

## Supplemental Figure 1.

**Hp-Zfhx** -----MGATMADSAIIRCKRRKQANPQRKNVDIDGNPKGMTQAILA 41  
 Saccoglossus-Zfhx -----MAEGP--RCTRKRQANPRRKKELLEENE-----A 27  
 amphioxus-Zfhx MVPLTMNQSRQLMQLSPRRHPANMHAGVTPVSERSICLNKVKVEARNCVTPVSERSICLN 60  
 humanDeltaEF1b -----MADGP--RCKRRKQANPRRNN--VTNYNTVVETNSDS 33  
 humanDeltaEF1a -----MK--VTNYNTVVETNSDS 16  
 mouseDeltaEF1 -----MADGP--RCKRRKQANPRRNN--VTNYNTVVEANSDS 33  
 chickenDeltaEF1 -----MADGP--RCKRRKQANPRRNN--VTNYNNVIEANSDS 33  
 XenopusDeltaEF1a -----MADGP--RCKRRKQANPRRNN--VTNYNSVLEANSDS 33  
 ZebraKheper -----MADGP--RCKRRKQANPRRTN--VSNYSHVLEGGQSDS 33  
 humanSIP1 -----MKQPIMADGP--RCKRRKQANPRRKN--VVNYDNVVDTGSET 38  
 XenopusSIP1 -----MKQEIADGP--RCKRRKQANPRRKN--VLTVDNVVDTGSET 38  
 zebraSIP1b -----MRELIADGP--RCKRRKQANPRRKNAAVLDVFNVEVETGSET 40  
 zebraSIP1a -----MKQEIADGP--RCKRRKQANPRRKN--VLSYENVVDAGSGS 38  
 flyZfh1 -----

**Hp-Zfhx** **DGNDPISPSPEN**-----**GYHSNSSTIEDSDGDDKGSFMGDEEDEAEMDK** 86  
 Saccoglossus-Zfhx EEKCNKENNSD-----GYHSN-----ENELNQDE 52  
 amphioxus-Zfhx NKVCPWGKTEYE-----EEDEGAVLDDADASSTAHMDSGVDADNNEPDQR 106  
 humanDeltaEF1b DDEDKLHIVEEE-----SVTDAADCEG---VPEDDLPTDQTVLPGRSSEREGNA 79  
 humanDeltaEF1a DDEDKLHIVEEE-----SVTDAADCEG---VPEDDLPTDQTVLPGRSSEREGNA 62  
 mouseDeltaEF1 DDEDKLHIVEEE-----SITDAADCEGG---MPDELDPADQTVLPG--GSDRGGGA 79  
 chickenDeltaEF1 DDEDKLHIVEEE-----SITDAADCDAS---VPEDDLPTDHTVLP--NSEREGST 79  
 XenopusDeltaEF1a DDEDKLHIVEEE-----SVTDAADGEGS---VPEDDLPTDQTVLPEGSSESGKGS 80  
 ZebraKheper DDEDKLHIVEEE-----SLLDGADCDV---APDDD-----PNTADPDGR 72  
 humanSIP1 DEEDKLHIAEDDGIANPLDQETSPASVPNHE----SSPHVSQALLPREE--EDEIREGGV 93  
 XenopusSIP1 EEEDKLHIAEDDSITTTLDQETSPASMLNHE----TSPQANQALLPRDE--EDELREGRM 93  
 zebraSIP1b EEEDRLVSEED---ALLNGAGSPASLVNHESEAPPSPTLSHTLLRKTVDDEDDMKDSGI 97  
 zebraSIP1a DDEDRLLGSEGE-----GSPAGVPSLE---ASPRVAHALLSCRGDENESQDGAG 85  
 flyZfh1 -----

**Hp-Zfhx** -----**STSDGDKDDGVDDLEPDKEFHRKNGMHLLHPPHPPHQQFR** 128  
 Saccoglossus-Zfhx -----MSSNDGSGYHGDDGYQSNKELGEDE-----CAAPG----- 81  
 amphioxus-Zfhx LDDSL-----HMENGTVPQSPAGDDISTTPTSTPGTPDHSNPTPGTPHRTDE 153  
 humanDeltaEF1b --KNCWE-----DDR--KEG--QEILGPEAQADEAGCTVKDDECESDAENEQNHD 123  
 humanDeltaEF1a --KNCWE-----DDTGKEG--QEILGPEAQADEAGCTVKDDECESDAENEQNHD 107  
 mouseDeltaEF1 --KNCWQ-----DNV-----KDNECDSDAENEQNHD 103  
 chickenDeltaEF1 --NSCWE-----DEG--KET--KEILGPEAQSDVEGCTVKEDECDSDAENEQNHD 123  
 XenopusDeltaEF1a --KSCWE-----DEEGADCGDEILGPEAEADELGCCTVKDEECDSVNEQNHD 126  
 ZebraKheper -----WD-----DVK-----EECVSD--EDERSRD 90  
 humanSIP1 --EHPWHNNEILQASVDGPEEMKEDYDTMGPEATIQTAINNGTVKNANCTSDFEYFAKR 151  
 XenopusSIP1 --DHNWHNNVILKASVDGSDMKEDYDTLGPQVTHVTTINNGTVKNPNCSTDFEYFVKR 151  
 zebraSIP1b --ENVVHENDLLNASIDGTDELKADYDTMGTDVSLSE--IGNGTVKSVHCHDTEDFDFGKR 154  
 zebraSIP1a --AHVWR-----HGLNGSEERKAEYNSMSPDISLHG--IGNGTVKGIDASSELESFFAKR 137  
 flyZfh1 -----

