

Supplemental Information (Three Tables and Eight Figures)

Table S1. Sequences, subfamilies and accession numbers.

Subfamily	Name (synonym) - Accession Number - Description - Species
Activin	CeTIG-3 NP_497318.2 transforming growth factor beta family [C elegans]
Activin	DmActivin-beta NP_651942.2 activin-beta [D melanogaster]
Activin	DmMyoglianin NP_726604.1 myoglianin, isoform A [D melanogaster]
Activin	MmBmp3 NP_001297606.1 bone morphogenetic protein 3 isoform 1 [M musculus]
Activin	MmGdf10 NP_665684.2 growth/differentiation factor 10 preproprotein [M musculus]
Activin	MmGdf11 NP_034402.1 growth/differentiation factor 11 preproprotein [M musculus]
	Synonym BMP11
Activin	MmInhba NP_032406.1 inhibin beta A chain preproprotein [M musculus]
Activin	MmInhbb NP_032407.1 inhibin beta B chain preproprotein [M musculus]
Activin	MmInhbc NP_034695.1 inhibin beta C chain preproprotein [M musculus]
Activin	MmInhbe NP_032408.2 inhibin beta E chain preproprotein [M musculus]
Activin	MmMstn NP_034964.1 growth/differentiation factor 8 preproprotein [M musculus]
11 Activin	Synonym GDF8
BMP	CeDBL-1 NP_504709.1 Dpp/BMP-Like [C elegans]
BMP	CeTIG-2 NP_504271.1 transforming growth factor beta family [C elegans]
BMP	DmDPP NP_477311.1 decapentaplegic, isoform A [D melanogaster]
BMP	DmGBB NP_477340.1 glass bottom boat, isoform A [D melanogaster]
BMP	DmSCW NP_524863.3 screw, isoform A [D melanogaster]
BMP	MmBmp2 NP_031579.2 bone morphogenetic protein 2 preproprotein [M musculus]
BMP	MmBmp4 NP_001303289.1 bone morphogenetic protein 4 preproprotein [M musculus]
BMP	MmBmp5 NP_031581.2 bone morphogenetic protein 5 preproprotein [M musculus]
BMP	MmBmp6 NP_031582.1 bone morphogenetic protein 6 preproprotein [M musculus]
BMP	MmBmp7 NP_031583.2 bone morphogenetic protein 7 preproprotein [M musculus]
BMP	MmBmp8a NP_001242948.1 bone morphogenetic protein 8A isoform 1 [M musculus]
BMP	MmBmp8b NP_031585.2 bone morphogenetic protein 8B preproprotein [M musculus]
BMP	MmBmp10 NP_033886.2 bone morphogenetic protein 10 preproprotein [M musculus]
BMP	MmBmp15 NP_033887.1 bone morphogenetic protein 15 preproprotein [M musculus]
BMP	MmGdf1 NP_032133.2 embryonic growth/differentiation factor 1 [M musculus]
BMP	MmGdf2 NP_062379.3 growth/differentiation factor 2 preproprotein [M musculus]
	Synonym BMP9
BMP	MmGdf3 NP_032134.2 growth/differentiation factor 3 preproprotein [M musculus]
BMP	MmGdf5 NP_032135.2 growth/differentiation factor 5 preproprotein [M musculus]
BMP	MmGdf6 NP_038554.1 growth/differentiation factor 6 preproprotein [M musculus]
BMP	MmGdf7 NP_001299805.1 growth/differentiation factor 7 isoform 1 [M musculus]
BMP	MmGdf9 NP_032136.2 growth/differentiation factor 9 precursor [M musculus]
BMP	MmNodal NP_038639.2 nodal preproprotein [M musculus]
22 BMP	
TGF-β	CeDAF-7 NP_497265.1 dauer larva development growth factor daf-7 [C elegans]
TGF-β	CeUNC-129 NP_501566.1 uncharacterized protein CELE_C53D6.2 [C elegans]
TGF-β	DmDawdle NP_523461.1 dawdle, isoform A [D melanogaster]
TGF-β	DmMaverick NP_524626.1 maverick [D melanogaster]
TGF-β	MmAmh NP_031471.2 muellerian-inhibiting factor precursor [M musculus]
	Synonym MIS
TGF-β	MmGdf15 NP_035949.2 growth/differentiation factor 15 preproprotein [M musculus]
TGF-β	MmInha NP_034694.3 inhibin alpha chain isoform 1 preproprotein [M musculus]
TGF-β	MmLefty1 NP_034224.1 left-right determination factor 1 preproprotein [M musculus]
TGF-β	MmLefty2 NP_796073.1 left-right determination factor 2 preproprotein [M musculus]
TGF-β	MmTgfb1 NP_035707.1 transforming growth factor beta-1 preproprotein [M musculus]
TGF-β	MmTgfb2 NP_001316036.1 transforming growth factor beta-2 isoform 2 [M musculus]
TGF-β	MmTgfb3 NP_033394.2 transforming growth factor beta-3 precursor [M musculus]
12 TGF-β	
45 total TGF-β family sequences	
outgroup	MmGdnf NP_034405.1 glial cell line-derived neurotrophic factor 1 [M musculus]

Table S2. Cleavage site identified computationally separating prodomain and ligand.

Subfamily	Name	Residue	Prodomain	Cleavage site	Ligand
Activin	CeTIG-3	125	NVINALSVLR	//	NAPNFDVMVF
Activin	DmActivin-beta	822	TESSRTRRVR	//	RRAVDCGGAL
Activin	DmMyoglianin	483	GSQKKHRRKR	//	SVYMDCTEND
Activin	MmBmp3	276	ALSVERRKKR	//	STGILLPLQN
Activin	MmGdf10	328	LKPRTGRKDR	//	KKKDQDTFTA
Activin	MmGdf11	287	VLENTKRSRR	//	NLGLDCDEHS
Activin	MmInhba	298	SEDHPHRRRR	//	RGLECDGKVN
Activin	MmInhbb	285	RLGDSRHRIR	//	KRGLECDGRT
Activin	MmInhbc	226	RVEGKHVRVR	//	RGIDCQGASR
Activin	MmInhbe	227	EPGAGRARRR	//	TPTCEPETPL
Activin	MmMstn	258	VTDTPKRSRR	//	DFGLDCDEHS
BMP	CeDBL-1	227	SEPSSVRRKR	//	SAQTGNSERK
BMP	CeTIG-2	258	KPNENERCQR	//	KGLYVDFDIL
BMP	DmDPP	463	GGGKGGRNKR	//	QPRRPTRRKN
BMP	DmGBB	316	AHSSHRSKR	//	SASHPRKRKK
BMP	DmSCW	262	VKIQKLRFKR	//	DLEKRRAGGG
BMP	MmBmp2	271	GHPLHKREKR	//	QAKHKQKRKL
BMP	MmBmp4	283	HTLTRRRAKR	//	SPKHHPQRSR
BMP	MmBmp5	307	ASEVLLRSVR	//	AASKRKNQNR
BMP	MmBmp6	362	VSEVHVRTTR	//	SASSRRRQQS
BMP	MmBmp7	282	ATEVHLRSIR	//	STGGKQRSQN
BMP	MmBmp8a	251	ASQSPVRAPR	//	AARPLKRRQP
BMP	MmBmp8b	254	SPVRAPRTAR	//	PLKKKQLNQI
BMP	MmBmp10	304	IDDSSARIRR	//	NAKGNKYCKKT
BMP	MmBmp15	258	ESSFLMRSVR	//	QACSIEDAS
BMP	MmGdf1	246	GPVGTCRTRR	//	LHVSFREVGVW
BMP	MmGdf2	309	VGPLLARRKR	//	STGASSHCQK
BMP	MmGdf3	243	HCHPSSRKRR	//	AAISVPKGFC
BMP	MmGdf5	365	EYLFSQRRKR	//	RAPLANRQGGK
BMP	MmGdf6	346	GKKSRLRCSR	//	KPLHVNFKEL
BMP	MmGdf7	348	AGRGHGRRGR	//	SRCSRKSLHV
BMP	MmGdf9	297	EVERSPRRRR	//	GQKAIRSEAK
BMP	MmNodal	234	ERGGWGRRQR	//	RHHLPPDRSQL
TGF- β	CeDAF-7	225	TRPKGSRKRR	//	SHAKPVCNAE
TGF- β	CeUNC-129	280	FGEETSREER	//	ERIANEELAN
TGF- β	DmDawdle	457	IVIDMQNRRR	//	KSRQKRSINC
TGF- β	DmMaverick	577	HRSNHDSTWR	//	KDKWTNNCYK
TGF- β	MmAmh	437	GREGRGRTGR	//	SAGTGTGPGC
TGF- β	MmGdf15	179	LRVAAGRGRR	//	SAHAHPRDSC
TGF- β	MmInha	224	APSAGERARR	//	STPSVPWPWS
TGF- β	MmLefty1	211	GTWSSHKLVR	//	FAAQGTPDGK
TGF- β	MmLefty2	211	GTWSAHKLVR	//	FAAQGTPDGK
TGF- β	MmTgfb1	269	QHLHSSRHRR	//	ALDTNYCFSS
TGF- β	MmTgfb2	321	SQQSSRRKKR	//	ALDAAYCFRN
TGF- β	MmTgfb3	291	PGQGSQRKKR	//	ALDTNYCFRN
outgroup	MmGdnf	111	QAAALPRRER	//	NRQAAAASPE

