Figure S3 clustal W alignment of Pl-foxo with other FoxO proteins.

```
                                                                    1           14
PL-FOXO-MT799801.2          ------------------------------------MVDNDPDFEPQARP
SP-FOXO1-XP_030850453       ------------------------------------MVDNDPDFEPQARP
HL-FOXO-KAJ8026986.1        ------------------------------------MDDIDADFEPQDRP
AR-FOXO-XP_033635399.1      ------------------------------------MAEIDPDFEPQSRP
SK-FOXO3-NM_001164968.1     ----------------------------------MADILEIDPDFEPQSRP
HS-FOXO3-NM_001415139.1     --------------------------------------------------
CC-FOXO-XM041212798.1       ----------------------------MEEAVAPHVDIDPDFEPQSRP
BF-FOXO-XP_035685890.1      ----------------------------MDMEDPQLEIDPDFEPQSRP
DM-FOXO-NM_001275628.1      ----------MMDGYAQEWPRLTHTDNGLAMDQLGGDLPLDVGFEPQTRA
Ce-DAF16-AF032112.1         MMEMLVDQGTDASSSASTSTSSVSRFGADTFMNTPDDVMMNDDMEPIPRD

                            15                                          56
PL-FOXO-MT799801.2          RSCTWP-LRRPDFLDSKPQQPGNAAAAPPVDHPHGALSPAVLT-------
SP-FOXO1-XP_030850453       RSCTWP-LRRPDFLDSKPGQPGNAAGAPPVDHAHSALSPAVLA-------
HL-FOXO-KAJ8026986.1        RSCTWPSLRRPEFLDKKPSQAGADQQAQAAQQAQLPEEAQSQA-------
AR-FOXO-XP_033635399.1      RSCTWP-LRRPDFLEKPSQPS--PGEGAPSTGTGAPDEIQDPV-------
SK-FOXO3-NM_001164968.1     RSCTWP-LPRPDFSAQKPSPPPSDQAATPETEIPQEGIEIKQD-------
HS-FOXO3-NM_001415139.1     --------------------------------------------------
CC-FOXO-XM041212798.1       RSCTWP-LPRPEFPVAEGKGEESASHNEPAAATESGGGSGGGGGGVK---
BF-FOXO-XP_035685890.1      RSCTWP-LPRPEVCTNESKTEGSPENEQTTTGEGGGIEPKTEAGTVPG--
DM-FOXO-NM_001275628.1      RSNTWPCPRPENFVEPTDELDSTKASNQQLAPGDSQQAIQNAN-------
Ce-DAF16-AF032112.1         RCNTWP-MRRPQLEPPLNSSPIIHEQIPEEDADLYGSNEQCGQLGGASSN

                                     57                    77  81    87        97
PL-FOXO-MT799801.2          ---------EESVDIKPILPLEGGENRELSTPSSQRRNGSRRNAWGNLSY
SP-FOXO1-XP_030850453       ---------EEPLDIKPVLPLEGGENRELSTPSSQRRNGSRRNAWGNLSY
HL-FOXO-KAJ8026986.1        ---------VASPQITPES------KVDLTTPTTQRKNGSRRNAWGNLSY
AR-FOXO-XP_033635399.1      ---------LSQQVESPDI------KQDLAAVATNRKNCSRRNAWGNLSY
SK-FOXO3-NM_001164968.1     ---------QSTPS----------------------RKNSSRRNAWGNLSY
HS-FOXO3-NM_001415139.1     ----------------------MRLPRSLGHGQVRRGGRGRRRGKGERTG
CC-FOXO-XM041212798.1       --------------AEAKALAATHSPLRLSECSQHRKKSSRRNAWGNLSY
BF-FOXO-XP_035685890.1      ------LAAEPTAPVAAAPTTVDATSLQAELQAPQPKKSSRRNAWGNLSY
DM-FOXO-NM_001275628.1      ---------------------------------AAKKNSSRRNAWGNLSY
Ce-DAF16-AF032112.1         GSTAMLHTPDGSNSHQTSFPSDFRMSESPDDTVSGKKTTTRRNAWGNMSY

                            98                                        135       146