**Hp-Zfhx** **NGEVGGDGVINLEDYMNRSDTAIYPEPVEDMDGVNGDTPNTPEGN--DNETEIEGEL** 186  
 Saccoglossus-Zfhx GGGGGGRAGLNLQEYLSRGDTAIYPEAPDEN-----SDPSGQNGE--SNDDTIL--- 130  
 amphioxus-Zfhx LAGDGTQAEHDIREYANRSDTAIYVPEASDDPMVG---HAPANGTGN--MLEDQLLS-- 205  
 humanDeltaEF1b -----PNVEEFLOQQDQDAVIFPEAPEEDQR--OGTPEASGHDEN-----GTPDAF 166  
 humanDeltaEF1a -----PNVEEFLOQQDQDAVIFPEAPEEDQR--OGTPEASGHDEN-----GTPDAF 150  
 mouseDeltaEF1 -----PNVEEFLOQQDQDAVIFYPEAPEEDQR--OGTPEASSHDEN-----GTPDAF 146  
 chickenDeltaEF1 -----PNVEEFLOQEDTAVIFYPEAPEEDQR--OGTPEASGDEN-----GTPDAF 166  
 XenopusDeltaEF1a -----PNVEEFLOQSDTAVIFYPEAPDEQR--OGTPEAVGQDEN-----GTPDAF 169  
 ZebraKheper -----ALVEEMLQQGDQDAVIFPEAPDEPR--OGTPEASGHDEN-----GTPDSF 133  
 humanSIP1 KLEERDGHAVSIEEYLQRSDTAIYPEAPELSR--LGTPEANGQEEN--DLPPGTPDAF 207  
 XenopusSIP1 KMDAGSNGVSAEYLQRSDTAIYPEAPEELCR--LGTPEANGHEEN--DLPPGTPDAF 207  
 zebraSIP1b KLVDTESHVVSIAEYLQRGDTAIYPEAPELSRSLATPEATGHEEN--DLPPGTPDAF 212  
 zebraSIP1a KLDDGEGHAASIAEYLQ--DTVIYPEPDEEGTR--LGTPEANGQDENENDLALRTPDAF 193  
 flyZfh1 -----

### Zinc-finger domains

**Hp-Zfhx** **GKPEDCPYCDRSYKRLTSLKEHIKYRHEKTFNNSFCPECNYCFAYKSQLERHMATHMPGR** 246  
 Saccoglossus-Zfhx ---SCPYCDRVYKRATSLKEHIKYRHEKNANNYACSECNYSFAYKSQLERHMATHMPGR 186  
 amphioxus-Zfhx ---CPYCDRGGYKRLTSLKEHIKYRHERDSSYACNECNYSFAYKSQLERHMATHMPGR 260  
 humanDeltaEF1b SQLLTCPCYCDRGGYKRLTSLKEHIKYRHEKNEEDNFSCSLCSYTFAYRTQLERHMTSHKSGR 226  
 humanDeltaEF1a SQLLTCPCYCDRGGYKRLTSLKEHIKYRHEKNEEDNFSCSLCSYTFAYRTQLERHMTSHKSGR 210  
 mouseDeltaEF1 SQLLTCPCYCDRGGYKRLTSLKEHIKYRHEKNEEDNFSCSLCSYTFAYRTQLERHMTSHKSGR 206  
 chickenDeltaEF1 SQLLTCPCYCDRGGYKRLTSLKEHIKYRHEKNEEDNFSCSLCSYTFAYRTQLDRHMTSHKSGR 226  
 XenopusDeltaEF1a SQLLTCPCYCDRGGYKRLTSLKEHIKYRHEKNEEDNFSCMCSYTFAYRTQLDRHMTSHKSGK 229  
 ZebraKheper SQLLTCPCYCDRGGYKRLTSLKEHIKYRHEKNEEDNFSCSLCSYTFAYRTQLDRHMTAHKAGR 193  
 humanSIP1 AQLLTCPCYCDRGGYKRLTSLKEHIKYRHEKNEENFSCPLCSYTFAYRTQLERHMVTHKPGT 267  
 XenopusSIP1 AQLLTCPCYCDRGGYKRLTSLKEHIKYRHEKNEENFSCPLCSYTFAYRTQLERHMVTHKPGR 267  
 zebraSIP1b AQLLTCPCYCDRGGYKRLTSLKEHIKYRHEKNEENFACPLCSYTFAYRTQLERHMATHKPGR 272  
 zebraSIP1a AQLLTCPCYCDRGGYKRLTSLKEHIKYRHEKNEEDNFPCPLCSYTFAYRTQLERHMATHKPAR 253  
 flyZfh1 -----MSAAACLSSSTSSFEKT-----CRICKKAFANVYRORHMTSHDESA 43

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**Hp-Zfhx**

Saccoglossus-Zfhx  
amphioxus-Zfhx  
humanDeltaEF1b  
humanDeltaEF1a  
mouseDeltaEF1  
chickenDeltaEF1  
XenopusDeltaEF1a  
ZebraKheper  
humanSIP1  
XenopusSIP1  
zebraSIP1b  
zebraSIP1a  
flyZfh1