Table S3. Spacer between cleavage site and first cysteine of the ligand is hypervariable.

Subfamily	Name	Residues between cleavage site and first cysteine	Length
Activin	CeTIG-3	NAPNFDVMVFQPNTVTAGTSD	21
Activin	DmActivin-beta	RRAVD	5
Activin	DmMyoglianin	SVYMD	5
Activin	MmBmp3	STGILLPLQNNELPGAIEYQYKEEGAWEEKPYKSLQTQPPEKSRN	80
Activin	MmGdf10	KKKORKGSHOKGOTLOFDEOTLKKARRKOWVEPRN	36
Activin	MmGdf11	KKKDQDTFTAASSQVLDLDFDEKTMQKARRRQWDEPRV	36
Activin	MmInhba	NLGLD	5
Activin	MmInhbb	RGLE	4
Activin	MmInhbc	KRGLE	5
Activin	MmInhbe	RGID	4
Activin	MmMstn	TPT	3
Activin	MmMstn	DFGLD	5
BMP	CeDBL-1	SAQTGNSEKRNKGRKHHNTEAESNL	27
BMP	CeTIG-2	KGLYVDFDILGWKQWVIAPEGFSFY	26
BMP	DmDPP	QPRRPTRRNHDDT	14
BMP	DmGBB	SASHPRKRKKSVPNNVPLLEPMESTRS	28
BMP	DmSCW	DLEKRRAGGGSPPPPPPPVDLYRPPQS	28
BMP	MmBmp2	QAKHKQRKRLKSS	13
BMP	MmBmp4	SPKHPQRSRKKNKN	15
BMP	MmBmp5	AASKRKNQNRNKSNSHQDPSRMPSAGDYNTSEQKQA	36
BMP	MmBmp6	SASSRRRQQSRNRSTQSQDVSRGSGSSDYNGSELKTA	37
BMP	MmBmp7	STGGKQRSQNRSKTPKNQEALRMASVAENSSSDQRQA	37
BMP	MmBmp8a	AARPLKRRQPKKTNELPHPNKLPGLFDDGHGSRGREV	37
BMP	MmBmp8b	PLKKKQLNQLNQLPHSNKHLGILDDGHGSHGREV	34
BMP	MmBmp10	NAKGNV	6
BMP	MmBmp15	QA	2
BMP	MmGdf1	LHVSFREVGVHRWVIAPRGFLANF	24
BMP	MmGdf2	STGASSH	7
BMP	MmGdf3	AAISVPKGF	9
BMP	MmGdf5	RAPLANRQGKRPSKNLKR	19
BMP	MmGdf6	KPLHVNFKELGWDDWIIAPLEYEAYH	26
BMP	MmGdf7	SR	2
BMP	MmGdf9	GQKAIRSEAKGPLLTASFNLSEYFKQFLFPQNE	33
BMP	MmNodal	RHHLPPDRSQL	10
Unexpected conservation between MmNodal and CeDBL-1 in red			
TGF-β	CeDAF-7	SHAKPV	6
TGF-β	CeUNC-129	ERIANEELANDVRVLLQNKNR	22
TGF-β	DmDawdle	KSRQKRSIN	9
TGF-β	DmMaverick	KDKWTNN	7
TGF-β	MmAmh	SAGTGTGDP	9
TGF-β	MmGdf15	SAHAHPRDS	9
TGF-β	MmInha	STPSVPWPWSPAALRLLQRPPEEPAAHAF	29
TGF-β	MmLefty1	FAAQGTPDGKGQGEPQLELHTLDLKDYGAAQGN	32
TGF-β	MmLefty2	FAAQGTPDGKGQGEPQLELHTLDLKDYGAAQGN	32
TGF-β	MmTgfb1	ALDTNY	6
TGF-β	MmTgfb2	ALDAAY	6
TGF-β	MmTgfb3	ALDTNY	6
outgroup	MmGdnf	NRQAAAASPENSRGKGRRGQRGKNRG	26