PL-FOXO-MT799801.2          ADLITKAIQSAPDQRLTLSQIYDWMVKNVPFFKDKGDSNSSAGWKN-SIR
SP-FOXO1-XP_030850453       ADLITKAIQSAPDQRLTLSQIYDWMVKNVPFFKDKGDSNSSAGWKN-SIR
HL-FOXO-KAJ8026986.1        ADLITKAIQGAPEQRLTLAQIYEWMVKNVPFFKDKGDSNSSAGWKQNSIR
AR-FOXO-XP_033635399.1      ADLITKAIQSAPEQRLTLSQIYDWMVKNVPFFKDKGDSNSSAGWKN-SIR
SK-FOXO3-NM_001164968.1     ADLITKAIESAPDKRLTLSQIYEWMVKSVPYFKDKGDSNSSAGWKN-SIR
HS-FOXO3-NM_001415139.1     VHLLDSPDSTE---------------------------------EN-SIR
CC-FOXO-XM041212798.1       ADLITKAIESSPEKRLTLSQIYDWMVRHVPYFKDKGDSNSSAGWKN-SIR
BF-FOXO-XP_035685890.1      ADLITKAIQSSPEGRLTLSQIYDWMVRCVPYFRDKGDSNSSAGWKN-SIR
DM-FOXO-NM_001275628.1      ADLITHAIGSATDKRLTLSQIYEWMVQNVPYFKDKGDSNSSAGWKN-SIR
Ce-DAF16-AF032112.1         AELITTAIMASPEKRLTLAQVYEWMVQNVPYFRDKGDSNSSAGWKN-SIR

                            147                                           187  193
PL-FOXO-MT799801.2          HNLSLHSRFVRVQNEGTGKSSWWMINPDAKP---GKSSRRRASSMDTTNS
SP-FOXO1-XP_030850453       HNLSLHSRFVRVQNEGTGKSSWWMINPDAKP---GKSSRRRASSMDTTNS
HL-FOXO-KAJ8026986.1        HNLSLHSRFVRVQNEGTGKSSWWMINPDAKP---GKNSRRRSSSMDTSNA
AR-FOXO-XP_033635399.1      HNLSLHSRFVRVQNEGTGKSSWWMINPDAKP---GKSSRRRASSMDTSNP
SK-FOXO3-NM_001164968.1     HNLSLHSRFVRVQNEGTGKSSWWMINPDATKT--GKSSRRRATSMDTSNK
HS-FOXO3-NM_001415139.1     HNLSLHSRFMRVQNEGTGKSSWWIINPDGGKS--GKAPRRRAVSMDNSNK
CC-FOXO-XM041212798.1       HNLSLHSRFIRVQNEGTGKSSWWMLNPDGGKT--GKSPRRRAVSMDSNSK
BF-FOXO-XP_035685890.1      HNLSLHSRFIRVQNEGTGKSSWWMLNPD-AKG--GKSPRRRASSMDTNNS
DM-FOXO-NM_001275628.1      HNLSLHNRFMRVQNEGTGKSSWWMLNPEAKP---GKSVRRRAASMETSRY
Ce-DAF16-AF032112.1         HNLSLHSRFMRIQNEGAGKSSWWVINPDAKPGRNPRRTRERSNTIETTTK
```

```
                                194                         219        227
PL-FOXO-MT799801.2              KFERKRGRVKKKVLEERAKWGNTSPTP----KLEGEEG------------
SP-FOXO1-XP_030850453           KFERKRGRVKKKVLEERAKWGNTSPTP----KLEGEEG------------
HL-FOXO-KAJ8026986.1            KWEKKRGRAKKKAEEKAKNCY-PNSSP----KLEGADD------------
AR-FOXO-XP_033635399.1          KWEKKRGRAKKKVLEEHAKWN-TSPTP----KFEGGEP------------
SK-FOXO3-NM_001164968.1         QFEKKRGRAKKKAAELAAKLAAAGERP----KWSPQTPDGSDTGM-----
HS-FOXO3-NM_001415139.1         YTKSRGRAAKKKAALQTAPESADDSPS-QLSKWPGSP-------------
CC-FOXO-XM041212798.1           YLKSKRGANKKKATLQATQEGNEGSPSSQHTKWSGSP-------------
BF-FOXO-XP_035685890.1          KYEKKRGRAKKKAQEAREAAAAANAGS-PTGKWPGSPQDSKSEGGTPSGD
DM-FOXO-NM_001275628.1          EKRRGRAKKRVEALRQAGVVGLNDATPSPSSSVSEGLDHFPES-------
Ce-DAF16-AF032112.1             AQLEKSRRGAKKRIKERALMGSLHSTLNGNSIAGSIQTISHDLYD-----

                                228                     246          255 259      269
PL-FOXO-MT799801.2              -----ASPLPFNLATTDFRSRASSNASSCG---RLSPIMTTHPEMDMHDN