**NQICDICNKA FVNIYRLQRHMLTHTSG-NRKFKCGECGKAFYKHHLKEHLRIHSGEKPY** 305  
DQICEICNKA FVNIYRLQRHMLTHTSG-NRKFKCGECHKAFYKHHLKEHLRIHSGEKPY 245  
DQVCERCNKA FVNIYRLQRHMLTHTSG-NRKFKCHECGKAFYKHHLKEHLRIHSGEKPY 319  
D-----QRHVTSQGC--NRKFKTECGKAFYKHHLKEHLRIHSGEKPY 268  
D-----QRHVTSQGC--NRKFKTECGKAFYKHHLKEHLRIHSGEKPY 252  
E-----QRHVTSQGC--NRKFKTECGKAFYKHHLKEHLRIHSGEKPY 248  
D-----QRHVTSQGC--NRKFKTECGKAFYKHHLKEHLRIHSGEKPY 268  
D-----QRHVTSQGC--NRKFKTECGKAFYKHHLKEHLRIHSGEKPY 271  
E-----QRHVTSQGGGNRKFKTECGKAFYKHHLKEHLRIHSGEKPY 237  
D-----QHQLTQAG-NRKFKTECGKAFYKHHLKEHLRIHSGEKPY 310  
D-----QHEMLTQAG-NRKFKTECGKAFYKHHLKEHLRIHSGEKPY 310  
D-----QHQLNQGSG-NRKFKTECGKAFYKHHLKEHLRIHSGEKPY 315  
D-----QPQLNEGAG-NRKFKTECGKAFYKHHLKEHLRIHSGEKPY 296  
L-----LRKFCKECKD KAFYKHHLKEHVRHSGEKPF 76  
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**Hp-Zfhx**

Saccoglossus-Zfhx  
amphioxus-Zfhx  
humanDeltaEF1b  
humanDeltaEF1a  
mouseDeltaEF1  
chickenDeltaEF1  
XenopusDeltaEF1a  
ZebraKheper  
humanSIP1  
XenopusSIP1  
zebraSIP1b  
zebraSIP1a  
flyZfh1

**ECPTCLKRFSHSGSYSSHISSKKCS-----PVKEQPPALTRITGVP** 346  
ECTTCKKRF SHSGSYSSHISSKKCT-----PSKYP-SLLLSTKAA 285  
ECPNCKKRF SHSGSYSSHISSKKCTIGLISFRNKMAE-----MPNVVPTSMHLLMAQA 373  
ECPNCKKRF SHSGSYSSHISSKKCTISLIPVNGRPR-----GLKTSQCSSPPLSASPGSP 323  
ECPNCKKRF SHSGSYSSHISSKKCTISLIPVNGRPR-----GLKTSQCSSPPLSASPGSP 307  
ECPNCKKRF SHSGSYSSHISSKKCTISLMPVNGRPRS-----GLKTSQCSSPPLSASPGSP 303  
ECPNCKKRF SHSGSYSSHISSKKCTIGLMPVNGRARS-----GLKTSQCSSPPLSASPGSP 323  
ECSNCKKRF SHSGSYSSHISSKKCTISVAVNGRVR-----GLKTPQCSSPPLSASPGSP 326  
ECSNCKKRF SHSGSYSSHISSKKCTIGLISVNGRPRSPATGAAKTPQCSSPYLPTSS-PT 296  
ECPNCKKRF SHSGSYSSHISSKKCTIGLISVNGRMRN-----NIKGTSSPNSVSSPTNS 364  
ECPNCKKRF SHSGSYSSHISSKKCTIGLISVNGRMRN-----NMKTGSSPNSVSSPTNS 364  
ECPNCKKRF SHSGSYSSHISSKKCTIGLIAINGVRN-----NLKTGSSPTSASSPTNS 369  
ECSNCKKRF SHSGSYSSHISSKKCTIGLISINGVRHG-----VNNKPGSSPNSAASSPGSP 352  
GCDNCGKRF SHSGSFSHMTSKKCTISMG-----LKLNNRA 112  
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**Hp-Zfhx**

Saccoglossus-Zfhx  
amphioxus-Zfhx  
humanDeltaEF1b  
humanDeltaEF1a  
mouseDeltaEF1  
chickenDeltaEF1  
XenopusDeltaEF1a  
ZebraKheper  
humanSIP1  
XenopusSIP1  
zebraSIP1b  
zebraSIP1a  
flyZfh1