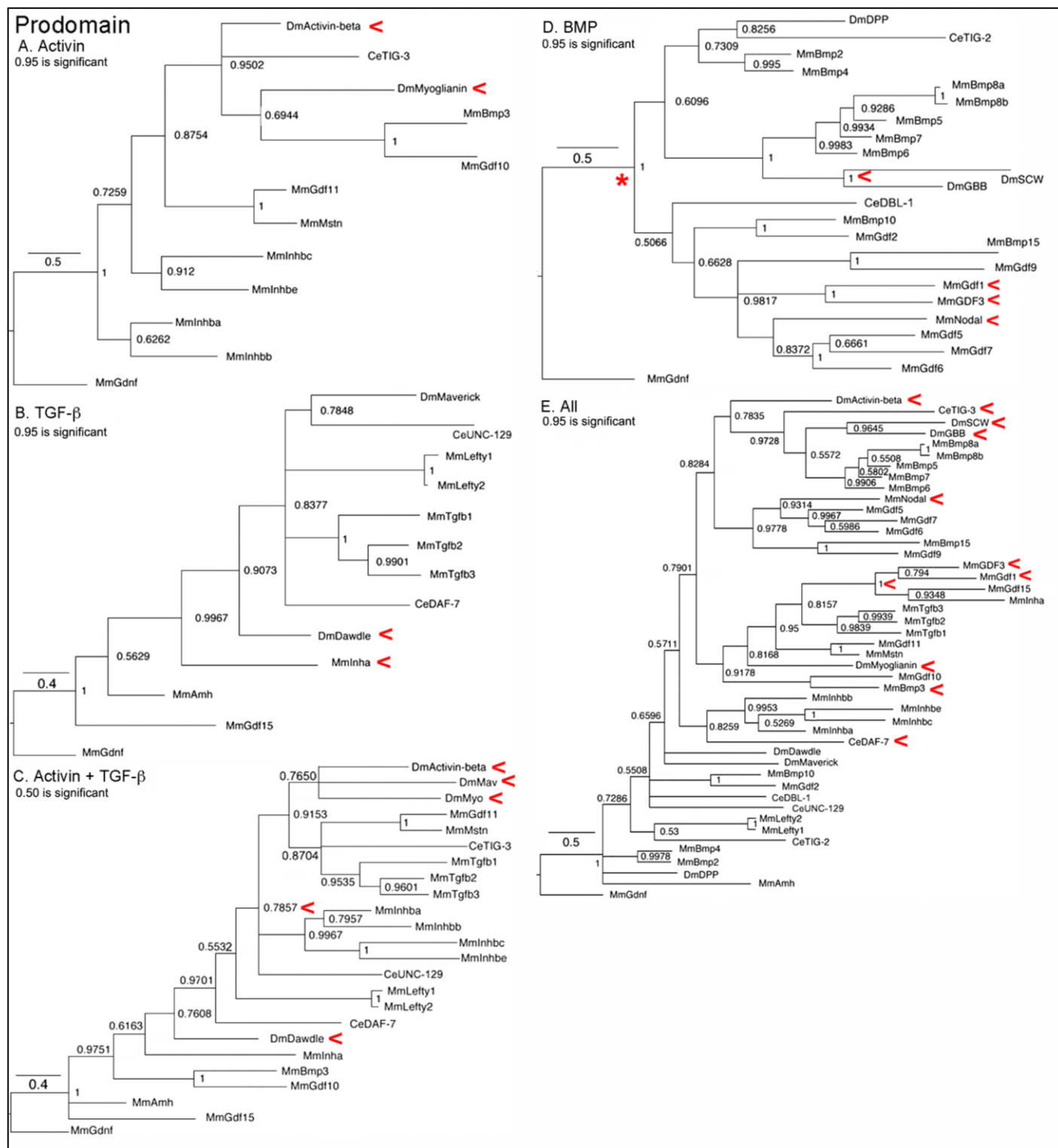


Fig. S1. Prodomain trees. Trees for this domain are displayed as in Fig. 1. Red arrowheads indicate a cluster that may reflect common regulation. For every tree except Activin+TGF- β nodes above 0.95 are significant. For Activin+TGF- β nodes above 0.50 are significant. A) Activin. The significant cluster of Activin and Myoglianin

is unexpected. B) TGF- β . The significant cluster of Dawdle and Inhibin- α was unexpected. C) Activin+TGF- β . The significant cluster of Activin, Maverick and Myoglianin that is clustered with the four Inhibin- β proteins and Dawdle's location near Inhibin- α were unexpected but consistent with cysteine conservation in the "Association region" and β 8. D) BMP. The significant cluster of Gbb/Screw in all trees was unexpected. The cluster of heterodimerizing Nodal and GDF1/GDF3 was expected. Red asterisk indicates node leading to two symmetric secondary clusters. E) All family members. The not quite significant cross-subfamily cluster of Activin, TIG-3, Gbb and Screw with Nodal was unexpected but three are known to heterodimerize and two have conserved cysteines. The absolute cluster of GDF3/GDF1 with GDF15/Inhibin- α and this group's not quite significant cluster with Myoglianin was unexpected. The not quite significant cluster of DAF-7 with the four Inhibin- β proteins was unexpected but is consistent with "Association region" cysteine conservation. The cluster of BMP3/GDF10 with Myoglianin was unexpected.

