Figure S2.

```
hsSIRT6      1 GAGISTASGIPDFRG-PHGVW-----------------------------TMEERGL-AP
dmSRT408     1 GAGISTSAGIPDFRG-PKGVW-----------------------------TLEEKGE-KP
atSRT1       1 GAGISTSCGIPDFRG-PKGIW-----------------------------TLQREGKDLP
leSRT1105    1 GARISTSCGIPDFRG-PKGIW-----------------------------TLQREGKALP
zmSRT101     1 GAGISTSSGIPDFRG-PMGVW-----------------------------TLQRAGKGIP
taSRT803     1 GAGISTSSGIPDFRAQPKGVW-----------------------------TLQRAGKGVP
osSRT701     1 GASISTSSGIPDFRG-PKGVW-----------------------------TLQRSGKGVP
hsSIRT7      1 GAGISTAASIPDYRG-PNGVW-----------------------------TLLQKGR--S
dmSRT409     1 GAGISTAALIPDYRG-SQGIW-----------------------------TLLQKGQ--D
hsSIRT4      1 GAGISTESGIPDYRSEKVGLYARTDRRP---------IQHGDF--VRSAPIRQRYWARNF
dmSRT407     1 GAGISTESGIPDYRSEGVGLYARSNHKP---------VQHMEF--VKSSAVRKRYWARNF
ceSRT310     1 GAGISTESGIPDYRSKDVGLYTKTALEP---------IYFQDF--MKSKKCRQRYWSRSY
ceSRT311     1 GAGISTESGIPDYRSKDVGLYARIAHKP---------IYFQDY--MRSNRCRQRYWSRNF
atSRT2       1 GAGVSTECGIPDYRS-PNGAY-SSGFKP---------ITHQEF--TRSSRARRRYWARSY
leSRT1104    1 GAGMSTESGIPDYRS-PNGAY-STGFKP---------ITHQEF--LRSIKARRRYWARSY
mtSRT1303    1 GAGISTECGIPDYRS-PNGAY-SSGFQP---------ITHQEF--LRSTRARRRYWARSY
scSIR2       1 GAGVSTSLGIPDFRSSE-GFYSKIKHLG--LDDPQDVFNYNIF--MHDP---SVFYNIAN
scHST1       1 GAGVSTSLGIPDFRSSE-GFYSKIRHLG--LEDPQDVFNLDIF--LQDP---SVFYNIAH
spSIR2       1 GAGISTSLGILDFRSDN-GFYARLARHG--LSEPSEMFDIHTF--RENP---EIFYTFAR
hsSIRT1      1 GAGVSVSCGIPDFRSRD-GIYARLAVDFPDLPDPQAMFDIEYF--RKDP---RPFFKFAK
dmSRT406     1 GAGVSVSCGIPDFRSTN-GIYARLAHDFPDLPDPQAMFDINYF--KRDP---RPFYKFAR
ceSRT309     1 GAGVSVSCGIPDFRSKD-GIYARLRSEFPDLPDPTAMFDIRYF--RENP---APFYNFAR
scHST2p      1 GAGISTSCGIPDFRSPGTGLYHNLARLK--LPYPEAVFDVDFF--QSDP---LPFYTLAK
spHST2       1 GAGISTAAGIPDFRSPETGIYNNLQRFN--LPYAEAVFDLSYF--RKNP---RPFYELAH
hsSIRT2      1 GAGISTSAGIPDFRSPSTGLYDNLEKYH--LPYPEAIFEISYF--KKHP---EPFFALAK
hsSIRT3      1 GAGISTPSGIPDFRSPGSGLYSNLQQYD--LPYPEAIFELPFF--FHNP---KPFFTLAK
scHST4       1 GAGISVAAGIPDFRSSE-GIFSTVNGG-----SGKDLFDYNRV--YGDESMSLKFNQLMV
spHST4       1 GAGISCDAGIPDFRSSE-GLFSSLRAEYKLNCSGKELFDG-SV--YRDLKSVNIFHAMIR
scHST3       1 GAGISCNAGIPDFRSSD-GLYDLVKKDCSQYWSIKSGREMFDISLFRDDFKISIFAKFME
hsSIRT5      1 GAGVSAESGVPTFRG-AGGYWRKWQAQDLATP-------------LAFAHNPSRVWEFYH
ceSRT312     1 GAGVSTGSKLPDFRG-KQGVW-------------------------------TLQAEGKH

hsSIRT6     30 KFDTTFESARPTQTHMALVQLER----VGLLRFLVSQNVDGLHVRSGFPRD---------
dmSRT408    30 DFNVSFDEARPTKTHMAIIALIE----SGYVQYVISQNIDGLHLKSGLDRK---------
atSRT1      31 KASLPFHRAMPSMTHMALVELER----AGILKFVISQNVDGLHLRSGIPRE---------
leSRT1105   31 EASLPFHRATPSMTHMALVELEK----AGFLKFLISQNIDGLHLRSGIPRE---------
