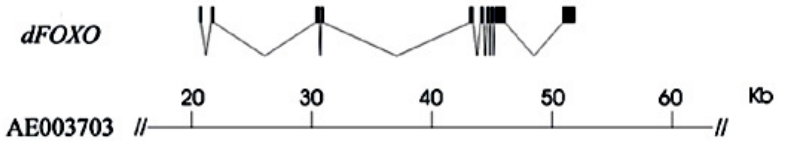
A



B

```
                                                                                T1
dFOXO           ------------------------------MDQLGGDLFLDVGFEPQTRARSNTWPCPRP 31
FOXO1a(FKHR)    -----------------------MAEAPQ--------VVEIDPDFEPLPRPRSCTWPLPRP 30
FOXO4(AFX)      ----------------------MRIQPQKAAAI----IDLDPDFEPQSRPRSCTWPLPRP 34
FOXO3a(FKHRL1)--------------------MAEAPASPAPLSPLEVELDFEPEPQSRPRSCTWPLQRP 38
Daf-16a1        MMEMLVDQGTDASSSASTSTSSVSRFGADTFMNTPDDVMMNDDMEPIPRDRCNTWPMRRP 60
                                                          : ::  :** .* *. *** **

dFOXO           BNFVEPTDELDSTKASN---------------------------------------- 48
FOXO1a(FKHR)    EFSQSNSATSSPAPSGS--AAANPDAAAGLPSASAAAVSADFMSNLSLLEESEDFPQAPG 88
FOXO4(AFX)      EIANQPSEP----------PEVEPD-----------------------LG--------E 52
FOXO3a(FKHRL1)ELQASPAKPSGETAADSMIPEEEDDEDDEDGGGRAGSAMAIGGGGGSGTLGSGLLLEDSA 98
Daf-16a1        QLEPPLNSSPIIHEQIP-------------------------------EEDADLYGSNE 88
                 :

dFOXO           QQLAPGDSQQAIQN------------------------------------------ANA 65
FOXO1a(FKHR)    SVAAAVAAAAAAAATGGLCGDFQGPEAGCLHPAPPQPPPPGPLSQHPPVPPAAAGPLAGQ 148
FOXO4(AFX)      KVHTEGRSEPILLPSRLS--------------EPAGGPQPG----------ILGA--VTG 86
FOXO3a(FKHRL1)RVLAPGGQDPGSGPATAAGGLSGGTQALLQPQQPLPPPQPG----------AAGG--SGQ 146
Daf-16a1        QCGQLGGASSNGSTAMLHTPDGSNSHQTSFPSDFRMSESPD----------------DTV 132

dFOXO           AKKNSS-RRNAWGNLSYADLITHAIGSATDKRLTLSQIYEWMVQNVPYFKDKGDSNSSAG 124
FOXO1a(FKHR)    PRKSSSSRRNAWGNLSYADLITKAIESSAEKRLTLSQIYEWMVKSVPYFKDKGDSNSSAG 208
FOXO4(AFX)      PRKGGS-RRNAWGNQSYAEFISQAIESAPEKRLTLAQIYEWMVRTVPYFKDKGDSNSSAG 145
FOXO3a(FKHRL1)PRKCSS-RRNAWGNLSYADLITRAIESSPDKRLTLSQIYEWMVRCVPYFKDKGDSNSSAG 205
Daf-16a1        SGKKTTTRRNAWGNMSYAELITTAIMASPEKRLTLAQVYEWMVQNVPYFRDKGDSNSSAG 192
                . *  : ******* ***::*: ** ::.:*****.*:*****: ****:**********

                                                                  S1
dFOXO           WKNSIRHNLSLHNRFMRVQNEGTGKSSWWMLNP-EAKPGKSVRR---RAASMETS-RYEK 169
FOXO1a(FKHR)    WKNSIRHNLSLHSKFIRVQNEGTGKSSWWMLNPEGGKSGKSPRR---RAASMDNNSKFAK 265
FOXO4(AFX)      WKNSIRHNLSLHSKFIKVHNEATGKSSWWMLNPEGGKSGKAPRR---RAASMDSSSKLLR 202
FOXO3a(FKHRL1)WKNSIRHNLSLHSRFMRVQNEGTGKSSWWIINPDGGKSGKAPRR---RAVSMDNSNKYTK 262
Daf-16a1        WKNSIRHNLSLHSRFMRIQNEGAGKSSWWVINP-DAKPGRNPRTTRPSNTLETTTKAQL 251
                ************.*:::::**.:*******::**  .*.*:  **    *: ::::.. :

dFOXO           RRGRAKKRVEALRQAGVVGLNDATPSPSSSVSEGLDHFPESP-LHSGGGFQLSPDFRQRA 238
FOXO1a(FKHR)    SRSRAAKKKASLQSG------QBGAGDSPGS--QFSKWPASPGSHSNDDFDNWSTFRPRT 317
FOXO4(AFX)      GRSKAPKKKPSVLPA------PPEGATPTSPVGHFAKWSGSPCSRNREEADMWTTFRPRS 256
FOXO3a(FKHRL1)SRGRAAKKKAALQTA------PBSADDSPS---QLSKWPGSPTSRSSDELDAWTDFRSRT 313
Daf-16a1        EKSRRGAKKRIKERA------LMGSLHSTLNGNSIAGSIQTISHDLYDDDSMQGAFDNVP 305
                 :.:  :                                 :   :          .   *  .