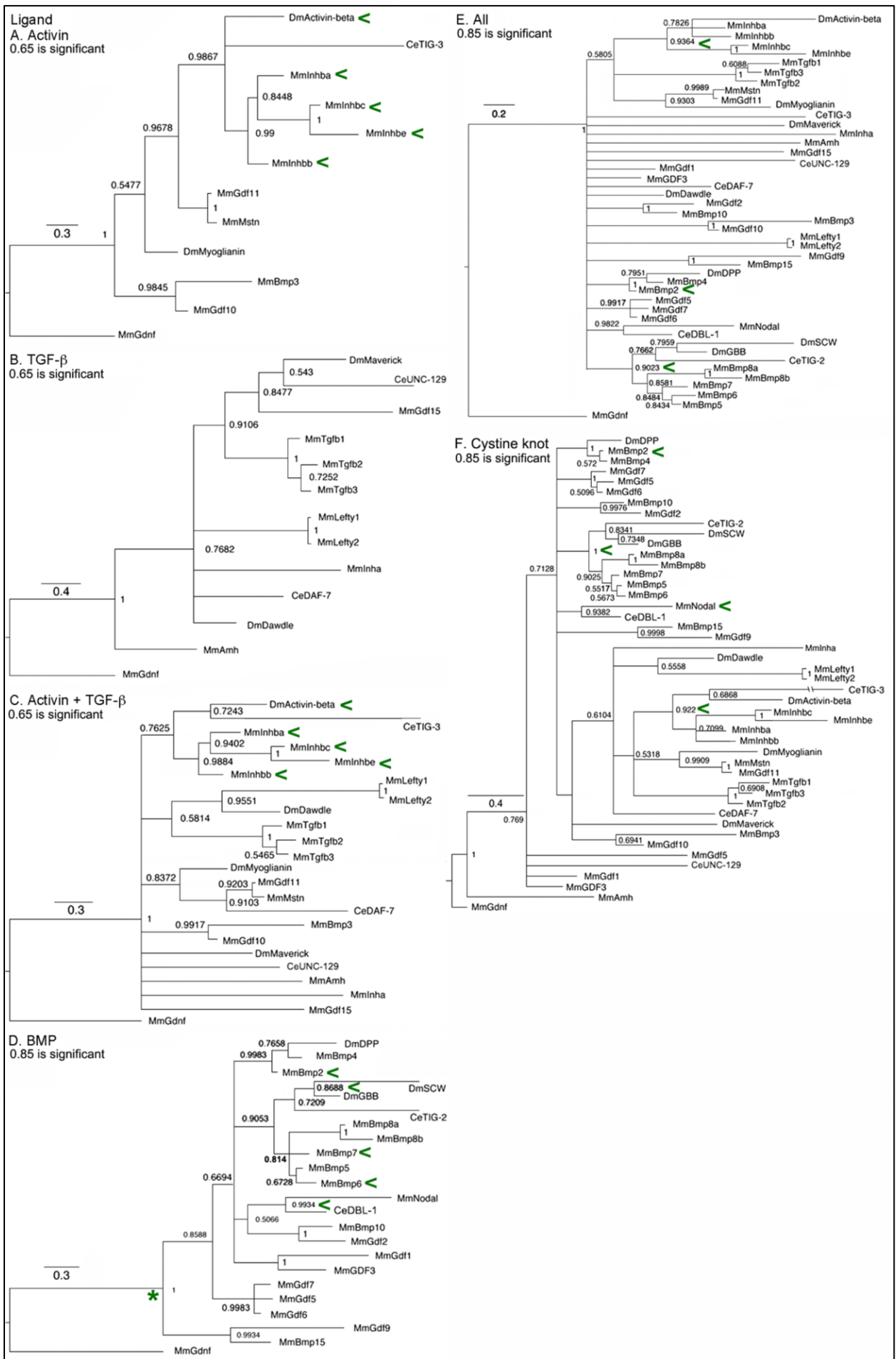


Fig. S2. Ligand trees. Trees for this domain are displayed as in Fig. 1. Green arrowheads indicate a cluster that may reflect common function. For Activin, TGF- β and Activin+TGF- β nodes above 0.65 are significant. For BMP subfamily and All family members trees nodes above 0.85 are significant. A) Activin. The significant cluster of Activin and the four Inhibin- β proteins was expected. B) TGF- β . The significant clusters of TGF- β 1-3 and Lefty1,2 were expected. C) Activin+TGF- β . The significant cluster of Activin and the four Inhibin- β proteins was expected. D) BMP. The significant cluster of BMP2-8a,b with Gbb/Screw was expected and consistent with functional heterodimers of BMP2-BMP6 and BMP2-BMP7 that have been reported. The significant cluster of Nodal and DBL-1 was unexpected. Green asterisk indicates node leading to two asymmetric secondary clusters. E) All family members. Several significant clusters are expected such as the four Inhibin- β proteins and Dpp/BMP2/BMP4. A significant cluster of Nodal and DBL-1 was unexpected. F) Cystine knot nodes above 0.85 are significant. Several significant clusters are expected such as Activin with four Inhibin- β proteins, Dpp/BMP2/BMP4 and Gbb/Screw/BMP5-8a,b. A significant cluster of Nodal and DBL-1 was unexpected.

Myostatin/GDF11 was expected. B) TGF- β . The significant clusters of TGF- β 1-3 and Lefty1,2 were expected. C) Activin+TGF- β . The significant cluster of Myoglianin and Myostatin/GDF11 was expected. D) BMP. Clustering of GBB/Screw, BMP10-GDF9, BMP15-GDF9 and Nodal-GDF1/GDF3 are consistent with heterodimerization that has been reported. Green asterisk indicates node leading to two asymmetric secondary clusters. E) All family members. The not quite significant clustering of BMP3 and GDF1 with all of the BMP subfamily proteins was unexpected. The not quite significant cluster between Nodal and GDF1/GDF3 was expected.