zmSRT101    31 NASLPFHHAVPSLTHMALVELER----AGFLKFVISQNVDSLHLRSGFPRE---------
taSRT803    32 DASLPFHRAAPTLTHMALVELER----AGLLKFVISQNVDSLHLRSGFPRE---------
osSRT701    31 GATLPFQRAVPTLTHMALVELEK----TGRLKFVISQNVDSLHLRSGLPRE---------
hsSIRT7     29 VSAADLSEAEPTLTHMSITRLHE----QKLVQHVVSQNCDGLHLRSGLPRT---------
dmSRT409    29 IGEHDLSSANPTYTHMALYELHR----RRLLHHVVSQNCDGLHLRSGLPRN---------
hsSIRT4     50 VGWPQFSSHQPNPAHWALSTWEK----LGKLYWLVTQNVDALHTKAGSR-----------
dmSRT407    50 VGWPKFSATQPNATHHALARFER----EERVQAVVTQNVDRLHTKAGSR-----------
ceSRT310    50 LNWPRFAQALPNFNHYALSKWEA----ANKFHWLITQNVDGLHLKAGSK-----------
ceSRT311    50 LAWPRFGQAAPNINHYALSKWEA----SDRFQWLITQNVDGLHLKAGSK-----------
atSRT2      48 AGWRRFTAAQPGPAHTALASLEK----AGRINFMITQNVDRLHHRAGS------------
leSRT1104   48 AGWRRFTAAQPSTGHIALSSLEK----AGHISFMITQNVDRLHHRAGS------------
mtSRT1303   48 AGWRQFTAAQPSAAHCALAAFEN----AGPIDFMVTQNVDRLHHRAGS------------
scSIR2      53 MVLPP--EKIYSPLHSFIKMLQM----KGKLLRNYTQNIDNLESYAG----------IST
scHST1      53 MVLPP--ENMYSPLHSFIKMLQD----KGKLLRNYTQNIDNLESYAG----------IDP
spSIR2      53 DLLPE--TNHYSPSHAFIRLLEK----KNKLSTLFTQNIDNLEKKTG----------LSD
hsSIRT1     55 EIYP--GQFQPSLCHKFIALSDK----EGKLLRNYTQNIDTLEQVAG----------IQR
dmSRT406    55 EIYPGEFQFQPSPCHRFIKMLET----KGKLLRNYTQNIDTLERVAG----------IQR
ceSRT309    55 EIFPG--QFVPSVSHRFIKELET----SGRLLRNYTQNIDTLEHQTG----------IKR
scHST2p     54 ELYPG--NFRPSKFHYLLKLFQD----KDVLKRVYTQNIDTLERQAG----------VKD
spHST2      54 ELMPE--KYRPTYTHYFIRLLHD----KRLLQKCYTQNIDTLERLAG----------VPD
hsSIRT2     54 ELYPG--QFKPTICHYFMRLLKD----KGLLLRCYTQNIDTLERIAG----------LEQ
hsSIRT3     54 ELYPG--NYKPNVTHYFLRLLHD----KGLLLRLYTQNIDGLERVSG----------IPA
scHST4      53 SLFRLSKNCQPTKFHEMLNEFAR----DGRLLRLYTQNIDGLDTQLPHLSTN-----VPL
spHST4      57 KLHMLSNNARPTDFHLFLSQLAQ----ESKLLRLYTQNIDFLETRLEGLQTC-----IPL
scHST3      60 RLYSNVQLAKPTKTHKFIAHLKD----RNKLLRCYTQNIDGLEESIGLTLSNRKLPLTSF
hsSIRT5     47 YRREVMGSKEPNAGHRAIAECETRLGKQGRRVVVITQNIDELHRKAGTKN----------
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ceSRT312     29 AEGVDFQVARPGVSHKSILALHK----AGYIKTIITQNVDGLDRKVGIP-----------

hsSIRT6      77 -------KLAELHGNMFVEECAK--CKTQYVRDTVVGTMGLKAT----------------
dmSRT408     77 -------YLSELHGNIYIEQCKK--CRRQFVSPSAVETVGQKSL----------------
atSRT1       78 -------KLSELHGDSFMEMCPS--CGAEYLRDFEVETIGLKET----------------
leSRT1105    78 -------KLSELHGDSFMERCPS--CGIEYMRDFEIETIGLKET----------------
zmSRT101     78 -------KLAELHGNSFKEICPC--CKTEYLRDFEIETIGLKDT----------------
taSRT803     79 -------KLAELHGNSFKEVCPC--CKTEYLRDFEIETIGLKDT----------------
osSRT701     78 -------KLAELHGNSFKEICPS--CKKEYLRDFEIETIGLKDT----------------
hsSIRT7      76 -------AISELHGNMYIEVCTS--CVPNREYVRVFDVTERTAL----------------