**PVKVINSLPSPVLQSP LSDIDTSES-----LPLTEPKKSAPAYMPLHIKI** 392  
PVKLISEDMSPVTG-PHNIHNYIPG-----SFYDQSDKPSNDDDDALSINV 330  
AANPTVSLPNGSANPATNGLHASSTGLLQALNLTLP SLLAATPPLGAASTLQNPVMVKT 433  
TRPQIRQKIEN---KPLQEQLSVNQIKTEP-----VDYEFKPIVVAS--GINCSTPLQN 372  
TRPQIRQKIEN---KPLQEQLSVNQIKTEP-----VDYEFKPIVVAS--GINCSTPLQN 356  
TRPQIRQKIEN---KPLQEQLSVNQIKTEP-----VDYEFKPIVVAS--GINCSTPLQN 352  
ARPQIRQKIEN---KPLQEQLPVNQIKTEP-----VDYEFKPIVVAS--GINCSTPLQN 372  
ARPQIRQKIEN---KPLQEQLPVNQIKTEP-----VDYEFKPIVVAS--GINCSTPLQN 375  
ARVQVRDKLDNS--KPLQEQLPVQIKSEP-----LDYEFKPIVVAS--SARGVN 342  
AITQLRNKLENGKPLSMSEQTGLLKI KTEP-----LDFNDYKVLMT-HGFSGTSPFMM 417  
AITQLRHKLENGKPLGMSEPSGLLKI KTES-----LDYNDYKLLMAASHAFNGAHPFM 418  
AISQLRHKLENGKPLQDQSNHLNLIKSEP-----LDFNDYKLLMAS-HGYATGSPFLN 422  
ALALRHKLENGRSMQLDPSAHTDIKSEP-----MDFNEYRLMIASQEQY GASGAFLN 406  
LLKRLEKSPGSAASSARRSPSDHGKGLPE-----QPSLPGLPHPM SYFASDAQVQG 164

**Smad-binding domain**

**Hp-Zfhx**

Saccoglossus-Zfhx  
amphioxus-Zfhx  
humanDeltaEF1b  
humanDeltaEF1a  
mouseDeltaEF1  
chickenDeltaEF1  
XenopusDeltaEF1a  
ZebraKheper  
humanSIP1  
XenopusSIP1  
zebraSIP1b  
zebraSIP1a  
flyZfh1

**PNADGSVQGHPSNETLENGTTP L TSPAN-----DAVKKVLQIVAS-TVCRQOK** 440  
NTSDDQSQ-----DKSITITSPPN-----DAVKKVLQIVGA-TVSRQOM 368  
EPMDTLSPPMSRSSISPSGGYVSSGSGSTESPVKGDINQVKKVLQIVEN-TVTRQOK 492  
GVFTGGGPLQATSSPQGMVQAVVLPVGLVLS---PISINLSDIQNLKVAVDGNVIRQVL 429  
GVFTGGGPLQATSSPQGMVQAVVLPVGLVLS---PISINLSDIQNLKVAVDGNVIRQVL 413  
GVFSSGGQLQATSSPQGVVQAVVLPVGLVLS---PISINLSDIQNLKVAVDGNVIRQVL 409  
GVFSSGGPLQATSSPQGVVQAVVLPVGLVLS---PISINLSDIQNLKVAVDGNVIRQVL 429  
GVFTSGSLQATNSPQGVVQAVVLPVGLVLS---PISINLSDIQNLKVAVDGNVIRQVL 432  
GMFQGG---AAAPLQAVQAVVLPVGLVLS---PISINLGDQLQNLKVAVDGNVIRQVL 395  
GGLGATSP LGVHPSAQSP<sup>MOHLGVGMEAPLLGFPPTMNSNLSEVQKVLQIVDN-TVSRQKM</sup> 476  
GGLGATSP LGIHSSAPSP<sup>MOHLGVGMEAPLLGFPPTMNSNLSEVQKVLQIVDN-TVSRQKM</sup> 477  
GGVGGSP LGIHN-SQSP<sup>LQHLGMBIEGOMLGYPSLGNLSEVQKVLQIVDN-TVCRQKM</sup> 480  
GGGRGSP PMHSSSNQNP<sup>LQHLGIGSDSHPLGYTGF INNMSEVQKVLQIVDN-TVCRQKM</sup> 465  
GSAAPAPFPFPHNYMNAALLAFPHNFMAAAGLDPVRVHPYSIQRLQLSAAAGQQOREEE 224  
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**Hp-Zfhx**

Saccoglossus-Zfhx  
amphioxus-Zfhx  
humanDeltaEF1b  
humanDeltaEF1a  
mouseDeltaEF1  
chickenDeltaEF1  
XenopusDeltaEF1a  
ZebraKheper  
humanSIP1  
XenopusSIP1  
zebraSIP1b  
zebraSIP1a  
flyZfh1

**DGQKTDISKLKKTKTSDTAPVVASPF EIRPFKLEKMAAVTLPKATPPPPSENTPEKTP** 500  
EGQKNVAKLKKAKQPPMERESKDPVNEVK-----TAEKIVPEIPRETPAKSP 418  
ETGAMSDTWPRAVDNAAGNLSDEL SKIREN-----AKAMSLATEALSLSDAARLPL 543  
ENNQANLASKEQETINASPIQQGGH-----SVISAISLPLVDQDGTTKI 473  
ENNQANLASKEQETINASPIQQGGH-----SVISAISLPLVDQDGTTKI 457  
ETNQASLASKEQEAVSASPIQQGGH-----SVISAISLPLVDQDGTTKI 453  
ENNHANLASKEQETINASPIQQAGH-----SLISAISLPLVDQDGTTKI 473  
ENNHASLASKEQGLTTSATTQQAGH-----SVISAISLPLVDQDGTTKI 476  
ESTQAKGQAGTIVGAGGIAQTQ-----QVIQAIISLPLDQDGNAKI 439  
DCKAEIEISKLKGYHMKDPCSQPEEQ--GVT-----SPNIPPVGLPVVSHNGATKS 524  
ECKPEEITKLGKGYHMKDGGPOPEEQ--GVT-----SPGNPPVGLPVVSHNGATKS 525  
DCKPEEISKLKAY-MKELGSHIEEQKQGLN-----SSGGGQGLPLINHNNGATKS 529  
DGNPEEISKLRAY-MKELGSGMEEQ--N-----RVLASQQSFLGVGHNSPTKT 510  
REEQQKQQQHDEETPDEPKLVMDIE-----EPETKEMAPTEATEAATPI 270