                S2                  DYRK1a/mnb
dFOXO           LSNASSADF-LSPIRAQDLEPDWGFPVDYQNTTMTQAHAQALEELTG------------- 384
FOXO1a(FKHR)    SSNASTISGRLSPIMTE---QDDLGEGDVHSMVYPPSAAKMASTLP--------------- 360
FOXO4_AFX_      SSNASSVSTRLSPLRPE---SEVLAEEIPAS--VSSYAGGVPP----------------- 294
FOXO3a(FKHRL1)NSNASTVSGRLSPIMASTELDSVQDDDAPLSPMLYSSSASLSPSVSKPCTVELPRLTDMA 373
Daf-16a1        SSFRPRTQSNLSIPGSSSRVSPAIGSDIYDDLEPPSWVGESVPAIPS------------- 352
                 .  .  .  **   ..                .          .

dFOXO           ---------------TMADELTLCN-----------------QQQQGFSAASGLPSQPPP 312
FOXO1a(FKHR)    ---SLSEISNPENMENLLDNLNLLSSPTSLTVSTQSSPGTMMQQTPCYSFAPPNTSLNSP 417
FOXO4(AFX)      ---TLNEGL-------ELLDGLNLTS-------SHS-----LLSPSGLSGFSLQHPGVTGP 333
FOXO3a(FKHRL1)GTMNLNDGLTENLMDDLLDNITLPP-------SQPSPTGGLMQRSSSFPYTTKGSGLGSP 426
Daf-16a1        ---------------DIVDRTDQMR----------------------IDATTHIGGVQIK 375
                                  : *                                  :   .

dFOXO           PPYQ-------------PPQHQQAQQQ----------------QQQQSPYALNGPASGYN 343
FOXO1a(FKHR)    SPNYQKYTYGQQSMSPLPQMPIQTLQDNK-SSYGGMSQYNCAPGLLKELLTSDSPP--HN 474
FOXO4(AFX)      LHTYSSSLFSP------AEGPLSAGEG----CFSSS-------QALEALLTSDTPPPPAD 376
FOXO3a(FKHRL1)TSSFNSTVFGPSSLNSLRQSPMQTIQENKPATFSSMSHY--GNQTLQDLLTSDSLS-HSD 483
Daf-16a1        ------------------------------------------QESKPIKTEPIAPPPSY 392
                                                                  :   :   .

dFOXO           TLQPQSQCLLHRSLNCSCMHNARDGLSPNSVTTTMSPAYP--------------------- 483
FOXO1a(FKHR)    DIMTPVDPGVAQPNSRVLGQNVMMGPNSVMSTYGSQASHN--KMMNPSSHTHPGHAQQTS 532
FOXO4(AFX)      VLMTQVDPILSQAPTLLLLGGLPSSSKLATG--VGLCPKP--------------------- 414
FOXO3a(FKHRL1)VMMTQSDPLMSQASTAVSAQNSRRNVMLRNDPMMSFAAQPNQGSLVNQNLLHHQHQTQGA 543
Daf-16a1        HELNSVRGSCAQNPLLRNPIVPSTNPKPMPLPGAYGNYQN--------------------- 432
                                  :                 .

dFOXO           --NSEPSSDSLNTYSNVVLDGPADTAAMVQQQQQQQQ------------------------ 418
FOXO1a(FKHR)    AVNGRPLPHTVSTMPHTSGMNRLTQVKTPVQVPLPHPMQMSALGGYSSVSSCNGYGRMGL 592
FOXO4(AFX)      -LEARGPSSLVPTLSMIA--PPPVMASAPIPKALGTPVLTPPTEAAS-------------- 458
FOXO3a(FKHRL1)LGGSRALSNSVSNMGLSE--SSSLGSAKHQQQSPVSQSMQTLSDSLSGSSLYSTSANLPV 601
Daf-16a1        --GGITPINWLSTSNSSPLPGIQSCGIVAAQHTVASS------------------------ 467
                    .      : .

dFOXO           --QQQLSASLEG-QCLEV---LNNEAQPIDEFNLENFPVGNLECNVEEVSG--------- 463
FOXO1a(FKHR)    LHQEKLPSDLDG-MFIER---LDCDMESIIRNDLMDGDTLDFNFDNVLPNQ--------S 640
FOXO4(AFX)      --QDRMPQDLDLDMYMEN---LECDMDNIISDLMDEGEGLDFNFEPDP------------ 501
FOXO3a(FKHRL1)MGHEKFPSDLDLDMFNGS---LECDMESIIRSELMDADGLDFNFDSLISTQNVVGLNVGN 658
Daf-16a1        ---SALPIDLENLTLPDQPLMDTMDVDALIRHELSQAGGQHIHFDL--------------- 510
                   . :. .*:                 : : :    : :    .:. :

dFOXO           ---------------
FOXO1a(FKHR)    FPHSVKTTTHSWVSG 655
FOXO4(AFX)      ---------------
FOXO3a(FKHRL1)FTGAKQASSQSWVPG 673
Daf-16a1        ---------------
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