		--α1----- -LatencyLasso- ----α2-----	
MmBmp3	124	-----	
MmGdf10	123	-----	
CeTIG-3	1	-----	
DmMyoglianin	205	DS ¹ EST ² KMH ³ ILM ⁴ RL ⁵ NE ⁶ KK ⁷ LP ⁸ NT ⁹ TK ¹⁰ PS ¹¹ V ¹² PQ ¹³ NI ¹⁴ ID ¹⁵ NY ¹⁶ -RD ¹⁷ YN ¹⁸ ASS ¹⁹ KT ²⁰ TV ²¹ WN ²² R ²³ ME ²⁴ S ²⁵ DES ²⁶ H	
MmGdf11	72	LR ¹ EST ² KS ³ QIL ⁴ SK ⁵ LR ⁶ KE ⁷ AP ⁸ NI ⁹ S ¹⁰ RE ¹¹ V ¹² K ¹³ QL ¹⁴ EP ¹⁵ -K ¹⁶ AP ¹⁷ PL ¹⁸ Q ¹⁹ Q ²⁰ IL ²¹ DL ²² -----H ²³ DF ²⁴ Q ²⁵ G ²⁶ DA	
MmMstn	52	SR ¹ TE ² AT ³ KI ⁴ QIL ⁵ SK ⁶ LR ⁷ ET ⁸ AP ⁹ NI ¹⁰ SK ¹¹ DA ¹² IR ¹³ QL ¹⁴ EP ¹⁵ -R ¹⁶ AP ¹⁷ PL ¹⁸ RE ¹⁹ LID ²⁰ Q-----Y ²¹ D ²² WORD ²³ DD	
DmActivin-beta	369	VR ¹ EST ² KR ³ QIL ⁴ TK ⁵ LG ⁶ SH ⁷ K ⁸ PN ⁹ V ¹⁰ SH ¹¹ PK ¹² Q ¹³ FW ¹⁴ -ET ¹⁵ IY ¹⁶ -----R ¹⁷ Y ¹⁸ D ¹⁹ G ²⁰ GR	
MmGdnf	92	DV ¹ MD ² FT ³ QAT ⁴ IK ⁵ R---L ⁶ K ⁷ RS ⁸ PD ⁹ KQ---A ¹⁰ A ¹¹ LP ¹² -RR ¹³ ER-----	
MmInhba	53	EM ¹ VE ² AV ³ KK ⁴ HL ⁵ N ⁶ ML ⁷ HL ⁸ KK ⁹ RP ¹⁰ DV ¹¹ TP ¹² VP ¹³ KA ¹⁴ AL ¹⁵ -N ¹⁶ AI ¹⁷ R-----K ¹⁸ TH ¹⁹ V ²⁰ G ²¹ K	
MmInhbb	77	DF ¹ EA ² VR ³ KR ⁴ HL ⁵ SL ⁶ QL ⁷ GR ⁸ PN ⁹ ITH ¹⁰ AV ¹¹ PK ¹² AA ¹³ V ¹⁴ -T ¹⁵ AL ¹⁶ R-----K ¹⁷ TH ¹⁸ AG ¹⁹ K	
MmInhbc	42	LL ¹ DL ² LAK ³ SI ⁴ LD ⁵ KL ⁶ HL ⁷ SR ⁸ PI ⁹ LS ¹⁰ RP ¹¹ VS ¹² RG ¹³ AK ¹⁴ -T ¹⁵ AL ¹⁶ Q-----R ¹⁷ Y ¹⁸ RG ¹⁹ PR	
MmInhbe	42	LV ¹ LE ² LAK ³ Q ⁴ ILE ⁵ GL ⁶ HT ⁷ SR ⁸ PR ⁹ IT ¹⁰ RP ¹¹ LQ ¹² AA ¹³ LT ¹⁴ -R ¹⁵ AL ¹⁶ R-----R ¹⁷ Y ¹⁸ Q ¹⁹ PK ²⁰ S	
		end straitjacket--β1--	
MmBmp3	124	-----	
MmGdf10	123	-----	
CeTIG-3	1	-----	
DmMyoglianin	264	S ¹ IND ² TY ³ GD ⁴ -----H ⁵ IM ⁶ T ⁷ DE ⁸ DE ⁹ SS ¹⁰ SS ¹¹ Q ¹² M ¹³ Q ¹⁴ G ¹⁵ DD ¹⁶ AN-----	
MmGdf11	122	Q ¹ PED ² F ³ LEED ⁴ -----E ⁵ Y ⁶ HAT ⁷ TET ⁸ VI ⁹ SM ¹⁰ AQ-----E ¹¹ T ¹² DP ¹³ AV ¹⁴ Q ¹⁵ TD	
MmMstn	102	S ¹ -SD ² GS ³ LEDD ⁴ -----D ⁵ Y ⁶ HAT ⁷ TET ⁸ II ⁹ MT ¹⁰ P-----E ¹¹ S ¹² DF ¹³ LM ¹⁴ Q ¹⁵ AD	
DmActivin-beta	411	W ¹ IP ² NN ³ AF ⁴ GS ⁵ -----S ⁶ G ⁷ KN ⁸ LD ⁹ Q ¹⁰ K ¹¹ TI ¹² K ¹³ RA ¹⁴ FA ¹⁵ SP ¹⁶ GS ¹⁷ HL ¹⁸ F ¹⁹ NG ²⁰ R ²¹ GG ²² RT ²³ D ²⁴ Q ²⁵ R ²⁶ SER ²⁷ DP ²⁸ SH ²⁹ HK ³⁰ Y	
MmGdnf		-----	
MmInhba	95	V ¹ GEN ² GY ³ VE ⁴ IED ⁵ D ⁶ IG ⁷ RA ⁸ EM ⁹ NEL ¹⁰ ME ¹¹ QT ¹² SE ¹³ II ¹⁴ FA ¹⁵ ES ¹⁶ G-----T ¹⁷ --A	
MmInhbb	119	V ¹ RED ² GR ³ VE ⁴ I ⁵ PH ⁶ LD ⁷ G ⁸ HAS ⁹ PG ¹⁰ AD ¹¹ G ¹² Q ¹³ ERV ¹⁴ SE ¹⁵ II ¹⁶ SA ¹⁷ ET ¹⁸ D ¹⁹ GLA-----S ²⁰ --S	
MmInhbc	84	RE ¹ T---L ² LE ³ H-----D ⁴ QR ⁵ EE ⁶ YE ⁷ II ⁸ S ⁹ FAD ¹⁰ TL ¹¹ SS-----I ¹² --N	
MmInhbe	84	V ¹ --P-----G ² N---RE ³ K ⁴ V ⁵ IS ⁶ FAT ⁷ II ⁸ DKS-----T ⁹ ST ¹⁰ Y	
		begin arm-β2--- -β3--	
MmBmp3	124	-----NIL ¹ SA ² TI ³ YF ⁴ YV ⁵ GEL ⁶ VNI ⁷ ---SL ⁸ SC	
MmGdf10	123	-----MIL ¹ TA ² AF ³ HY ⁴ SE ⁵ PP ⁶ RP ⁷ PR ⁸ AE ⁹ VFC	
CeTIG-3	17	-----IT ¹ LE ² PN ³ R ⁴ KS ⁵ WT ⁶ CT ⁷ PES-	
DmMyoglianin	330	SI ¹ YIF ² PEE ³ I ⁴ Q ⁵ PH ⁶ VR ⁷ NR ⁸ K ⁹ VD ¹⁰ V ¹¹ RF ¹² QI-----D ¹³ SS ¹⁴ Y ¹⁵ DL ¹⁶ SY ¹⁷ AT ¹⁸ HL ¹⁹ YL--R ²⁰ Q ²¹ WD ²² W ²³ SA ²⁴ HQ ²⁵ P	
MmGdf11	179	-----W ¹ V ² YL ³ RP ⁴ V ⁵ PR	
MmMstn	158	-----W ¹ I ² YL ³ RP ⁴ V ⁵ KT	
DmActivin-beta	643	EI ¹ IT ² FA ³ EE ⁴ GT---Q ⁵ Y ⁶ R ⁷ Q ⁸ Y ⁹ RI ¹⁰ LE ¹¹ FS ¹² AQ ¹³ NR ¹⁴ RV ¹⁵ PS ¹⁶ Q ¹⁷ LS ¹⁸ IRS ¹⁹ Q ²⁰ TH ²¹ IR ²² ID ²³ K ²⁴ PH ²⁵ SL ²⁶ WE ²⁷ KA ²⁸ KS	
MmGdnf		-----	
MmInhba	153	-----AE ¹ V-----W ² L ³ FL ⁴ M ⁵ VP ⁶ KA	
MmInhbb	180	-----AS ¹ L-----W ² Y ³ YL ⁴ K ⁵ LL ⁶ PY	
MmInhbc	132	-----TR ¹ F-----M ² FF ³ V ⁴ Q ⁵ FP ⁶ HN	
MmInhbe	125	-----AR ¹ -----L ² WL ³ RP ⁴ PP ⁵ S	
		-α3- ----β4--	
MmBmp3	145	P-E---PQ ¹ GCS ² HHT ³ QR ⁴ Q-----HI ⁵ Q ⁶ ID ⁷ SA ⁸ W ⁹ L ¹⁰ KS ¹¹ NQ ¹² SQ ¹³ LL ¹⁴ G-----	
MmGdf10	147	K ¹ PR ² AK ³ -NAS ⁴ CR ⁵ LL ⁶ TP ⁷ GL-----P ⁸ AR ⁹ LH ¹⁰ IF ¹¹ RS ¹² LS ¹³ -Q ¹⁴ NT ¹⁵ AT ¹⁶ QG-----	
CeTIG-3	34	---LV ¹ KDC ² F ³ QYS ⁴ INS ⁵ IN ⁶ HE ⁷ IL ⁸ SAS ⁹ LI ¹⁰ ID ¹¹ PK ¹² DN ¹³ SI ¹⁴ V ¹⁵ YEV ¹⁶ DEL ¹⁷ F-----	