dmSRT409     76 -------SLSEIHGNMYVEVCKN--CRPNSVYWRQFDTTEMTARY---------------
hsSIRT4      95 -------RLTELHGCMDRVLCLD--CGEQTPRGVLQERFQVLN--PTWSAEAHGLA----
dmSRT407     95 -------NVVEVHGSGYVVKCLS--CEYRIDRHEFQSILASLN--PAFKDAPDMIR----
ceSRT310     95 -------MITELHGNALQVKCTS--CEYIETRQTYQDRLNYAN--PGFKEQFVSPGQ---
ceSRT311     95 -------MVTELHGSALQVKCTT--CDYIESRQTYQDRLDYAN--PGFKEEHVAPGE---
atSRT2       92 -------DPLELHGTVYTVMCLE--CGFSFPRDLFQDQLKAINPKASWAEAIESIDHGDP
leSRT1104    92 -------NPLELHGTVYIVACTN--CGFSLPRDLFQDQVKAHN--PKWAEAIENLDYDSR
mtSRT1303    92 -------NPLELHGTVYNVICIN--CGYSLCRSLFQDQLKSLN--PKWAEAIENLDHGNA
scSIR2       97 DK------LVQCHGSFATATCVT--CHWNLPGERIF----NKIRNLE-------------
scHST1       97 DK------LVQCHGSFATASCVT--CHWQIPGEKIF----ENIRNLE-------------
spSIR2       97 NK------IIQCHGSFATATCIK--CKHKVDGSELY----EDIRNQR-------------
hsSIRT1      99 --------IIQCHGSFATASCLI--CKYKVDCEAVR----GDIFNQV-------------
dmSRT406    101 --------VIECHGSFSTASCTK--CRFKCNADALR----ADIFAQR-------------
ceSRT309     99 --------VVECHGSFSKCTCTR--CGQKYDGNEIR----EEVLAMR-------------
scHST2p      98 DL------IIEAHGSFAHCHCIG--CGKVYPPQVFKSKL-AEHPIKD-------------
spHST2       98 KA------LIEAHGSFQYSRCIE--CYEMAETEYVR----ACIMQKQ-------------
hsSIRT2      98 ED------LVEAHGTFYTSHCVSASCRHEYPLSWMK----EKIFSEV-------------
hsSIRT3      98 SK------LVEAHGTFASATCT--VCQRPFPGEDIR----ADVMADR-------------
scHST4      104 AK--PIPSTVQLHGSIKHMECN--KCLNIKPFDPELFKCDDKFDSRTEI-----------
spHST4      108 PQSAPWPTTIPLHGTLEVVSCT--RCSFLKKFNPDIFDRNG-------------------
scHST3      116 SSHWKNLDVVQLHGDLKTLSCT--KCFQTFPWSRYWSRCLRRG----E------------
hsSIRT5      97 --------LLEIHGSLFKTRCT--SCGVVAENYKSPICPALSGKGAPEPGTQDASIP---
ceSRT312     74 -----VEDLIEVHGNLFLEVCQ--SCFSEYVREEIVMSVGLCPT----------------

hsSIRT6     112 ----------------------------GRLCTVAKARGLRACR----------------
dmSRT408    112 ----------------------------QRACKSSMDSKGRSCRS----------------
atSRT1      113 ----------------------------SRKCSVEK------CG----------------
leSRT1105   113 ----------------------------ARRCS--K------CG----------------
zmSRT101    113 ----------------------------PRRCSDKN------CG----------------
taSRT803    114 ----------------------------PRRCTDK-------CG----------------
osSRT701    113 ----------------------------PRRCSDKN------CG----------------
hsSIRT7     111 -----------------------HRHQTGRTCHK--------CG----------------
dmSRT409    112 ------------------------CHKTHRLCHR--------CS----------------
hsSIRT4     140 -----------PDGDVFLSEEQVR-SFQVPTC--------VQCG----------------
dmSRT407    140 -----------PDGDVEIPLEYIEXXXXXPXC--------XXCG----------------
