Additional File 1.

MH1 Domain

Nuclear localization signal

```
HS2    MSSILP----------------FTPPVVKRLLGWKKSAGGSGGAGGGEQNGQEEKWCEKAVKSLVKKLKKTGR-LDELEKAITTQNCNTKCVTIPSTCSEIWGLSTPNTIDQWDTTGLYS [103]
XS2    MSSILP----------------FTPPVVKRLLGWKKSASGTTGAGGGEQNGQEEKWCEKAVKSLVKKLKKTGQ-LDELEKAITTQNCNTKCVTIPSTCSEIWGLSTPNTIDQWDTTGLYS [103]
HS3    MSSILP----------------FTPPIVKRLLGWKK----------GEQNGQEEKWCEKAVKSLVKKLKKTGQ-LDELEKAITTQNVNTKCITIP------------------------- [68]
XS3    MSSILP----------------FTPPIVKRLLGWKK----------GEQNGQEEKWCEKAVKSLVKKLKKSGQ-LDELEKALTTQSISTKCITIP------------------------- [68]
dSmad2 M---LP----------------FTPQVVKRLLALKK---------GNEDNSVEGKWSEKAVKNLVKKIKKNSQ-LEELERAISTQNCQTRCVTVP------------------------- [66]
NvS23  MTSLLP----------------FTPPVVKRLLGWKR---------GGDE---DDKWAEKAVKSLVKKLKKTGG-LEELEKAITNPGVATKCVTIP------------------------- [66]
HS9a   MHSTTPIS----------SLFSFTSPAVKRLLGWKQ----------GDE---EEKWAEKAVDSLVKKLKKKKGAMDELERALSCPGQPSKCVTIP------------------------- [72]
HS9b   MHSTTPIS----------SLFSFTSPAVKRLLGWKQ----------GDE---EEKWAEKAVDSLVKKLKKKKGAMDELERALSCPGQPSKCVTIP------------------------- [72]
XS8a   MHASTPIS----------SLFTFTSPAVKRLLGWKQ----------GDE---EEKWAEKAVDSLVKKLKKKKGAMEELERALSCPGQPSKCVTIP------------------------- [72]
XS8b   MHASTPIS----------SLFSFTSPAVKRLLGWKQ----------GDE---EEKWAEKAVDSLVKKLKKKKGAMEELERALSCPGQPSKCVTIP------------------------- [72]
HS1    MNVT--------------SLFSFTSPAVKRLLGWKQ----------GDE---EEKWAEKAVDALVKKLKKKKGAMEELEKALSCPGQPSNCVTIP------------------------- [68]
XS1    MNVT--------------SLFSFTSPAVKRLLGWKQ----------GDE---EEKWAEKAVDALVKKLKKKKGAMEELEKALSCPGQPSNCVTIP------------------------- [68]
HS5    MTSMA-------------SLFSFTSPAVKRLLGWKQ----------GDE---EEKWAEKAVDALVKKLKKKKGAMEELEKALSSPGQPSKCVTIP------------------------- [69]
dMAD   MDTDDVESNTSSAMSTLGSLFSFTSPAVKKLLGWKQ----------GDE---EEKWAEKAVDSLVKKLKKRKGAIEELERALSCPGQPSKCVTIP------------------------- [82]
NvS15  MSSMA-------------SLFSFTPPAVKRLLGWKQ----------GDE---EEKWAEKAIESLVKKLKKKKGALEDLEKALSNPNQQSKCVTIA------------------------- [69]
```