SP-FOXO1-XP_030850453           -----ASPLPFNLATTDFRSRASSNASSCG---RLSPIMTTHPEIDMHDN
HL-FOXO-KAJ8026986.1            -----QNSLAFSLS-TDFRSRASSNASSCG---RLTPIMAN-ELTDMHDS
AR-FOXO-XP_033635399.1          -----ETSLSLALS-SEFRSRASSNASSCG---RLSPINQMVELTDMHDN
SK-FOXO3-NM_001164968.1         ----VESPLPAFQLSPDFRPRTSSNASSCG---RLSPIMANQELDDMHDN
HS-FOXO3-NM_001415139.1         ----TSRSSDELDAWTDFRSRTNSNASTVSG--RLSPIMASTELDEVQDD
CC-FOXO-XM041212798.1           ----SSHASDEFDAWTDFRSRANSAASTLSG--RLSPIMANSELDELEDD
BF-FOXO-XP_035685890.1          GNLSASTASPLSFNISDFRQRTSSNASSLSG--RLSPIMGPDLDDDNQVP
DM-FOXO-NM_001275628.1          ----PLHSGGGFQLSPDFRQRASSNASSCG---RLSPIRAQDLEPDWGFP
Ce-DAF16-AF032112.1             ---DDSMQGAFDNVPSSFRPRTQSNLSIPGSSSRVSPAIGSDIYDDLEFP

                                270                   290  294             314  317
PL-FOXO-MT799801.2              EVPPMSPIP--FQDIAPSQAYDSPDPYQSTDQLAKLAKAMTLDSSLSVEP
SP-FOXO1-XP_030850453           EVPPMSPIP--FQDLPPSQAYDSPDPYQSTDQLAKLAKAMTLDSSLSVEP
HL-FOXO-KAJ8026986.1            EAPPMSPVPFVDHIGPPHHSFGDSQDSNHTAELTSLAKAMSLNSAMNSPL
AR-FOXO-XP_033635399.1          EAPPMSPG---AYDIGHHTQPYESPDHLHTDQLTSLAQAMSLNASLNGSV
SK-FOXO3-NM_001164968.1         EVPPMSPGPIDWNSTVPVSNYPGAELLRQTTDQLTSALAETMTLNSPDPM
HS-FOXO3-NM_001415139.1         D-APLSPMLYSS-SASLSPSVSKPC-TVELPRLTDMAGTMNLNDGLTENL
CC-FOXO-XM041212798.1           DRTPSSPLLYPSPSNTLSPSVSTRR-TVELPRLADMASTINLNEGLTENL
BF-FOXO-XP_035685890.1          PMSPGWSDFGSNNNLSYG-TSDFLN-QSTDQLTQSLQQTMKLNSPDQLLG
DM-FOXO-NM_001275628.1          VDYQNTTMTQAHAQALEELTGTMADELTLCNQQQQGFSAASGLPSQPPPP
Ce-DAF16-AF032112.1             SWVGESVPAIPSDIVDRTDQMRIDATTHIGGVQIKQESKPIKTEPIAPPP

                                                                318        328      335
PL-FOXO-MT799801.2              -------------------------------AIRHPHNNGGYLFS--PQSY
SP-FOXO1-XP_030850453           -------------------------------AIRHTHNNGGYLFS--PQSY
HL-FOXO-KAJ8026986.1            NPDQ---MEQLTVPG---YHVSPQNNGGHYHSSGTSNGNGYIYSPSSSQY
AR-FOXO-XP_033635399.1          SSDLNSSVEQLRVPAPRRPSPQHTSRGPLFQNGVSNNSNGYMFSPSPS-F
SK-FOXO3-NM_001164968.1         TIDQLTLSPQPQIQP------AQSPSPGLPAVYTNQNGSTFTLSTQAPTF
HS-FOXO3-NM_001415139.1         MDDLLDNITLPPSQP-------------SPTGGLMQRSSSFPYTTKGSGL
CC-FOXO-XM041212798.1           LEDLQDNYNMSPSQQ-------------IPSGCLRQRSSSFSFGSKCSTR
BF-FOXO-XP_035685890.1          DSGLSGMSSMDSVGS-------------LGLGGFDSQPDPFMRRCHSVGS
DM-FOXO-NM_001275628.1          PYQPPQHQQAQQQQQ---------QQSPYALNGPASGYNTLQPQSQCLLH
Ce-DAF16-AF032112.1             ---------------------------------SYHELNSVRGSCAQNPL

                                336                                                 376
PL-FOXO-MT799801.2              SGSDMSPVHSNTQSPYYS---------QQGTPAVSPLGQCSPMQELPPNQ