DmMyoglianin	383	G---L ¹ LEE ² IKK---Q ³ PR ⁴ K-----D ⁵ IV ⁶ VT ⁷ H ⁸ RA ⁹ IR ¹⁰ VA-----N ¹¹ T	
MmGdf11	188	-PAT-----V ¹ YL ² QL ³ L ⁴ R ⁵ L ⁶ K ⁷ PL ⁸ T ⁹ GEG ¹⁰ TAGG---G	
MmMstn	167	-PTT-----V ¹ F ² V ³ QL ⁴ L ⁵ R ⁶ L ⁷ IK ⁸ PM ⁹ KD-----	
DmActivin-beta	699	L ¹ PE ² KH ³ LL ⁴ NT ⁵ K ⁶ R ⁷ K ⁸ WG ⁹ ANK ¹⁰ PHH-----R ¹¹ K ¹² I ¹³ W ¹⁴ F ¹⁵ QL ¹⁶ ST ¹⁷ SI-----N ¹⁸ ITE ¹⁹ K	
MmGdnf		-----	
MmInhba	165	N---R-----T ¹ RT-----K ² V ³ T ⁴ IR ⁵ F ⁶ QQ ⁷ Q ⁸ K ⁹ HP ¹⁰ Q ¹¹ GS ¹² LD ¹³ TG ¹⁴ DE ¹⁵ AEE ¹⁶ EM	
MmInhbb	192	V ¹ LE ² KG-----S ³ RR-----K ⁴ V ⁵ R ⁶ V ⁷ K ⁸ Y ⁹ F ¹⁰ QE-----	
MmInhbc	144	AT ¹ QT-----V ² NR ³ VL ⁴ LRP-----	
MmInhbe	135	FP ¹ GT-----Y ² LR ³ F ⁴ RC ⁵ GT-----	
		---β5- -β6-- --α4--- --β7--- no-β8	
MmBmp3	178	-----H ¹ LS ² VD ³ V ⁴ RP ⁵ YR ⁶ DS ⁷ VS ⁸ W ⁹ LS ¹⁰ KD ¹¹ IT ¹² QL ¹³ R ¹⁴ K ¹⁵ AK ¹⁶ QNE---E ¹⁷ FL ¹⁸ IG ¹⁹ FN ²⁰ ITS ²¹ RA ²² HE ²³ LP	
MmGdf10	182	-----L ¹ RG ² AM ³ AL ⁴ TP ⁵ PP ⁶ RG ⁷ LW ⁸ Q ⁹ ARD ¹⁰ ISS ¹¹ IK ¹² AARR ¹³ DG---E ¹⁴ LL ¹⁵ SA ¹⁶ QL ¹⁷ DT ¹⁸ GE ¹⁹ KD ²⁰ PG	
CeTIG-3	76	---GEL ¹ QYV---DR ² FE ³ IR ⁴ -ET ⁵ LD ⁶ KY ⁷ H ⁸ FD ⁹ ISH ¹⁰ F ¹¹ HK ¹² WM ¹³ K ¹⁴ OK ¹⁵ SS ¹⁶ DKV---K ¹⁷ IE ¹⁸ IT ¹⁹ NS ²⁰ NT-----	
DmMyoglianin	410	TS ¹ FN ² PK ³ V ⁴ K ⁵ MF ⁶ FR ⁷ HS ⁸ PS ⁹ GL ¹⁰ QW ¹¹ AV ¹² DL ¹³ KS ¹⁴ LL ¹⁵ GN ¹⁶ LS ¹⁷ NMT ¹⁸ Q---E ¹⁹ EL ²⁰ LK ²¹ -GAET-----	
MmGdf11	211	GG ¹ RR ² H ³ IR ⁴ IR ⁵ SL ⁶ KIE ⁷ HS ⁸ RS ⁹ GH ¹⁰ W ¹¹ QS ¹² ID ¹³ F ¹⁴ Q ¹⁵ V ¹⁶ L ¹⁷ HS ¹⁸ W ¹⁹ FR ²⁰ OP ²¹ -Q ²² SN ²³ WG ²⁴ IE ²⁵ IN ²⁶ AF ²⁷ DP ²⁸ SG	
MmMstn	184	--G ¹ TRY ² TG ³ IR ⁴ SL ⁵ KLD ⁶ SP ⁷ GT ⁸ GI ⁹ W ¹⁰ QS ¹¹ ID ¹² V ¹³ KT ¹⁴ VL ¹⁵ Q ¹⁶ N ¹⁷ WL ¹⁸ K ¹⁹ OP ²⁰ -E ²¹ SN ²² L ²³ G ²⁴ IE ²⁵ KAL ²⁶ DENG-----	
DmActivin-beta	737	G--ID ¹ KAI ² L ³ FR ⁴ AS ⁵ FQ ⁶ W ⁷ DP ⁸ KN ⁹ L ¹⁰ GW ¹¹ Q ¹² K ¹³ FD ¹⁴ LT ¹⁵ DT ¹⁶ REW ¹⁷ YG ¹⁸ HT ¹⁹ S ²⁰ HE ²¹ K ²² LR ²³ LL ²⁴ DC ²⁵ TG ²⁶ CGG-----	
MmGdnf		-----	
MmInhba	196	GL ¹ KGER ² SE ³ LL ⁴ SE ⁵ KV ⁶ D ⁷ ARK ⁸ ST ⁹ WH ¹⁰ IF ¹¹ VS ¹² SS ¹³ OR ¹⁴ LL ¹⁵ DQ ¹⁶ -G ¹⁷ K ¹⁸ SS ¹⁹ LD ²⁰ RI ²¹ ACE ²² QC ²³ QE-----	
MmInhbb	210	--Q ¹ GH ² DR ³ NN ⁴ V ⁵ VE ⁶ KK ⁷ DL ⁸ K ⁹ RS ¹⁰ GH ¹¹ TF ¹² PI ¹³ EA ¹⁴ Q ¹⁵ AL ¹⁶ FER ¹⁷ -G ¹⁸ ERR ¹⁹ LN ²⁰ D ²¹ V ²² Q ²³ DC ²⁴ SC ²⁵ QE-----	
MmInhbc	158	--Y ¹ DT ² N ³ L ⁴ T ⁵ LS ⁶ QY ⁷ V ⁸ QV ⁹ NAS ¹⁰ GW ¹¹ Y ¹² QL ¹³ LG ¹⁴ PE ¹⁵ AQA ¹⁶ ACS ¹⁷ -G ¹⁸ HL ¹⁹ TLE ²⁰ T---V ²¹ PS ²² QVA-----	
MmInhbe	149	--TR ¹ CR ² GF ³ RT ⁴ FL ⁵ AE ⁶ HQT ⁷ TSS ⁸ GH ⁹ ALT ¹⁰ PS ¹¹ SG ¹² LR ¹³ SED ¹⁴ S ¹⁵ -G ¹⁶ V ¹⁷ V ¹⁸ KL ¹⁹ Q ²⁰ E ²¹ FR ²² PL ²³ DL ²⁴ NS	
		no bowtie -β9--- no-β9'- --β10- no-α5	
MmBmp3	226	K ¹ R ² ML ³ FF ⁴ PE ⁵ PY ⁶ LV ⁷ YAND ⁸ A-----A ⁹ ISE ¹⁰ PES ¹¹ V ¹² SS ¹³ L ¹⁴ QR ¹⁵ HR ¹⁶ DF ¹⁷ TAG ¹⁸ TG---P	
MmGdf10	230	V ¹ PR ² PS ³ SH ⁴ MP ⁵ Y ⁶ LV ⁷ YAND ⁸ L-----A ⁹ ISE ¹⁰ PNS ¹¹ V ¹² AV ¹³ SL ¹⁴ Q ¹⁵ RY ¹⁶ DF ¹⁷ PAG ¹⁸ DFE ¹⁹ PGA ²⁰ AP	
CeTIG-3	124	-----Q ¹ N ² INAL ³ S---V ⁴ LR-----	
DmMyoglianin	460	-----W ¹ M-----K ² SL ³ V ⁴ VT ⁵ T ⁶ D ⁷ NT ⁸ SE ⁹ NP ¹⁰ TV ¹¹ HIE ¹² IG ¹³ S--	
MmGdf11	265	-----T ¹ D ² AV ³ TS-----L ⁴ GP ⁵ GA ⁶ EL ⁷ HP ⁸ FE ⁹ LR ¹⁰ V ¹¹ LE ¹² NT-----	
MmMstn	236	-----H ¹ DL ² AV ³ TF-----P ⁴ GP ⁵ GED ⁶ GL ⁷ N ⁸ PF ⁹ EV ¹⁰ K ¹¹ VT ¹² DP-----	
DmActivin-beta	790	-----R ¹ YS ² L ³ HL ⁴ F ⁵ Q ⁶ TS ⁷ K ⁸ LR---G-----N ⁹ SS ¹⁰ D ¹¹ YL ¹² ST ¹³ NP ¹⁴ NR ¹⁵ PF ¹⁶ VL ¹⁷ HT ¹⁸ ESS ¹⁹ R--	
MmGdnf		-----	
MmInhba	250	-----S ¹ GAS ² LV ³ LL ⁴ G ⁵ K ⁶ K ⁷ K ⁸ KE ⁹ VD ¹⁰ GD ¹¹ G ¹² K ¹³ K ¹⁴ D ¹⁵ GS ¹⁶ DG ¹⁷ GLEE ¹⁸ E ¹⁹ KE ²⁰ Q ²¹ SH ²² RP ²³ FM ²⁴ QAR ²⁵ QSE--	
MmInhbb	262	-----LA ¹ V ² VP ³ V ⁴ F ⁵ VD-----P ⁶ GE ⁷ ESH ⁸ RP ⁹ FF ¹⁰ V ¹¹ QAR ¹² LG--	
MmInhbc	207	-----H ¹ SSL ² -IL ³ GW ⁴ FS ⁵ HR ⁶ PF ⁷ VAA ⁸ Q ⁹ VR ¹⁰ VE-----	
MmInhbe	200	-----TA ¹ AG-----L ² PR ³ LL ⁴ LD ⁵ TAG ⁶ Q ⁷ RP ⁸ FE ⁹ L ¹⁰ KIR ¹¹ ANE--	