DNA binding β hairpin

Hydrophobic core

Coordinate a zinc atom at the center

```
HS2    FSEQTRSLDGRLQVSHRKGLPHVIYCRLWRWPDLHSHHELKAIENCEYAFNLKKDEVCVNPYHYQRVETPVLPPVLVPRHTEILTELPPLDDYTHSIPENTNF----------------- [206]
XS2    FSEQTRSLDGRLQVSHRKGLPHVIYSRLWRWPDLHSHHELKAVENCEYAFNLKKDEVCVNPYHYQRVETPVLPPVLVPRHTEILTELPPLDDYTHSIPENTNF----------------- [206]
HS3    -----RSLDGRLQVSHRKGLPHVIYCRLWRWPDLHSHHELRAMELCEFAFNMKKDEVCVNPYHYQRVETPVLPPVLVPRHTEIPAEFPPLDDYSHSIPENTNF----------------- [166]
XS3    -----RSLDGRLQVSHRKGLPHVIYCRLWRWPDLHSHHELRAMEVCEYAFSMKKDEVCVNPYHYQRVETPVLPPVLVPRNTEIPAEFPSLDDYSHSIPENTNF----------------- [166]
dSmad2 -----RSKPAPAGEHLRKGLPHVIYCRLWRWPDLQSQNELKPLDHCEYAFHLRKEEICINPYHYKKIELSILVPKSLPTPPDSIVDYP-LDNHTHQIPNNTDYNAAIIRSASLSPPQYME [180]
NvS23  -----RSLDGRLQVSHRKGLPHVIYCRLWRWPDLQSHHELRPIEACEFAFSLKKEEVCVNPFHYQRVETPVLPPVLVPRQQSDVPHELPILPEYTR-PENVPF----------------- [163]
HS9a   -----RSLDGRLQVSHRKGLPHVIYCRVWRWPDLQSHHELKPLECCEFPFGSKQKEVCINPYHYRRVETPVLPPVLVPRHSEYNPQLSLLAKFRSASLHSEPLMPHNATYPDSFQQPPCS [187]
HS9b   -----RSLDGRLQVSHRKGLPHVIYCRVWRWPDLQSHHELKPLECCEFPFGSKQKEVCINPYHYRRVETPVLPPVLVPRHSEYNPQLSLLAKFRSASLHSEPLMPHNATYPDSFQQPPCS [187]
XS8a   -----RSLDGRLQVSHRKGLSHVIYCRVWRWPDLQSHHELKPMECCEFPFGSKQKDVCINPYHYRRVETPVLPPVLVPRHSEFNPQLSLLAKFSNTSLNNEPLMPHNATFPESFQQPPRT [187]
XS8b   -----RSLDGRLQVSHRKGLPHVIYCRVWRWPDLQSHHELKPMECCEFPFGSKQKDVCINPYHYRRVETPVLPPVLVPRHSEFNPQLSLLAKFRNTSLNNEPLMPHNATFPESFQQPPCT [187]
HS1    -----RSLDGRLQVSHRKGLPHVIYCRVWRWPDLQSHHELKPLECCEFPFGSKQKEVCINPYHYKRVESPVLPPVLVPRHSEYNPQHSLLAQFRNLGQN-EPHMPLNATFPDSFQQPNSH [182]
XS1    -----RSLDGRLQVSHRKGLPHVIYCRVWRWPDLQSHHELKPLECCEYPFGSKQKEVCINPYHYKRVESPVLPPVLVPRHSEYNPQHSLLAQFRNLEPS-EPHMPHNATFPDSFQQPNSH [182]
HS5    -----RSLDGRLQVSHRKGLPHVIYCRVWRWPDLQSHHELKPLDICEFPFGSKQKEVCINPYHYKRVESPVLPPVLVPRHNEFNPQHSLLVQFRNLSHN-EPHMPQNATFPDSFHQPNNT [183]
dMAD   -----RSLDGRLQVSHRKGLPHVIYCRVWRWPDLQSHHELKPLELCQYPFSAKQKEVCINPYHYKRVESPVLPPVLVPRHSEFAPGHSMLQFNHVAEPSMPHNVSYSNSGFNSHSLSTSN [197]
NvS15  -----RSLDGRLQVSHRKGLPHVIYCRVWRWPDLQSHHELKPLECCEYAFGLKQKEVCINPYHYHRVESPGLPPVLVPRQSEYPRPPPPLPPPFRATDDPPMPYNASFPFTNRQNTSEQS [184]
