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CBR-CHUP-1 ---MKALQAI F I L I F S E L I-----S T Q K P E V I P A K W D V L Y E--K E T E
CBN-CHUP-1 ---M K K L S I I F I L I F F Q I V-----S S Q V P E V I P A K W D V L Y Q--K E T G
CRE-CHUP-1 ---M K A T Q C I F L L I F L E V V-----K S Q L P Q V I P A K W D V M Y G--K E T G
CEL-CHUP-1 ---M R T S Q A I F I L I F L D S V-----R N Q S P Q V I P A K W D V V Y E--K E T G
CJP-SID-1 ----M Y N E I I L R V V R A V L G R L A D P N V T Q Y A S-----N N E P E S I I K H L N K K L T--N E T L
CEL-SID-1 ----M I R V Y L I I L M H L V I G L T Q N N S T P S P I I----T S S N S S V L V F E I S S K M K M I E K K L
CBN-SID-1 M K G S G S I L G C L L I V L L G Q L G L S D N I T D K E P S E L D F T K N N E T G P I I V R Q L H S K T K M F N A T L
CRE-SID-1 M V G S R F F A S C L L L V L L G K L N C S G N N T D N G V Q E-----T D E E N P V I T R E F P S K K V Y E T T L
CBR-SID-1 M I G S R Y F V S G V L L L L L G R F L S E Q D-----N N E T S P I S V R E F P A R R R Q I N D T L

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M I I

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CBR-CHUP-1 KNMSLTIFRFNVEKQY--SVARIIMSCNES----TEHNPLLAV-FREKVAI L S L Q V P L I V
CBN-CHUP-1 KNMSMTIFRFVVEEQY--SVARIIMSCNES----TEHNPLLAV-FREKLA I L S L Q V P L I V
CRE-CHUP-1 KNMSLTIFRFKVEEKY--SVARIIMSCNES----TEHNPLLAV-FREKLA V L S L Q V P L I V
CEL-CHUP-1 HNMSLTVFRFQVKEQY--SVARIIMSCNES----TEHNPLLAV-FREKLA I L S L Q V P L I V
CJP-SID-1 KAHTVNVLYNSLYTQSILDLTRVSVTIDEPWKFDTVHGHTLEATVSNGRDNFLLKLPVVY
CEL-SID-1 EANTVHVLRLELDQSFILDLTKVAAEIVDSSKYSKEDGVI LEVTVSNGRDSFLLKLPVY
CBN-SID-1 KPGKVHLYYLSLDDSYVLDLMRIAEEVIDPVLYKNEKDAI LEVTVSNGRDNFNKLPVIY
CRE-SID-1 KPNAVHVYYLKMNETYILDLIRVAAEITHPTLFEKEEDTIL DVTVSNGRDNFVIKLPVVY
CBR-SID-1 VANTVHVYYLKLDETFILDLTRISADVSEPALFRKEVDTI LEVTVSNGRDNF I L K L P M I Y

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P108S

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CBR-CHUP-1 DN--VEYSQVARTLCP--FTEYKEGEA-----FTVEVTS SRPVHYNFRA
CBN-CHUP-1 DN--VEYSQVARTLCP--FTEYKEGEA-----FTVEVTS SRPVHYNFRA
CRE-CHUP-1 DN--VEYSQVARTLCP--FTEYKEGEA-----FTVEVTS AQPVRYNFRA
CEL-CHUP-1 DN--VEYSQVARTLCP--FTEYKEGEA-----FTVEVTS SRPVHYNFRA
CJP-SID-1 KNVTLYSDGKVLNPLLPEDFGDRKLRKNQRFLPDNDENYHQNLIITVHSTLHEDIKYSV
CEL-SID-1 PNLKLYTDGKLLNPLVEQDFGAHRKRHR-----IGDPHFHQNLIVTVSRLNADIDYRL
CBN-SID-1 PNLTLVSYGKLLNPLISDDFGPKRSKKN-----RNSTGNTLIVTVSRLKVDLDYRL
CRE-SID-1 PEGSLTYGKLLNPLIPDDFGPKRSKKN-----TENSTGNTLIVTVSRLRVDIDYKL
CBR-SID-1 PDLTLVSYGKLLNPLRKEDEFGPKRSKKN----IPSENSTLSQNLVITVQSRRLRVDIDYQL