**Hp-Zfhx**  
 Saccoglossus-Zfhx **ESEKPKTFLNGNGVHQEKSYNIVDYTLKKVHEAQAINRCLERFSPSQINLNPDRTGCK** 560  
 amphioxus-Zfhx **QVQNQNR-----VDKKGKSYDIVDYTLRKNVNEAKAVEAF'N-----IHFKRDKNACR** 465  
 humanDeltaEF1b **NLNGFHAG-----DPTSASNYLKYTLEKFNQAKALQAFLEPRERSF'PGKEMKDYTCR** 596  
 humanDeltaEF1a **IINYSLEQPSQLQVVPQ-----NLKKE-NPVATNSCKSEKLPEDLTVKSEKDKS** 521  
 mouseDeltaEF1 **IINYSLEQPSQLQVVPQ-----NLKKE-NPVATNSCKSEKLPEDLTVKSEKDKS** 505  
 chickenDeltaEF1 **IINYSLEQPSQLQVVPQ-----NLKKE-IPAPTNSCKSEKLPEDLTVKSETDKS** 501  
 XenopusDeltaEF1a **IINYSLEQPSQLQVVPQ-----NLKKE-HSVPTNSCKNEKLPEDLTVKSEKDKN** 521  
 ZebraKheper **IINYSLEQPTQLPVVAQ-----NLKKE-VTAPAEVCKTEKLPEDLTIKTEKDTK** 524  
 humanSIP1 **FINYSLD-PSQAQAVLQ-----SPKKEPLGSNTEVCKGQKLPEDLTVKTNR---** 484  
 XenopusSIP1 **IIDYTLKVNKAEKACLSLTTDSRRQISNIKKEKRLTLIDLVTDDKMIENHNI'STPFSCQ** 584  
 zebraSIP1b **IIDYTLKVNKAEKACLSLTTDSRRQIGNIKKEKRLTLIDLVSEKMLESHHIST'PFSCQ** 585  
 zebraSIP1a **IIDYTLKVNKAEKACLSLTTDSRRQISNIKKEKANHMLDLGMEEKAHENNL'MFT'PFSCQ** 589  
 flyZfh1 **IIDYTLKVNKAEKACLSLTTEDSKRRLMDIKKERPSHAMDLLSEDKALERDAQY'APFSCQ** 570  
**KREESREASPDPE'SYR'SSS-----QAIKQEQLVNAEERQ'TPVEEHAPVEHADLRCS** 324

**Hp-Zfhx**  
 Saccoglossus-Zfhx **YCGREFHSPIDLHQHERYLCDLNEDVLKMKLFNGNPPQPSIGNFTLDRYEMQOEF'LAQ** 620  
 amphioxus-Zfhx **YCQEMFFNP IELHQHERYLCDENEDVQKVNHVSLTKYIN-FQREVVMQNDL'QSRKQ** 524  
 humanDeltaEF1b **YCGEAFPGAIPLHQHERYLCKQNEEILAAAQLQKN-----** 631  
 humanDeltaEF1a **FEGGVNDSTCLLCCDDCPGDINALPELKHLDLQPTQPPPL-----** 561  
 mouseDeltaEF1 **FEGGVNDSTCLLCCDDCPGDINALPELKHLDLQPTQPPPL-----** 545  
 chickenDeltaEF1 **FEGARDSDSTCLLCCDDCPGDINALPELKHLDLQPTQPPPL-----** 540  
 XenopusDeltaEF1a **FEGE'TNDSTCLLCCDDCPGDINALPELKHLDLQPTQPPPL-----** 561  
 ZebraKheper **FT---DKSTCLLGDHPGD'TNALQEPKHYDPKKN'LLPES-----** 561  
 humanSIP1 **-----DKTTLTVDEKSM'LHNDIL-LKHCG-----** 507  
 XenopusSIP1 **FC'KESFPGPIPLHQHERYLCKMNEEIKAVLQPHENIV'PNK-----** 624  
 zebraSIP1b **FC'KESFPGPIPLHQHERYLCKMNEEIKAVLQPHENIIL'NK-----** 625  
 zebraSIP1a **YCKE'TFPGPIPLHQHERYLCKMNEEIKAVLQPAQNAL'TNK-----** 629  
 flyZfh1 **YCKE'TFSGPIPLHQHERYLCKMNEEIKAVLQPN'DTVP'TGR-----** 610  
**RC'SKQFNHPT'ELVQHEKVL'CGLIKEELEQHF'QQQAT'SFALASAS-----** 369