```

```
HS2    --------------------------------------------------------PAGIEPQSNYIPE--TPPPGYISEDGETSDQQLNQSMDTGSPAE-LSPTTLSPVNHSLDLQPVT [267]
XS2    --------------------------------------------------------PAGIEPQSNYIPE--TPPPGYISEDGETSDQQLNQSMDTGSPAE-LSPSTLSPVNHNLDLQPVT [267]
HS3    --------------------------------------------------------PAGIEPQSN-IPE--TPPPGYLSEDGETSDHQMNHSMDAGSPN--LSPNPMSPAHNNLDLQPVT [225]
XS3    --------------------------------------------------------PAGIEPQINYIPE--TPPPGYLSEDGETSDQ-MNHSIDTGSPN--LSPNSMSPAHSNMDLQPVT [225]
dSmad2 LGGAGPVSVSSSASSTPATAAGGGGGPSSSSSSSSSAASAYQQQQQQLSFGQNMDSQSSVLSVGSSIPNTGTPPPGYMSEDGDPIDPNDNMNMSRLTP-----PA-DA-A-------PVM [286]
NvS23  --------------------------------------------------------PTQEPTNSQYHIQPGTPTD-YISDDACS-DMSGEHSQQNMQIDQQLSPAPDSNNLI--DAQPIQ [223]
HS9a   ALPPSPSHAFSQSPCTASYPHSPGSPSEPESPYQHSV-D--------------------------------TPPLPYHATEASETQSGQPVDATADRHVVLSIPNG--------DFRPVC [266]
HS9b   ALPPSPSHAFSQSPCTASYPHSPGSPSEPESPYQHS------------------------------------------------------------------------------DFRPVC [229]
XS8a   PFSSSPSNIFPQSPNTVGYPDSPRSSTDPGSPPYQI-TE--------------------------------TPPPPYNAPDLQGNQNRPTADPAECQLVLSALNR---------DFRPVC [265]
XS8b   PFSSSPSNIFSQSPNTVGYPDSPRSSTDPGSPPYQI-TE--------------------------------TPPPPYNAPDLQGNQNRPTADPAECQLVLSALNR---------DFRPVC [265]
HS1    PFPHSPNSSYPNSPGSSSSTYPHSPTSSDPGSPFQMPAD--------------------------------TPPPAYLPPEDPMTQDGSQPMDTNMMAPPLPSEINRG------DVQAVA [264]
XS1    PFPHSPNSSYPNSPGSSST-YPHSPASSDPGSPFQIPAD--------------------------------TPPPAYMPPEDQMTQDNSQPMDTNMMVPNISQD-INRA-----DVQAVA [263]
HS5    PFPLSPNSPYPPSPASST--YPNSPASSGPGSPFQLPAD--------------------------------TPPPAYMPPDDQMGQDNSQPMDTSNNMIPQIMPSISSR-----DVQPVA [264]
dMAD   TSVGSPSSVNSNPNSPYDSLA-------------------------------------------------GTPPPAYSPSEDGNSNNPNDGGQLLDAQMGDVAQVS-------------- [254]
NvS15  PSFDMADSGAGYMSEDGGSPRPEPNAMDVDPVN--------------------------------------SPP---SIS-QSAEAMSHVTAVN-------------------------- [236]
```