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D130N

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CBR-CHUP-1 ELVH-----NFYLYNDSKRLVTASASEPVYLR-----YDIPGVDSVAVHVL SNSTTC
CBN-CHUP-1 ELVQ-----NFHLYNDAKRLVTASASEPVYLR-----YDIPGDVDSVAVHVD SNSSIC
CRE-CHUP-1 ELVK-----NFFLYNNGKRLVTESASEPVYLR-----YDIPDDVDSVAVHVD SNSTTC
CEL-CHUP-1 ELVQ-----NFYLYNNSQRLVTASASEPVYLR-----YDIPGDVDSVAVHLD SNSTIC
CJP-SID-1 SVTHLDRSQYY-VKFKPGETRINQNDQHLLTVVKPLGYFLDAKEQNVNAFHITVTSDDDIC
CEL-SID-1 HVTHLDRSQYDFLKFKTGQTTKTLNSQKLTFFVKPIGFFLNCSEQNISQFHVTLYSEDDIC
CBN-SID-1 HLTRLDRSQYN-LKFKPGQSTKTLNSQKLTFFVKPIGFFLDAIEQNVKSFHITLSDDDFC
CRE-SID-1 FLTHLDRSQYD-LKFKPGQSEKTLNQKLTFFVKPMGFFLDAKEQDVKSFHITVSEDDIC
CBR-SID-1 HLTRLDRSQYN-LSFKEGQSTKTLNNSQKLTFFVKPIGFFLDTEEQIVKSFHITLTSADDIC

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R172W G201R
A173T G201E
P199L

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CBR-CHUP-1 MTVSQKIGCPVFDLPDNNVSMGLHQTMTSATIPV----EKSRMSSFYVVFVNTNDD
CBN-CHUP-1 MTVSQKIGCPIFDLPNNVSMGLHQTMTSATIPV----EKSRMSSFYVVFVNTNDD
CRE-CHUP-1 MTVSQKIGCPVFDLPDNNVSMGLHQTMTSATIPV----EKSRMSSFYVVFVNTNDD
CEL-CHUP-1 MTVSQKIGCPVFDLPDNNVSMGLHQTMTSATIPV----EKSRMSSFYVVFVNTNDD
CJP-SID-1 ANLITVPANESIYDRSVISDKTHNRRVLSFTKRADIFFTETEISMFKSERIFVFIAPDDS
CEL-SID-1 ASLITVPANESIYDRPVADKADNRRVITFTKRADIFFSQTEIETFKSERIFVFIAPDDS
CBN-SID-1 ANVITVPANESIYDRPVDSKADNRRVITFNRRADIFFSEKEIELFKSERIFVFIAPDDS
CRE-SID-1 ANVITVPANESIYERPVDSRADNRRVITFNRRADIFFSETEIQLFKSERIFVFIAPDVNA
CBR-SID-1 ANVITVPANESIYERPVDSRADNRRVITFNRRADIFFSETEIQLFKSERIFVFIAPDVNA

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CBR-CHUP-1 LCSEILSIKPNRPTKFLRLKSFNVTIE-SSMKIFDYIIPVFWACILLVTLVVFVYHY
CBN-CHUP-1 LCSEISSIKPIRPTKFLRLKSFNVTIE-SSMKTSDYTIPIVFWACILFLVTIVVFVYHY
CRE-CHUP-1 LCSEIMSIKPN-----PFNVTIE-SSMKIFDYTIPIVFWACVLLVTLVVFVYHY
CEL-CHUP-1 LCSEILSIKPNKPTKFLPRMKSFNVTIE-SSMKIFDYTIPIVFWACILLVTLVVFVYHY
CJP-SID-1 LC-GASRKTALQNK-----KLSLEFVKLNDASVPLIA-MFTFLAIPALIFLP--
CEL-SID-1 GCSTNTRKSFNEKK-----KISFEFKLENQSMVAVPTAL-MMIFLTTPCLLFLPIV
CBN-SID-1 PCSTNSRKTFNENK-----KVTFEFAKLEPSSYFFPTAL-MMAFLATPVLLFVPAL
CRE-SID-1 PCSLKTRKTFNEQK-----KMTFEFKLEPDSYFMPPTLA-MIAFFISPCILIVASIL
CBR-SID-1 PCSGNTRKKNYNEIK-----KITFDTRLEPNSYFVPTLA-MLVFFASPCILIFIASL
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**P328L**