ceSRT310    141 ---------QELDADTALPLGSEQ-GFKIPEC--------LNCG----------------
ceSRT311    141 ---------LAPDGDIILPLGTEK-GFQIPEC--------PSCG----------------
atSRT2      143 GSEKSFGMKQRPDGDIEIDEKFWEEGFHIPVC--------EKCK----------------
leSRT1104   141 -SDKSFGMKQRPDGDIEIDEKFWEEDFYIPEC--------QSCQ----------------
mtSRT1303   141 GSDKSFGMKKRPDGDIEIDENFWEEGFCIPTC--------QXXX----------------
scSIR2      132 ----------------------------LPLC--------PYCYKKRREYFPEGYNNKVG
scHST1      132 ----------------------------LPLC--------PYCYQKRKQYFPMSNGNNTV
spSIR2      132 ----------------------------VSYC--------NECGKPPLKLRRVGQNKKEK
hsSIRT1     132 ----------------------------VPRC--------PRCPADEP------------
dmSRT406    134 ----------------------------IPVC--------PQCQPNKEQSVDASVAVTEE
ceSRT309    132 ----------------------------VAHC--------KRCEG---------------
scHST2p     136 ----------------------------FVKC--------DVCGE---------------
spHST2      133 ----------------------------VPKC--------NSCKG---------------
hsSIRT2     135 ----------------------------TPKC--------EDCQS---------------
hsSIRT3     133 ----------------------------VPRC--------PVCTG---------------
scHST4      149 ----------------------------IPSC--------PQCEEYETVRKMAGLRSTGV
spHST4      147 ----------------------------VTVC--------PDCKTENEVRRIAGKRSVIE
scHST3      158 ----------------------------LPLC--------PDCEALINKRLNEGKRTLGS
hsSIRT5     144 -------------------------VEKLPRCE------EAGCG----------------
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ceSRT312   111 ----------------------------GRNCE-GNKRTGRSCRG---------------

hsSIRT6    128 -------------------GELRDTILDWED---SLPDRDLALADEASRN----------
dmSRT408   129 -------------------GILYDNVLDWEH---DLPENDLEMGVMHSTV----------
atSRT1     123 -------------------AKLKDTVLDWED---ALPPKEIDPAEKHCKK----------
leSRT1105  121 -------------------ARLKDTVLDWED---ALPPKEMNPAERHCKM----------
zmSRT101   123 -------------------ARLKDTVLDWDD---ALPPEEMNLATEHCRS----------
taSRT803   123 -------------------ARLKDTVLDWED---ALPPEEMNSAEEQCRA----------
osSRT701   123 -------------------ARLKDTVLDWED---ALPPEEMDAAKEQCQT----------
hsSIRT7    124 -------------------TQLRDTIVHFGERGTLGQPLNWEAATEAASR----------
dmSRT409   124 -------------------EPLYDTIVHFGERGNVKWPLNWAGATANAQR----------
hsSIRT4    164 -------------------GHLKPDVVFFGDT---VNPDKVDFVHKRVKE----------
dmSRT407   165 -------------------GXXKXEIVFFGDS---VPRPRVDQIAGMVYN----------
ceSRT310   167 -------------------GLMKTDVTLFGEN---LNTDKIKVCGKKVNE----------
ceSRT311   167 -------------------GLMKTDVTFFGEN---VNMDKVNFCYEKVNE----------
atSRT2     179 -------------------GVLKPDVIFFGDN---IPKERATQAMEVAKQ----------
leSRT1104  176 -------------------GVLKPDVVFFGDN---VPKSRADAAMEAAKG----------
