSNTHEFVNLVKELALPGELTQNRSYDFEFMQVEKPYESYVGANVRLRYFLKVTIVRRLSDLVKEYDLIVH.....QLATYPDV
D.melanogaster (76)..YYDRGNHHEFKCLAKALARPGDLIQNNSYPFDFPKVEKQFEVYAGSNVRLRYFLRATIVRRISDITKEVDIAVH.....TLCSYPEM
C.elegans (80)..YYDRGNQQDFISLTRELARPGDLTQNAQFPFEFNNVEKPFETYMGTNVKLRYFLRVTVIRRLTDLTKELDLVVH.....ALSSYPDN
S.cerevisiae (106) SVDVRKNSVDQFLCQSYDLCPAGELQHSQSFPFLFRDLSKRYESYKGKNVDVAIYVKVTVMRKSTDISKIKRFWVYLY(50)VLPISRSNNE
β10
β11
β12
β13
β14
β15
β16
H.sapiens
H.sapiens (161) NNSIKMEVGIEDCLHIEFEYNKSKYHLKDVIVGKIYFLLVRIKIQHMELQLIKKEITGIGPSTTTETETIAKYEIMDGAPVKGESIPIRLFL
G.gallus (160) NNSIKMEVGIEDCLHIEFEYNKSKYHLKDVIVGKIYFLLVRIKIQHMELQLIKKEITGIGPSTTTETETIAKYEIMDGAPVKGESIPIRLFL
D.rerio (161) NNSIKMEVGIEDCLHIEFEYNKSKYHLKDVIVGKIYFLLVRIKIQHMELQLIKKEMTGIGPSTTTETETVAKYEIMEGAPVKGESIPIRLFL
D.melanogaster (158) NPIKMEVGIEDCLHIEFEYNKKYHLRDTIGKIYFLLVRIKIKHMEIAIIKKESTSTGPTMFNENETIAKYEIMDGAPVKGESIPIRLFL
C.elegans (162) DKSIKMEVGIEDCLHIEFEYNKNYHLQDVIVGKIYFLLVRIKIKYMEIAILKTEVVGSGPNTFKESETVAKFEIMDGAPVRGESIPIRLFL
S.cerevisiae (244) PKPVRLDIGIENCLHIEFEYAKSQYSLKEVIVGRIYFLLTRLRIKHMELSLITRESSGLQTSNVMTDSTAIRYEIMDGSSVKGETIPIRLFL
η2
β16´
β17
β18
H.sapiens
H.sapiens (253) AGYDPTPTMRDVNKKFSVRYFLNLVLVDEEDRRYFKQQEIILWRKAPEKLRKQRTNFHQR..FESPESQ.....A..SAEQ.....PEM...
G.gallus (252) AGYDPTPTMRDVNKKFSVRYFLNLVLVDEEDRRYFKQQEIILWRKAPEKLRKQRTNFHQR..FESPESQ.....A..SAEQ.....PEM...
D.rerio (253) AGYDLTPTMRDVNKKFSVRYFLNLVLVDEEDRRYFKQQEIVLWRKAPEKMRK..RNFHQR..YESPEPR.....PSLSAEQ.....PEM...
D.melanogaster (250) AGYNLTPTMRDINKKFSVRYFLNLVLMDTEEDRRYFKQQEITLWRKADKPRYHGAQQHQQQQHQHVPLHA.....PPHLVSGP..AAPTVAHS
C.elegans (254) AGYDLAPSMRDVGKKFSVKYFLNLVLVDEEDRRYFKQQEVTLWRKADKVMRRPGTEDDEEEKQTTSIPGTQKFTAPAPVEHPKPESPRSDP.
S.cerevisiae (336) SGYDLTPNMSC..NYFNVKNYISLVIIDEDGRRYFKQSEITLWRTR.....
Hydrogen bonds with VPS35
Salt bridges with VPS35
Hydrophobic interactions with VPS35
Hydrogen bonds with SNX3
Hydrophobic interactions with SNX3
Hydrogen bonds with DMT1
Hydrophobic interactions with DMT1
Mutations in this work
Mutations in the literature