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CBR-CHUP-1 FDGIWERRFLSRAYTHLEDNAQDERLRDFYEFKRMSEDDDLRDY----DILTDCCKDMM--
CBN-CHUP-1 FDGIWERRFISRAYTHLEDNAQEERIRDFYDFQRMSDEDELDKDY----DLLLDCCKDMM--
CRE-CHUP-1 FDGIWERRFLSRAYTHLEDNAQEERIRDFYDFQRMSDEDDDLKDY----DLLTDCCKDMM--
CEL-CHUP-1 FDGIWERRFVSRAYTHLEDNAQEQRIRDFYDFQRMSDEDDDLKDY----DLLTDCQDMM--
CJP-SID-1 FVTLTRFRSMPIATDHLDDLST-----DLSSSSQPSPLIVL----DESATDNSLIG--
CEL-SID-1 INIKNSRKLAPSQSNLISFSPVPSEQRDMDLSDHDEQQNTSSELENNGEIPAAENQIVVEE
CBN-SID-1 ILN--RIRNTSTSQSTLI-----SFAPDTPDQSYQVE----EGPSTDNDI---
CRE-SID-1 AVNVWRNRDPSENTSADLV-----SFESDEPNHP-----NANTSDEQLV--
CBR-SID-1 TVNVIRNR--SDLVADLI-----SFSSDQSANTSIAIA----ENNMAHEIA--
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CBR-CHUP-1 VVRAKT-TLTVAD----LSMTPY--ETREMQYDVYKIALAIIGIFYNITVLQLIISKAG
CBN-CHUP-1 VVRAKA-TLTVAD----LSMTPY--ETREQQYDVYKIALAIIGIFYNITVLQLIISKAG
CRE-CHUP-1 VVRAKA-SLTVAD----LSMTPY--ELREQKYDVYKIALAIIGIFYNITVLQLIISKAG
CEL-CHUP-1 VVRAKA-SLTVAD----LSMTPY--EERELKYDVYKIALAIIGIFYNITVLQLIISKAG
CJP-SID-1 IAEVNA-DITVLED----VKLT----DSLHLGEMLRYPVAIILPVLMTAVEYHNWSKS
CEL-SID-1 ITAENQ-ETSVEEGNREIQVKIPLKQDSLSLHGQMLQYYPVAIILPVLMTAIEFHKWTTS
CBN-SID-1 VVPEEE-NLQVQE----GNIIPLEDLSLHGQMLKYPVAIILPVFMHTAVEYHEWFTTS
CRE-SID-1 VMEEEEVNQNHENLQNHVEAVSVKQDSLSLHGQVLRYPVAIILPVLMTAVQFHNFTFS
CBR-SID-1 VIPEEE-NLQVQE----IEPIPIKQDSLSLHGQMFKYPVAIILPVLMTGVEFHNFTTS
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CBR-CHUP-1 NLRQSGDLDECTFNFCARPLWYFVAFNNVVSNGGYVYFGSLIIVMNYCRERSFRRLFVAV
CBN-CHUP-1 SLRQSGDLDECTFNFCARPLWYFVAFNNVVSNGGYVYFGSLIIVMNYCRERSFRRLFVAV
CRE-CHUP-1 SLRQSGDLDECTFNFCARPLWYFVAFNNVVSNGGYVYFGLLIIVMNYCRERSFRRLFVAV
CEL-CHUP-1 SLRQSGDLDECTFNFCARPLWYFVAFNNVVSNGGYVYFGLTIIVMNYCRERSFRRLFVAV
CJP-SID-1 SMANRDEM--CFYNHACANPYGEFRAWNNIISNIGYAIYGLAFVAITVGRRRRSRQLVGV-
CEL-SID-1 TMANRDEM--CFHNNHACARELGELELRAWNNIITNIGYTYLGAIFIVLSICRRGRHEYSHV-
CBN-SID-1 TMANRDEM--CFHNNACAREYGELELRAWNNIISNIGYAIYGLVFIATMCRWRWRHGSPPV-
CRE-SID-1 TMANRDEM--CFHNSACSKELGELELRAWNNIISNIGYAIYGFVFIITMFRWRHHSALV-
CBR-SID-1 TMANRDEM--CFHNNACAKELGELELRSWNNIISNIGYAIYGLVFIIVTMCRRWRHHSPLV-
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**C464Y G488E G493R**