**Hp-Zfhx**  
 Saccoglossus-Zfhx **HKNESDNHEIDDKSDEEDENPKQMLTSPRESEQHLSPKASPNSGSR'LS'PNAESPEPEAN** 680  
 amphioxus-Zfhx **SHDQDQKAEIDDI'ITMSHDKASSSDEFEEEEVEEKEGEEQE'QEKNEH'SRNIE'NEK'LME** 584  
 humanDeltaEF1b **-----TQLAEASLI'EQARSFKP'DLLD'QGG'FLQ** 659  
 humanDeltaEF1a **-----PAAEAEKPESSVSSATGDGNL'SPSQP---** 587  
 mouseDeltaEF1 **-----PAAEAEKPESSVSSATGDGNL'SPSQP---** 571  
 chickenDeltaEF1 **-----PAPATEKPESSASSA--GN'GDL'SPSQP---** 565  
 XenopusDeltaEF1a **-----SGTEAEKPESSPAPSET'GENNL'SPGQP---** 587  
 ZebraKheper **-----SKAEVIKSE--PSSANSE'GDL'T'PSQP---** 586  
 humanSIP1 **-----KDEHRINGKNLEEKMDLEGL'CPGQP---** 532  
 XenopusSIP1 **-----AGVFVDNKALLSSV'LSEKGM'TSPIN---** 650  
 zebraSIP1b **-----OGVFAEKQALLSSV'LSEKGM'TSPIN---** 651  
 zebraSIP1a **-----PGLFSEKHGL'LHPSI'PEKSLNGP'IS---** 655  
 flyZfh1 **-----RGLFGSE'QQAGV'ISSLERDAT'SPVN---** 636  
**-----EEDEEDEM'DVEE'EPQESGERKVRVR---** 396

**Homeodomain**

**Hp-Zfhx**  
 Saccoglossus-Zfhx **KT'TD'ISKLLG'IT'SKAQE'QALRAF'YAMQAKP'SEDGIEKISV'ALNLP'QMLV'NKWF'QR--TR'KL** 739  
 amphioxus-Zfhx **CEEEESDKV-LIGENQQHALSAYYAMSSNP'SDDIDKISQ'RLGLP'VHAIQ'TWFENKKA'QL** 643  
 humanDeltaEF1b **SSLEKAKSEL'DLSSEHLTVL'KAYALHAQPSPEELIKISSV'VGLPKDFV'ESW'FANMR'ERN** 719  
 humanDeltaEF1a **-----PLKNLLSLLKAYALNAQPSAEEL'SKIADSVNLP'LDVVKKWF'EKMQ---** 633  
 mouseDeltaEF1 **-----PLKNLLSLLKAYALNAQPSAEEL'SKIADSVNLP'LDVVKKWF'EKMQ---** 617  
 chickenDeltaEF1 **-----PLKNLLSLLKAYALNAQPSAEEL'SKIADSVNLP'LDVVKKWF'EKMQ---** 611  
 XenopusDeltaEF1a **-----PLKNLLSLLKAYALNAQPSAEEL'SKIADSVNLP'LDVVKKWF'EKMQ---** 633  
 ZebraKheper **-----PLKNLLSLLKAYALNAQPSAEEL'SKIADSVNLP'LDVVKKWF'EKMQ---** 632  
 humanSIP1 **-----PLKNLLSLLKAYALNAQPSAEEL'SKIADSVNLP'LDVVKKWF'EKMQ---** 578  
 XenopusSIP1 **-----PYKDHMSV'LKAYAMNMEPNSDELLKISIAVGLPQ'EFVKEWF'EQRK---** 696  
 zebraSIP1b **-----LYKDHMSV'LKAYAMNMEPNSDELLKISIAVGLPQ'EFVKEWF'EQRK---** 697  
 zebraSIP1a **-----PYKDHMSV'LKAYAMNMEPNSDELLKISIAVGLPQ'EFVKEWF'EQRK---** 701  
 flyZfh1 **-----PYKDHMSV'LKAYAMNMEPNSDELLKISIAVGLPQ'EFVKEWF'EQRK---** 685  
**-----TAINEEQ'QQLKQHYSLNARPSRDEF'RMIAARLQ'LDPRVVQ'VWFQ'NNR---** 444

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**Hp-Zfhx**  
 Saccoglossus-Zfhx **EEEGSDPSLKSLSLMRQSPVVTVVPTQRRIKEHTGAQAIDSKEACVKS'PAENC'DLETAS** 799  
 amphioxus-Zfhx **EHERDAHDEDDADENHTPLVNSHHVDSSEDSNHSNIESSRSDQMKRGNDE'PDCARPL** 703  
 humanDeltaEF1b **EP'SGGDEKTADAERTT'GNETEVLNLSAKATAPSTKPGENSEPTEAEIPRTQSP'CAKEE'EEA** 779  
 humanDeltaEF1a **AGQISVQ'SSEP-----SSPEPGKVINIPAKNNDQ'PQSANANEPQDST** 674  
 mouseDeltaEF1 **AGQISVQ'SSEP-----SSPEPGKVINIPAKNNDQ'PQSANANEPQDST** 658  
 chickenDeltaEF1 **AGQIPGQ'SPDP-----PSPGTGSVINIPTKTDEQ'PQPADGNEPQEDS** 652  
 XenopusDeltaEF1a **AGQISVQ'SSGP-----SSPEQVKISSP'TDNDQAAAT'NESE'PONST** 674  
 ZebraKheper **SGEIPVD'SSQP-----SSPKPQNSV'TENS'VKS'KTESGLNDG--TS** 671  
 humanSIP1 **LGQISMDP'SSP-----QHEE--EQ'TTPVDLDGT'KGASPKPDLDEQM** 617  
 XenopusSIP1 **VYQYNSRSP'SLERS--KPLAPNSNPPTKDSL--LPRSPVKP'MDSITSPSIAELHNSV** 751  
 zebraSIP1b **VYQYANSRSP'SLERTSAEMALATILN'TPTKDS----ARSP'IKSVDFIT'SQSAELHNRV** 752  
 zebraSIP1a **VFQY'TTSRTPPLDRSPVSIHPVSAHTPTKDSLGI'RSPMSLVKGS'DRITSPA'IPELHN--** 759  
 flyZfh1 **HHSFRKRSP'PPERSG-----ETNHVRDSAFARS'PVSLGQYGDSTAEI'QAITNGDSG** 737  
**SRERKMQ'SFQN-----NQAGAAPMPID'SQASLTREDQPLDLSV'KR** 486