MH2 Doman

Trimer stabilization

Trimerization sites

Hydrophobic pocket

```
HS2    YSEPAFWCSIAYYELNQRVGETFHASQPSLTVDGFTDPSN--SERFCLGLLSNVNRNATVEMTRRHIGRGVRLYYIGGEVFAECLSDSAIFVQSPNCNQRYGWHPATVCKIPPGCNLKIF [385]
XS2    YSEPAFWCSIAYYELNQRVGETFHASQPSLTVDGFTDPSN--SERFCLGLLSNVNRNATVEMTRRHIGRGVRLYYIGGEVFAECLSDSAIFVQSPNCNQRYGWHPATVCKIPPGCNLKIF [385]
HS3    YCEPAFWCSISYYELNQRVGETFHASQPSMTVDGFTDPSN--SERFCLGLLSNVNRNAAVELTRRHIGRGVRLYYIGGEVFAECLSDSAIFVQSPNCNQRYGWHPATVCKIPPGCNLKIF [343]
XS3    YCEPAFWCSISYYELNQRVGETFHASQPSMTVDGFTDPSN--SERFCLGLLSNVNRNAAVELTRRHIGRGVRLYYIGGEVFAECLSDNAIFVQSPNCNQRYGWHPATVCKIPPGCNLKIF [343]
dSmad2 YHEPAFWCSISYYELNTRVGETFHASQPSITVDGFTDPSN--SERFCLGLLSNVNRNEVVEQTRRHIGKGVRLYYIGGEVFAECLSDSSIFVQSPNCNQRYGWHPATVCKIPPGCNLKIF [404]
NvS23  YTEPTYWCSISYYEMNTRVGETFHASQPSLTVDGFTDPSS--SDRFCLGLLSNINRNPPIEMTRKHIGKGVRLYYIGGEVFAECLSDSSIFVQSPNCNQRYHWHPATVCKIPPGCNLKIF [341]
HS9a   YEEPQHWCSVAYYELNNRVGETFQASSRSVLIDGFTDPSNNRN-RFCLGLLSNVNRNSTIENTRRHIGKGVHLYYVGGEVYAECVSDSSIFVQSRNCNYQHGFHPATVCKIPSGCSLKVF [385]
HS9b   YEEPQHWCSVAYYELNNRVGETFQASSRSVLIDGFTDPSNNRN-RFCLGLLSNVNRNSTIENTRRHIGKGVHLYYVGGEVYAECVSDSSIFVQSRNCNYQHGFHPATVCKIPSGCSLKVF [348]
XS8a   YEEPLHWCSVAYYELNNRVGETFQASARSVLIDGFTDPSNNKN-RFCLGLLSNVNRNSTIENTRRHIGKGVHLYYVGGEVYAECVSDSSIFVQSRNCNYQHGFHPSTVCKIPSGCSLKIF [384]
XS8b   YEEPLHWCSVAYYELNNRVGETFQASARSVLIGGFTDPSNNKN-RFCLGLLSNVNRNSTIENTRRHIGKGVHLYYVGGEVYAECVSDSSIFVQSRNCNYQHGFHPSTVCKIPSGCSLKIF [384]
HS1    YEEPKHWCSIVYYELNNRVGEAFHASSTSVLVDGFTDPSNNKN-RFCLGLLSNVNRNSTIENTRRHIGKGVHLYYVGGEVYAECLSDSSIFVQSRNCNYHHGFHPTTVCKIPSGCSLKIF [383]
XS1    YEEPKHWCSIVYYELNNRVGEAFHASSTSVLVDGFTDPSNNRN-RFCLGLLSNVNRNSTIENTRRHIGKGVHLYYVGGEVYAECLSDSSIFVQSRNCNTHHGFHPTTVCKIPSGCSLKIF [382]
HS5    YEEPKHWCSIVYYELNNRVGEAFHASSTSVLVDGFTDPSNNKS-RFCLGLLSNVNRNSTIENTRRHIGKGVHLYYVGGEVYAECLSDSSIFVQSRNCNTHHGFHPTTVCKIPSSCSLKIF [383]
dMAD   YSEPAFWASIAYYELNCRVGEVFHCNNNSVIVDGFTNPSNN-SDRCCLGQLSNVNRNSTIENTRRHIGKGVHLYYVTGEVYAECLSDSAIFVQSRNCNYHHGFHPSTVCKIPPGCSLKIF [373]
NvS15  YQEPLSWCSIAYYELNNRVGELFHAKSTSLIVDGFTDPNTTNSERFCLGLLSNVNRNSTIENTRRHIGKGVHLYYVGGEVYAECLSDSAIFVQSRNCNHSHGFHPTTVCKIPSGCTLKIF [356]
```