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CBR-CHUP-1 QPTLAERYGLPQHSGLMTAIGLAVIMEGISSATYHVCPPNNINYQFDTALMYVIGMLGKLK
CBN-CHUP-1 QPTLAERYGLPQHSGLMTAIGLAVIMEGISSATYHVCPPNNINYQFDTALMYVIGMLGKLK
CRE-CHUP-1 QPALAERYGLPQHSGLMTAIGLAVIMEGISSATYHVCPPNNINYQFDTALMYVIGMLGKLK
CEL-CHUP-1 QPTLAERYGLPQHSGLMTAIGLAVIMEGISSATYHVCPPNNINYQFDTALMYVIGMLGKLK
CJP-SID-1 -----YGVHESTLIDVTIGVFMVLQAIASATYHICPSNVSFQFDTPCIQVTCGLLIIR
CEL-SID-1 -----FGTYECTLLDVTIGVFMVLQSIASATYHICPSDVAFQFDTPCIQVTCGLLMVR
CBN-SID-1 -----GIYEECTLLDVTIGVFMILQAIASATYHICPSDVAFQFDTPCIQVTCGLLIIR
CRE-SID-1 -----GTYEECTLLDITIGVFMILQAIASATYHICPSDIAFQFDTPCIQVTCGLLIIR
CBR-SID-1 -----GTYEECTLLDITIGLFMILQAIASATYHICPSDIAFQFDTPCIQVTCGLLIIR
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**I534N S536I C559Y R565C**

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CBR-CHUP-1  IWSLRHPDMVVSAMHAFGFLGIFLMAAIAGVYVHNMIWFIMFSTIYIGSMMLISLEFYFK
CBN-CHUP-1  IWSLRHPDMVVSAMHAFGFLGMFLMAAIAGVYVHNMIWFIMFSTIYIASMMLVSLLEFYFK
CRE-CHUP-1  IWSLRHPDMVVSAMHAFGFLGIFLMAAIAGVYVHNMIWFIMFSTIYIGSMMLISLEFYFK
CEL-CHUP-1  IWSLRHPDMVVSAMHAFGFLGVFLMAAIAGVYVHNMIWFALFSIYIASMMLVSLLEFYFK
CJP-SID-1    QWLVRLE-ESPSAAMSNLLLVVVSVNFLVLSALSKTWYIRYLIAGIHMFISSICL-----
CEL-SID-1    QWLVVRH-ESPSPAYTNILLVGVVSLNFLISAFSKTSYVRFIIAVIHWIVVGSICL-----
CBN-SID-1    QWRVRQ-ESPSASYTNLLLVGVVSLNFLISAFSKAKYVRYLIAMIHISAIASMCL-----
CRE-SID-1    QWLVVRK-ESPSPAYTNMLLLAVVSLNFLISTLSKSSRVRYVIATIHFIIVVATICL-----
CBR-SID-1    QWLVRQ-ESPSPAYTNILLFCVVSLNFLISACSKASGIRYLIATLHFGVVATVCL-----
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R570C