Fig. S4. Expanded Activin subfamily prodomain alignment indicating structural conservation. Sequences from Fig. 2 with no omissions, similar underlining and accurate numbering. Ungainly leaders and trailers were trimmed for brevity.

		-----α1----- -LatencyLasso- -----α2----
CeUNC-129	15	---IANCAKVDV-----LINETTRDLHFKSSD---PNVTSFHRSSHT---
CeDAF-7	19	GLTFNCTNSGICIKMKQHRTEYKNEELDQLNKEAKKGLKPMDEPKSVYLEMY---R
DmMaverick	245	-----SKRVDETRDKHLVLKGLGKKLDMRKVNISQAAYS-----S
MmTgfb1	27	AAG-LSTCKTDMELVKRKRIEATRGQILSKLRASPESSQGEVPPGPPEAVIALYNSTR
MmTgfb2	18	ALS-LSTCSTDMQFMKRRIEATRGQILSKLKTSPEDY-PEPEVPEVVISIYNSTR
MmTgfb3	21	SLS-LSTCTTDFGHIKKRVEATRGQILSKLRSTSPPEPS-V-MTHVPYQVIALYNSTR
MmLefty1	20	EAL-T-----GEO-----TLGSELQQLQDQPEVLDAKADVEGMVIPSHVRTQYV-
MmLefty2	20	AAM-T-----EQ-----VLSSLLQQLQSQATLDSADVEEMAIPTHVRSQYV-
MmInha	204	CSC-SGRPET-----
DmDawdle	233	CES-NRQVEHTEQLTHLRIEFYKQNTKTRKESKVSAAA-VEPKPIFDGM----
MmGdf15	118	AYR-VHRALLLTPTARPDITRPL-KRALSLRGPRALRLRL--TPPPDLA-----
MmGdnf		-----
MmAmh	351	AAT-EREFPMTGHPASAPWAAGLQR-RVAVETQAAASELRDLPGLPPTAPPLLARL----
		end straitjacket--β1---
CeUNC-129	53	-----TEHMKNLNENFIDEDESNEDGNLVRAIEPAVGKFEGQEVLVFDVE
CeDAF-7	76	DLLEKDEQDM-----GVEMSFYAKD-----
DmMaverick	282	KYLEYLSRLR---SNQEKGSYNFNMFGASFT-----
MmTgfb1	86	DRVAGESAD-----PEPEPEADYAKEV-----
MmTgfb2	76	DLLEKASRRRAACERERSDEEYAKEV-----
MmTgfb3	78	ELLEEMHGEREEGCTQETSESEYAKEI-----
MmLefty1	63	ALLQHSASR---SRGKRFSQNLREVA-----
MmLefty2	63	ALLQGSADR---SRGKRFSQNLREVA-----
MmInha	213	-----
DmDawdle	285	-TSSHPDDST---KNK-ELDDYARTS-----
MmGdf15	167	---MLPS-----GGTQLELR-----
MmGdnf		-----
MmAmh	405	-LALCPNDSR---SSGDPLRALLL-----
		begin arm --β2-- --α3-- --β3--
CeUNC-129	143	TLKKIRVGGDENLE---EYK--VIMDATKS-VFDSYHLDAKQAVFRITREHSMRPHYA
CeDAF-7	102	-----NPSQLVAKEDVTND---LERSDLQALTLTSIEIPAK---
DmMaverick	356	--L--LRGEQDT-----MNILLHPLTNAQDANFHHDKIDEANVRMLLYSSSL---
MmTgfb1	126	-----DISH---SIY---MRENTSDIREAVPEPPLSRAEIRQRLKS---
MmTgfb2	136	SQV--LCGYLDAIPPTFYRPFYFRIVREDVST---MEKNASNVKAEFRVRLQNPK---
MmTgfb3	126	-----GITSKVFRFNVSS---VEKNGTNTFRAEFRVLRVNPNS---
MmLefty1	95	-----STHLLVFGMEQ---RLPPNSELVQAVLRVFOQEPVPR---
MmLefty2	95	-----STHLLVFGMEQ---RLPPNSELVQAVLRVFOQEPVPR---
MmInha	213	-----
DmDawdle	327	-----SNPSMCFTKIID---ADAEGFDSTAVLWTFKNKQNR---
MmGdf15		-----
MmGdnf		-----
MmAmh		-----
		---β4--- --β5-- --β6-- --α4---
CeUNC-129	249	-----LDNEDREPIKRNKGNLSLSEEISSDVMQGEETSRREE---
CeDAF-7	138	GMLQDVQVQVYEKNE--DG-S-MGEMVTSGIFA--TK-GSERISIOLPIDTKSWFTIS
DmMaverick	441	NSSQQLTKVYQLLSANRRRKITSRKIEFGNVGF--QETRTQWIEFD-VTKAVRSWLNKS
MmTgfb1	163	--SVEQHVELYQKYS---NNSWRYLGNELL---TPTDTPEWLSFD-VTGVRQWLNQG
MmTgfb2	187	ARVAEQRELYQILKSKDLTSPQRYLDSKV---KTRAEGEWLSFD-VTDVQEWLHHK
MmTgfb3	161	SKRTEQRLELFQILRPD--H-IAQRYLGGNLL---PTRGTAEWLSFD-VTDVREWLLRR
MmLefty1	140	SARARVTLEWLRFRD--GSGNRTA-LDSRLV---SIHESGWKAFD-VTEANFQWQLS
MmLefty2	140	SARARVTLEWLRVRE--GSGNRTA-LDSRLV---SIHESGWKAFD-VTEANFQWQLS
MmInha	213	-----
DmDawdle	370	-TSAQQTIVVSEVEV--EQQKDSKYLAAATTAQSVNVQDEWMKID--LEWPKHWTSGH
MmGdf15		-----
MmGdnf		-----
MmAmh		-----
		---β7- --β8-----bowtie-----β9---
CeUNC-129	289	-----
CeDAF-7	190	PI-QGIFVKAMLDRNV-----ALHPQ
DmMaverick	498	HENLGIE--IQCDKCKSIGA--RILSDFSPSTPPRSTASSDEHLNMPVLNIIGHGTLS
MmTgfb1	212	DGIQGFRESAHCSCDSKDNK-----LHVEING---I
MmTgfb2	243	DRNLGFKISLHCPCCCTFVPSNNYIIPNKSEE-----LEARFAGIDGT
MmTgfb3	216	ESNLGLEISIHCPCHTFQPNGD-ILENVHEV-----MEIKFKGVDNE
MmLefty1	192	RP--R-----
MmLefty2	192	RP--R-----
MmInha	213	-----
DmDawdle	426	EL--SHLIQITCGGCDVSDMEEIISVD-----
MmGdf15		-----
MmGdnf		-----
MmAmh		-----
		no-β9' --β10- --α5--
CeUNC-129	289	-----R---
CeDAF-7	211	QTTADVDMRLQL-----S---TRPKG--S-RKRR---
DmMaverick	554	QQHGDADIHQIMLTNNRSDQYV-----HHRSNHDSWTW---
MmTgfb1	240	SPKRRGDLGTIH-----DMNRFFLLMATPLERAQHLSSRRHR---
MmTgfb2	285	STYASGDQKTIKSTRKKTSGKTEHLLMLLPSYRLESQQSSRRKKR---
MmTgfb3	257	DDHGRGDLGRLK---KQKDHHNPHLLMMIPPHRLDSPGGGSRKKR---
MmLefty1	195	-----CPLLT-QVSVQ---REHLGPGTWSSHKLV---
MmLefty2	195	-----CPLLT-QVSVQ---REHLGPGTWSSHKLV---
MmInha	213	-----TFELVAHTRAR--APSAGE--RARR---
DmDawdle	451	-----KDYRFFLLIDMQNR--RR---
MmGdf15		-----
MmGdnf		-----
MmAmh		-----