Loop strand pocket

Trimer sites

Goes in pocket

C-term Phos.

```
HS2    NNQEFAALLAQSVNQGFEAVYQLTRMCTIRMSFVKGWGAEYRRQTVTSTPCWIELHLNGPLQWLDKVLTQMGSPSVRCSSMS [467]
XS2    NNQEFAALLAQSVNQGFEAVYQLTRMCTIRMSFVKGWGAEYRRQTVTSTPCWIELHLNGPLQWLDKVLTQMGSPSVRCSSMS [467]
HS3    NNQEFAALLAQSVNQGFEAVYQLTRMCTIRMSFVKGWGAEYRRQTVTSTPCWIELHLNGPLQWLDKVLTQMGSPSIRCSSVS [425]
XS3    NNQEFAALLAQSVNQGFEAVYQLTRMCTIRMSFVKGWGAEYRRQTVTSTPCWIELHLNGPLQWLDKVLTQMGSPSIRCSSVS [425]
dSmad2 NNQEFAALLSQSVSQGFEAVYQLTRMCTIRMSFVKGWGAEYRRQTVTSTPCWIELHLNGPLQWLDRVLTQMGSPRLPCSSMS [486]
NvS23  NNQEFAQLLSQSVNQGFEAVYALTRMCTIRMSFVKGWGAEYRRQTVTSTPCWIELHLNGPLQWLDKVLTQMGSPSAPCSSVS [423]
HS9a   NNQLFAQLLAQSVHHGFEVVYELTKMCTIRMSFVKGWGAEYHRQDVTSTPCWIEIHLHGPLQWLDKVLTQMGSPHNPISSVS [467]
HS9b   NNQLFAQLLAQSVHHGFEVVYELTKMCTIRMSFVKGWGAEYHRQDVTSTPCWIEIHLHGPLQWLDKVLTQMGSPHNPISSVS [430]
XS8a   NNQLFAQLLSQSVNQGFEVVYELTKMCTIRMSFVKGWGAEYHRQDVTSTPCWIEIHLHGPLQWLDKVLTQMGSPHNPISSVS [466]
XS8b   NNQLFAQLLSQSVNQGFEVVYELTKMCTIRMSFVKGWGAEYHRQDVTSTPCWIEIHLHGPLQWLDKVLTQMGSPHNPISSVS [466]
HS1    NNQEFAQLLAQSVNHGFETVYELTKMCTIRMSFVKGWGAEYHRQDVTSTPCWIEIHLHGPLQWLDKVLTQMGSPHNPISSVS [465]
XS1    NNQEFAQLLAQSVNHGFETVYELTKMCTIRMSFVKGWGAEYHRQDVTSTPCWIEIHLHGPLQWLDKVLTQMGSPHNPISSVS [464]
HS5    NNQEFAQLLAQSVNHGFEAVYELTKMCTIRMSFVKGWGAEYHRQDVTSTPCWIEIHLHGPLQWLDKVLTQMGSPLNPISSVS [465]
dMAD   NNQEFAQLLSQSVNNGFEAVYELTKMCTIRMSFVKGWGAEYHRQDVTSTPCWIEIHLHGPLQWLDKVLTQMGSPHNAISSVS [455]
NvS15  NNQEFAQLLSQSVNYGFEAVYELTKMCSIRISFVKGWGAEYHRQDVTSTPCWIEVHLHGPLQWLDKVLSQMGSPRNPISSVS [438]
```