CBR-CHUP-1  GIWTLNIRELRNSIRMSWATSRHLSC--IVPAYKARFFVILLNLMANTAVVYGLDAHPK
CBN-CHUP-1  GIWTLNIRELRNSVRMAWASSRRLSC--VIPAYKARFFVILLNLANAVVYGLEAHPK
CRE-CHUP-1  GIWTLNIRELRNSVRMAWASSRRLSC--IMPAYKARFFVILLMLNIVNTAVVYGLEAHPK
CEL-CHUP-1  GIWTLNIRELRNSIRLSWSSRHLSC--VVPAYKARFFVILLNIANTAVVYGLEAHPK
CJP-SID-1    -----AKKRMGLGINESAFRQISLTFIIYYISICNITMLLVYLVSAKI-----HLN
CEL-SID-1    -----AKERSLGSEKLRTRF-----FIMAFSMGNFAAIVMYLTLTSAF-----HLN
CBN-SID-1    -----AKRRTLETKKTQV-----FTACFAAINFLIMLTYLAPSIL-----HLN
CRE-SID-1    -----KKQKKMGSRKDAK-----FMIFFAVANFILMMMYLTSSKI-----HLN
CBR-SID-1    -----AKRKTLRSKQYKV-----FVGTFAIFNFFAITTYVTSSYI-----HLN
. : . : . : . : . : . : . : . : . : . : . : . : . : . : . : * :
DFLSFLLIPIFIGNLFYIYYILMKMIYREKIPKRAVALLIAAVISWTCAGILFNORVSD
CBN-CHUP-1  DFLSFLLIPIFIGNLFYIYYILMKMIHREKIPKRAMALLMAAVISWTCAGILFNORVSD
CRE-CHUP-1  DFLSFLLIPIFIGNLFYIYYILMKMIYREKIPKRALALLFAAVISWTCAGILFNORVSD
CEL-CHUP-1  DFLSFLLIPIFIGNLFYIYYILMKMIYREKIPKRAIALLFAAVISWTCAGILFNORVSD
CJP-SID-1    QIVTYC---CIFNCIMYLIYYALIKYMCHERISHLAKLYGSLALVGFVSAWFFFODDMD
CEL-SID-1    QIATYC---FIINCIMYLMYYGCMKVLHSEBRTSKAKLKGSLSLLAWAVAGFFFODDTD
CBN-SID-1    QIVTYC---FISNCIMYLVYYAVMKLVSRERIGLKGKVCGLAVIGWIVAAVFFFODDTD
CRE-SID-1    QITTYC---FILNCIVYLYTYATMKAVSRESIGLKAKICGTLAIVGMIITAGYFFFODDTD
CBR-SID-1    QISTYC---FILNCILYLYTYALMKFASRESIELKAKVCGVSAIFGWLIIAGFFFODDTD
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WSKMPAISRELNKPCIFLNFDNHDIWHLSSAFAIFFSFTAINVIDDDLMFVVRNTIRVF
CBN-CHUP-1  WSKMPAISRELNKPCIFLNFDNHDIWHLSSAFAIFFSFTAINVIDDDLMFVVRNTIKVF
CRE-CHUP-1  WSKMPAISRELNKPCIFLNFDNHDIWHLSSAFAIFFSFTAINVIDDDLMFVVRNTIRVF
CEL-CHUP-1  WSKMPAISRELNKPCIFLNFDNHDIWHLSSAFAIFFSFTAINVIDDDLMFVVRNTIRVF
CJP-SID-1    WTQSAAVSRSLNKPCVLLQFFGSHDLWHIFGAMAGLFTFELFVSVVDDDLNIPKCSVTVF
CEL-SID-1    WTRSAASRALNKPCLLDFFGSHDLWHIFGALAGLFTFELFVSVVDDDLINTRKTSINIF
CBN-SID-1    WTRSAASRALNKPCLLNFFGSHDLWHIFGALAGLFTFELFVSVVDDDLVNTPKSAINVY
CRE-SID-1    WTRTAASRALNKPCLLDFFGSHDLWHIFGALAGLFTFELFVSVVDDDLVNTPKSSINIF
CBR-SID-1    WTRTAASRALNTPCLLDFFGSHDLWHMFGAIALGLFTFELFVSVVDDDLINTPKSSINMY
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H740Y G747R

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**Figure S1. A multiple sequence alignment of full-length SID-1 homologs.** Available full-length SID-1 and CHUP-1 homologs from *C. elegans*, *C. brenneri*, *C. briggsae*, *C. remanei*, and *C. japonica* were aligned by MUSCLE v3.8 with default parameters (Edgar 2004). Residues identically conserved in all nine aligned sequences (predicted SID-1 orthologs and paralogs) are highlighted in black; residues identically conserved only in the five putative SID-1 orthologs are highlighted in grey. The position and amino acid change of the recovered weak alleles (regular weight) and strong alleles (bold weight) is indicated below the substituted residue.