**Hp-Zfhx** **VSSSSAERVGADSLPPSPCSSINSLPKSSIRYTFHKEKSMVSPIGRATESARERLEP** 859  
 Saccoglossus-Zfhx QITTTTP---YANRLRTDDNRYGGLLMVSMPLDTCENGLNLSKKNVPHDEPIALTKKK 760  
 amphioxus-Zfhx QPQSDSD---APMDLTPKTEASKSKPNSVVTIYNKRKSAMFAPIDPDLTNPAAYYAA 835  
 humanDeltaEF1b VNLQSP-----KMTNSPVLVPGSTTNGSRSSSTP--SPSPLNLSSSR 714  
 humanDeltaEF1a VNLQSP-----KMTNSPVLVPGSTTNGSRSSSTP--SPSPLNLSSSR 698  
 mouseDeltaEF1 TRGQSPV-----KIRSSPVLVPGSAMNGSRSSCT--SPSPLNLSCSR 692  
 chickenDeltaEF1 NNSQNPA-----NTSKSQTSSTGGSTQNGSRSSSTP--SPSPLNLSSSR 714  
 XenopusDeltaEF1a VPLKSPK-----QEAEPEL---AVNGSESGHR--FSYTTKLSLE 706  
 ZebraKheper NSEKQEE-----RECCSPAEGIAASVNGIESVPA--SPSPLNLS--- 654  
 humanSIP1 TNCDPPL-----RLTKPSHFTNIKP-VEKLDHSRSNTSPSPLNLSSTS 792  
 XenopusSIP1 SNCDTPL-----RLTKSNHFASMKPVLDKLDHSRSNTSPSPLNLSSTS 794  
 zebraSIP1b -NCDTPL-----RLSKTPQYSNHKQLGDKMDHSRSNTSPSPLNLSSTS 800  
 zebraSIP1a HKLSRPH-----QITG--TRQTNKQP-LDSVDHLRGETPSPLNLSSTS 777  
 flyZfh1 DPLTFK-----SESSPPYIAPPSGEALNPEAINLSRKFSTASMS 525

**Hp-Zfhx** **MERDSRSPARSLTPAKETRDSPLDLSLPRKATPPPSLSRSSIPPKLVGYGNYALYSA** 919  
 Saccoglossus-Zfhx IVSESPSPSQERTKNNQ---PLDLSMPKPKLVKVS--SKARR-----FPQTSQYHQ 805  
 amphioxus-Zfhx LPFFGQGGIPAPFPGYIDFLASPMTGAFNLGLGSP----- 870  
 humanDeltaEF1b NTQGYLYTAEG---AQEEPQVEPLDLSLKPQGG-----EL 746  
 humanDeltaEF1a NTQGYLYTAEG---AQEEPQVEPLDLSLKPQGG-----EL 730  
 mouseDeltaEF1 NPQGYSCVAEG---AQEEPQVEPLDLSLKPQGG-----EL 724  
 chickenDeltaEF1 NSQGYTYTAEG---VQEEPQMEPLDLSLKPQHG-----EL 746  
 XenopusDeltaEF1a NSDGAACDGT---PDGEEQAEPLDLSLSPKQGG-----NV 738  
 ZebraKheper -ADGVPARTL---EEGE---GPLDLSLPKS----- 678  
 humanSIP1 SKNSHSSSYTPNSFSSEELQAEPLDLSLKPQMKEP-----KSI IATKN 835  
 XenopusSIP1 SKNSHSSSYTPNSFSSEELQAEPLDLSLKPQMKEP-----KTI IATKN 837  
 zebraSIP1b SKNSHTSSYTPNSFTSEDLQAEPLDLSLKPQMKEP-----KHILTVKS 843  
 zebraSIP1a SKNSHSSSYTPNSLTSSEDAHGEPLDLSLKPQVS-----KAER 814  
 flyZfh1 SPASISPSAAALYFGAAPPSPSPNSQLDSTP-----KAER 557