SP-FOXO1-XP_030850453           SGSDMSPVHS--NSPYYS---------QQGTPAVSPLGQCSPMQELPPSQ
HL-FOXO-KAJ8026986.1            SGSELSPAQNGVQSPFSSYS-------QPNTPVMSPINQPQPQQQQQCSP
AR-FOXO-XP_033635399.1          SGSDISPVHSNVQSPAYSPY-------GQNS-------AMSPMAQQRCSP
SK-FOXO3-NM_001164968.1         GTQNVTLANTSLFLPYNTQSGLCMTQAGQTSPSSLGMISENPSPPQLSMS
HS-FOXO3-NM_001415139.1         GSPTSSFNSTVFGPSSLNSL------------------RQSPMQTIQENK
CC-FOXO-XM041212798.1           GSQTSTYSATMYSQPPMTML------------------RHSPMQTIQENK
BF-FOXO-XP_035685890.1          RAQLPSPRRQNTGYSTPPPS------------------FKSPFSPVQVPQ
DM-FOXO-NM_001275628.1          RSLNCSCMHNARDGLSPNSVT----------------TTMSPAYPNSEPS
Ce-DAF16-AF032112.1             LRNPIVPSTNFKPMPLPGAYG---------------------------
```

```
                         377                                            406
PL-FOXO-MT799801.2       YG--------------------MRQTFTSLMHENNDAIIPQDPMFSQTAG
SP-FOXO1-XP_030850453    YG--------------------MQRSFTNLIHEN-ESIIPQDPMFAQSAV
HL-FOXO-KAJ8026986.1     INGVSDLNP--------QYIQQPPGLLSQSANILSQDPIQNRLNVPADSV
AR-FOXO-XP_033635399.1   SMSVTDMSQPFTMNVPQQQQQQTPSAFTMMPHQDPSVILSKRDPMLSHST
SK-FOXO3-NM_001164968.1  NIQQVSQTPLNEAMISQNDPILPSDLIISQQDPMLSQISGNDLMLQSDPM
HS-FOXO3-NM_001415139.1  PATFSSMS------HYGNQTLQDLLTSDSLSHSDVMMTQSDPLMSQASTA
CC-FOXO-XM041212798.1    QVTFSTIN------HYGNRMLQDLLTPESLRHKEVMMTQTDPLMPQANTV
BF-FOXO-XP_035685890.1   PAHSPNQQQ--GSLPSVNAPQQDPTQFSLQQLSDVMLTQTDPILTSGDPV
DM-FOXO-NM_001275628.1   SDSLNTYSNVVLDGPADTAALMVQQQQQQQQQQQLSASLEDNNCASTLIG
Ce-DAF16-AF032112.1      --------------NYQNGGITPINWLSTSNSSPLPGIQSCGIVAAQHTV

                         407           418  423                         427
PL-FOXO-MT799801.2       LRQQ----QSPRPMPSCREESM-------------------------IQH
SP-FOXO1-XP_030850453    LRQQ----QSPRPMPSCREESM-------------------------NQH
HL-FOXO-KAJ8026986.1     MMQQAVHNQS--MLSSCREQSN-------------------------MVH
AR-FOXO-XP_033635399.1   LGPGSMMHQRPTNLPTCRVQTS-------------------------ISQ
SK-FOXO3-NM_001164968.1  LSMAQEQKYVPSRLNFNIPSSVNLTQPN-----------------VMTGF
HS-FOXO3-NM_001415139.1  VSAQN---SRRNVMLRNDPMMS-----------------------FAAQP
CC-FOXO-XM041212798.1    VASQN---QRQMVMCSDPAISP-----------------------FNAQS
BF-FOXO-XP_035685890.1   MSSGDPLISQGNLMLRQDPMMSGCPDQGSQLSSLLQGTGMSYAFRQQQQQ
DM-FOXO-NM_001275628.1   QCLEVLNNEAQPIDEFNLENFPVG----------------------NLEC
Ce-DAF16-AF032112.1      ASSSALPIDLENLTLP----------------------------------

                         428                                            474
PL-FOXO-MT799801.2       TSPHRLMPS-GNQGSNLAMLLNNGHN--QTTSHHHPLPYPNGGTPHHIPH
SP-FOXO1-XP_030850453    TSPHRLMPSSMNQGSNLAMLLNNGHNTHTTSHHHHPQPYPNGGTPHHVHP
HL-FOXO-KAJ8026986.1     R--QRFVSPGQHQQVNQSSLALALGMS---QQGFTPASLQMSRNIQAYQQ