mtSRT1303  177 -------------------XXXXXXXXXXXXX---XXXXXXXXXXXXXXX----------
scSIR2     156 VAASQGSMSERPPYILNSYGVLKPDITFFGEA---LPN-KFHKSIREDIL----------
scHST1     156 QTNINFNSP-----ILKSYGVLKPDMTFFGEA---LPS-RFHKTIRKDIL----------
spSIR2     156 HYFSDGDSESSED-DLAQPGIMKPDITFFGEA---LPDSFFNKVGSGELE----------
hsSIRT1    144 -------LA-----------IMKPEIVFFGEN---LPE-QFHRAMKYDKD----------
dmSRT406   158 ELRQLVENG-----------IMKPDIVFFGEG---LPD-EYHTVMATDKD----------
ceSRT309   141 --------------------VIKPNIVFFGED---LGR-EFHQHVTEDKH----------
scHST2p    145 --------------------LVKPAIVFFGED---LPD-SFSETWLNDSEWLREKITTSG
spHST2     142 --------------------LIKPMIVFYGEG---LPM-RFFEHMEKDT--------K--
hsSIRT2    144 --------------------LVKPDIVFFGES---LPA-RFFSCMQSDFL-------K--
hsSIRT3    142 --------------------VVKPDIVFFGEP---LPQ-RFL-LHVVDFP-------M--
scHST4     173 G-------------------KLRPRVILYNEV---HPEGDFIGEIANNDLK---------
spHST4     171 G-------------------CLRPRIVLYNEI---HPDSESIGSVCSQDLK---------
scHST3     182 N-----------------VGILRPNIVLYGEN---HPSCEIITQGLNLDIIKG-------
hsSIRT5    157 -------------------GLLRPHVVWFGEN---LDPAILEEVDRELAH----------
ceSRT312   127 --------------------KLRDATLDWDTEIS-LNHLDRIRKAWKQTS----------

hsSIRT6    156 ----ADLSITLGTSLQIRP
dmSRT408   157 ----ADLNIALGTTLQIVP
atSRT1     151 ----ADLVLCLGTSLQITP
leSRT1105  149 ----ADVVLCLGTSLQITP
zmSRT101   151 ----ADLVLCLGTSLQITP
taSRT803   151 ----ADLVLCLGTSLQITP
osSRT701   151 ----ADLVLCLGTSLQITP
hsSIRT7    155 ----ADTILCLGSSLKVLK
dmSRT409   155 ----ADVILCLGSSLKVLK
hsSIRT4    192 ----ADSLLVVGSSLQVYS
dmSRT407   193 ----SDGLLVLGSSLLVFS
ceSRT310   195 ----CNGVLTLGTSLEVLS
ceSRT311   195 ----CDGILSLGTSLAVLS
atSRT2     207 ----SDAFLVLGSSLMTMS
leSRT1104  204 ----CDAFLVLGSSLMTMS
mtSRT1303  205 ----XXXXXXXXXXXXXXX
scSIR2     202 ---ECDLLICIGTSLKVAP
scHST1     197 ---ECDLLICIGTSLKVAP
spSIR2     202 ---ETDLLICIGTSLKVAP
hsSIRT1    172 ---EVDLLIVIGSSLKVRP
dmSRT406   193 ---VCDLLIVIGSSLKVRP
ceSRT309   167 ---KVDLIVVIGSSLKVRP
scHST2p    181 KHPQQPLVIVVGTSLAVYP
spHST2     168 ---VCDMALVIGTSLLVHP
hsSIRT2    171 ----VDLLLVMGTSLQVQP
hsSIRT3    168 ----ADLLLILGTSLEVEP
scHST4     202 -K-RIDCLIIVGTSLKIPG
spHST4     200 -S-RPDCLIVAGTSCKIPG
scHST3     215 ---NPDFLIIMGTSLKVDG
hsSIRT5    185 ----CDLCLVVGTSSVVYP
ceSRT312   156 ------HLLCIGTSLEIIP
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Multiple sequence alignment of SIR2 domains of SIR2 family proteins included in the phylogenetic analysis. The average length of the domain is approximately 175 amino acids. The numbers listed in front of the sequences indicates the location in the histone deacetylase domain and not in the given protein sequence.