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**Hp-Zfhx** **AAAAANGYLLPPAYAPSEPLPSSLYENSIKAHKSRTSPSP-----GKTPPSSTATTN** 973  
 Saccoglossus-Zfhx QQFDAARSVFMKGYHSTPNTTDFYFSSFKVDPRLAQPYF-----ENNIKAKHCNGQAH 859  
 amphioxus-Zfhx -----YLTPGFNAATLSTKRRLDTPTRGRRRRRRVY-----DNGSRVPMATQS 914  
 humanDeltaEF1b LERSTITSVYQNSVYSVQE---EPLNLSCA-KKEPQKDCV-----TDSEPVVNVIPP 795  
 humanDeltaEF1a LERSTITSVYQNSVYSVQE---EPLNLSCA-KKEPQKDCV-----TDSEPVVNVIPP 779  
 mouseDeltaEF1 LERSTITSVYQNSVYSVQE---EPLNLSCA-KKEPQKDCV-----TDSEPVVNVIPP 773  
 chickenDeltaEF1 LERSTITSVYQNSVYSVQE---EPLNLTCA-KKEPQKDCV-----TSDP I VNVIPP 795  
 XenopusDeltaEF1a PERPSITSVYQSSYSVQE---EPLNLSCA-KKEPQKDCV-----AKAETL-IINP 786  
 ZebraKheper ATTASVASGHANTVYSAQE---EPLNLTCT-KKELLSN-----ASTNAAIYASQP 724  
 humanSIP1 KTKASSISLDHNSVSSSENSEDEPLNLTFTI-KKEF--SNSNLL--DNKSTNPFVSMNPF 889  
 XenopusSIP1 KSKPNNITVDHNSVLSSETVDEPLNLTFTI-KKEF--CNAN-----MDKSTSPFLGFLNPF 889  
 zebraSIP1b RLKLSNGMPDHNHVATPREHADEPLNLTFTI-KKEF--LDKSSSPMFLGFLNPF 900  
 zebraSIP1a RAKPNGFSIEHTSNSTAREPGTEPLNLAHI-KKEFNGPNLSLGNENQMDKSSSPIFSINPF 873  
 flyZfh1 -----

**Hp-Zfhx** **TSSASDASILLKRSYPEPLYAYLPTMGGYAAKRMRFADGVDPVAPPMPYGSHLQVPDVY** 1033  
 Saccoglossus-Zfhx NPSA--ARILTHAIELPHLYAAHHHPG-----LHNSLLAAAAPTQGPTKKLKMLDMSL 909  
 amphioxus-Zfhx -----VTPVQAPSPMHPMSMDPDTQSPAL 938  
 humanDeltaEF1b SANP-----INIAIPTVTAQLPTIVAIADQNSVPC 825  
 humanDeltaEF1a SANP-----INIAIPTVTAQLPTIVAIADQNSVPC 809  
 mouseDeltaEF1 SANP-----INIAIPTVTAQLPTIVAIADQNSVPC 803  
 chickenDeltaEF1 SANP-----INIAIPTVTAQLPTIVAIADQNSVPC 825  
 XenopusDeltaEF1a SANP-----INIAIPTVTAQLPTIVAIADQNSVPC 816  
 ZebraKheper SANP-----INIMT---TQLPTLVAITDQGGQAC 750  
 humanSIP1 SAKP-----LYTALPPQSAPFPATFMPVQTSIPG 919  
 XenopusSIP1 SGKP-----LYSALPPQSAPFPATFMPVQTSIPG 919  
 zebraSIP1b AAKP-----MYTSLPPQSAPFPATFMPVQTSIPG 930  
 zebraSIP1a GGGH-----MYTSLPPHGAPFPPTFMSTTQASIPG 903  
 flyZfh1 -----RSGQAFPLPYPYMLPMSLPMEAL 580

**Hp-Zfhx** **SALAKTGFMPTMAHLGAAYGPTNPFPLPMLNGGG-LHPNHAGADNLSDIASEDSLSDIG** 1092  
 Saccoglossus-Zfhx G-LMSTGSPDPDIMP--AGRHFMTTEDEIRNSLGSNP-MSSYHPGAVHRDDSLSEGLDES- 964  
 amphioxus-Zfhx AQETAEGSPSIPSPSPSGTYPGYIGDSASSPGSPA-LSTGTP----- 979  
 humanDeltaEF1b LRALAANKQTILIPQVAYTYSTTVS-PAVQEPPLK-VIQPNQDERQDTSSEGVSNVED 883  
 humanDeltaEF1a LRALAANKQTILIPQVAYTYSTTVS-PAVQEPPLK-VIQPNQDERQDTSSEGVSNVED 867  
 mouseDeltaEF1 LRALAANKQTILIPQVAYTYSATVS-PAVQEPVVK-VIQPNQDERQDTSSEGVSTVED 861  
 chickenDeltaEF1 LRALAANKQTILIPQVAYTYSTTVS-PAVQETPPK-QTQANGSQUERQDTSSEGVSNVED 883  
 XenopusDeltaEF1a LRALAANKQTILIPQVAYTYSTTVS-PAVPEPQVK-NIQPNQDERQDTSSEGVSNVED 874  
 ZebraKheper LRALTTTKQTILIPQVAYTYSTTVS-PAVQETPPK-QTQANGSQUERQDTSSEGVSNVED 810  
 humanSIP1 LRPYPGLDQMSFLPHMAYTYPTGAATFADMQRK-YORKQGFQGEELLDGADYMSGLDD 978  
 XenopusSIP1 LRSYPGLDQMSFLPHMAYTYPTGAATFADMQRK-YORKQGFQGEELLDGADYMSGLDD 978  
 zebraSIP1b LRPYPGLDQMSFLPHMAYTYPTGAATFADMQRK-YORKQGFQGEELLDGADYMSGLDD 989  
 zebraSIP1a LRPYPGLDQMSFLPHMAYTYPTGAATFADMQRK-YORKQGFQGEELLDGADYMSGLDD 962  
 flyZfh1 FKMRPGDFASNHMNSIKLPDYRGTSLSPGGSE-KRSWRDDSRISHDEFAGVLM 639