AR-FOXO-XP_033635399.1   GRSLQGFSPQTSPSNPLSGLLLPNAVT---ASQTNHMSSPTHVSLNAHYA
SK-FOXO3-NM_001164968.1  GNNLQPFQQQQQQQQHSRLLAQLIGGNALQQQLQQQQQQQQQQQQQQQQQ
HS-FOXO3-NM_001415139.1  NQGSLVNQNLLHHQHQTQGALGGSRALSNSVSNMGLSESSSLGSAKHQQQ
CC-FOXO-XM041212798.1    PRLMNSNPFHHPSTAQQNSAVNNGALSNPIGLMHMHSDAGNINSVAHHLQ
BF-FOXO-XP_035685890.1   QLQQQQQQQQQPQQQPQQQNYNLGCALNQMLGGNMGIMAGQLAPTQQQQQ
DM-FOXO-NM_001275628.1   NVEELLQQEMSYGGLLDINIPLATVNTNLVNSSSGPLSISNISNLSNISS
Ce-DAF16-AF032112.1      -------------------------------DQPLMDTMDVDALIRHELS

                         475                 495                       505
PL-FOXO-MT799801.2       IHAH-HQHHHHPGIGHQDRFPSDLES------------------VQIDPL
SP-FOXO1-XP_030850453    HHIHPHIHHHHPGMVHVDRFPSDLES------------------VQIDPL
HL-FOXO-KAJ8026986.1     QSTQQNLQSQLVPN-----GPIPNDL------------------VSIEVE
AR-FOXO-XP_033635399.1   QSMNQLLQSSPMTTNTSDRVPTDLQS------------------LNVDMF
SK-FOXO3-NM_001164968.1  QQQQQMLSNQRTNFSMLQSMNMNMNMPGLATDQLTNMHDKFPSDLELDMF
HS-FOXO3-NM_001415139.1  ---SPVSQSMQTLSDSLSGSSLYSTS----ANLPVMGHEKFPSDLDLDMF
CC-FOXO-XM041212798.1    NQLHSLASHGMQMEASDSRLSSCPGG----INISTMSQDKFPTDLDLDMF
BF-FOXO-XP_035685890.1   TPLPQISTFGMMHQQSPASLHQQAMANSQANQLLSMHQEKFPSDLELDMF
DM-FOXO-NM_001275628.1   NSGSSLSLNQLQAQLQQQQQQQQAQQ------------------QQQAQQ
Ce-DAF16-AF032112.1      QAGGQHIHFDL---------------------------------------

                         506                                            543
PL-FOXO-MT799801.2       KGWSDLDVETILRNE-----------QDLTEG-PDASFDNIGTIGTTATT
SP-FOXO1-XP_030850453    KGWSDLDVETILRNE-----------QDLTEG-PDASFDNIGTIGTTATT
HL-FOXO-KAJ8026986.1     P-EFDIDMDSFIRNE-----------VNLGDGFNNVNFDNINTGNPTSTA
AR-FOXO-XP_033635399.1   K-DMHCDIESVIHDE-----------LKMDDGNLDFNFD-----GPINNQ
SK-FOXO3-NM_001164968.1  NGGLECDVDSIIRNEPDITETAALDFNNLEGNTSSTMGMNLTFSTSSATS
HS-FOXO3-NM_001415139.1  NGSLECDMESIIRSELMDAD--GLDFNFDSLISTQNVVGLNVGNFTGAKQ
CC-FOXO-XM041212798.1    HGSLECDVESIILNEFMDSE--ELDFNFDCAMPTQSVG-INMATLPTAPQ
BF-FOXO-XP_035685890.1   SGGLECDMDSIINTELMEDG--GLEFNFQQDPNNQMGSCAPTSAGMTQSM
DM-FOXO-NM_001275628.1   QQQHQQHQQQLLLNNNNNSS----SSLELATQTATTNLNARVQYSQPSVV
Ce-DAF16-AF032112.1      --------------------------------------------------
```

```
                                544   551
PL-FOXO-MT799801.2              MAAPSWVH----------
SP-FOXO1-XP_030850453           MAAPSWVH----------
HL-FOXO-KAJ8026986.1            NIGTNWVH----------
AR-FOXO-XP_033635399.1          TVAPNWVH----------
SK-FOXO3-NM_001164968.1         SSTQSWVH----------
HS-FOXO3-NM_001415139.1         ASSQSWVPG---------
CC-FOXO-XM041212798.1           TTNQSWVPG---------
BF-FOXO-XP_035685890.1          TMSQTQTNAGRLGYRETVI
DM-FOXO-NM_001275628.1          TSPPSWVH----------
Ce-DAF16-AF032112.1             ------------------
```