Fig. S5. Expanded TGF-β subfamily prodomain alignment indicating structural conservation. Sequences from Fig. 4 including underlining and presented as in Fig. S4.

		--α1-----	--LatencyLasso-	-----α2-----
DmMaverick	245	SKRVDETR-LKHLVLKGLGKIKKL-FDVRKVNISQA	----	EYSSKYIEYLSRLRS-----
DmMyoglianin	202	AKVDSIES-ISKMHILMRNLKKL-PNITKPI	-----	SVPMNIIDNFYRDYNASS-KT
MmGdf11	69	SRELRLS-ISKQILSKRLKEA-PNLSREVVKQLLPKAPPLQQILDHDFQGDALQ-P-		
MmMstn	49	TRYSRLEA-ISKQILSKRLLETA-PNLSKDAIRQLLPAPPLRELIDQYDVQRDDSS-S-		
CeTIG-3	1	MSTSR-----		
MmTgfb1	41	VKRKRLEA-IRGQILSKRLASP-PSQGEVPPG	-----	PLPEAVLALYNSTRDRVA-G-
MmTgfb2	32	FMRKRLEA-IRGQILSKRLTSP-PEDY-PEPD	-----	EVPPEVISIYNSTRDLLQ-E-
MmTgfb3	35	IKKKRVEA-IRGQILSKRLTSP-PEPS-V-MT	-----	HVPYQVLALYNSTRELLE-E-
CeUNC-129	25	-----L-INETIRDLLEHFKSSDPN	-----	TSFHRS-----
CeDAF-7	34	MKQHRTE-YLKNEILDQENMKEA-PKGLKPMDEPMKSVYLE-M-YRDLLEK-D	-----	EQ
MmBmp3	56	VSEHMTWLYDRYSGSSRQATRT-PGSQLPGPQPL	-----	
MmGdf10	71	VAIHMERLYEKYNRRG-----		APP-----
MmInhba	50	SQPEMVEA-VKKHILNMLHKKR-PDVTQVPVKAALLNAIRKL	-----	H-----VG
MmInhbb	74	VDGDFLEA-VKRHILSRQLRGR-PNTHAVPKAAMVTALRKL	-----	H-----AG
MmInhbc	39	QRELLDL-AKKSILDKHLSQR-PILSRPVSRGALKTALQRL	-----	R-----GP
MmInhbe	39	ERALVLEL-AKQQLLEGLHLTSR-PRITRPLPQAALTRALRL	-----	Q-----PK
DmActivin-beta	546	MNE-----		NALKKSTYPIDINHSDNKTHTG
MmLefty1	27	-----ILGSELQQQLDQF-PVLDKADVEGMVIPSHVRTQYVALLQSHAS	-----	R
MmLefty2	27	-----VLSSILQQQLSQA-PTLDSADVEEMAIPTHVRSQYVALLQGSHAD	-----	R
MmInha	213			
DmDawdle	247	LTHLRTEF-VKQQLLEKRLKES-PKNSA	----	VELPKPIFDGM----T
MmGdf15	132	ARPWDITR-PL-KRALSRGPRAPALRLRL	----	TPPPDLA-----MLPS-----
MmGdnf				
MmAmh	365	SAPWAAGL-QR-RVAVEIQAAAS-ELRDLPLGLPPTAPPLLRL	----	LALCPNDS----R
		end straitjacket -β1-- TGF-β		
DmMaverick	293	-----NQEKGSYFNFMGASFTRDHLFLSITTNFNDISNKRRLHRRSLKKIN		
DmMyoglianin	251	TVVNRMESIDESHLISINDTYGDHIMTDFDESSSSQMGGDANTVNEFLIDLNKNQAKKS		
MmGdf11	125	EDF-----LEEDEYHAT-----		TETVISMAQETDPAV
MmMstn	104	DGS-----LEDDDYHAT-----		TETIITMPTESDFLM
CeTIG-3	6	-----KHDLYGG-----		VLDKITLEPNRK--
MmTgfb1	91	ESAD-----PEPEPEADYYAK-----		EVTRVLMVDRNNAIY
MmTgfb2	81	KASRRAAA-CERERSDEEYYAK-----		EVYKIDMPSHLPSET
MmTgfb3	83	MHGEREEG-CTQETSESEYYAK-----		EIHKFDMIQGLAEHN
CeUNC-129	50	--SHT-----		
CeDAF-7	84	DMGVE-----MSFYTA-----		KDPSYGEN-----
MmBmp3	90	RGG-----		NTVRSFRAAAA-----
MmGdf10	90	GGG-----		NTVRSFRARLE-----
MmInhba	94	KVG-----		EN-----G-----Y
MmInhbb	118	KVR-----		ED-----G-----R
MmInhbc	83	RRE-----		T-----
MmInhbe	83	SMV-----		
DmActivin-beta	572	KNG-E-----MSHNDYEFNDYSVQ-----		THDKNRYHEGRSSIGYQPAIHN
MmLefty1	73	SRGKR-----FSQNLREVAGRFLVS-----		ET-----S----
MmLefty2	73	SRGKR-----FSQNFREVAGRFLMS-----		ET-----S----
MmInha	213			
DmDawdle	294	KNK-E-----LDDYYARTSKKFILL-----		NR--EEVECNARDGKSNP--
MmGdf15	171	-GGTQ-----LELR-----		LRVAAGRGR--
MmGdnf				
MmAmh	414	SSGDP-----LRALLL---LKALQG-----		LRAEWHGREGRGRTGR-----
		end straitjacket -β1-- Activin		
DmMaverick	342	RLNQNPKKHQNYGD-----		LLRGEQD---TMNILLHPLTN-----AQ
DmMyoglianin	311	DIPINTNDE-EYES-----		ILSHISS-----IY---IPPEIQPHVRHNRKVD
MmGdf11	152	Q-----TD-----		GS---PLC-----
MmMstn	131	Q-----AD-----		GK---PKC-----
CeTIG-3	25	-SWTCLTPE-----		
MmTgfb1	122	EK-----TK-----		DI-SH---SIY--
MmTgfb2	117	VCPVVTPSGSLGS-----		FCSRQSQ---VLC---GLDAI-PPTFYRPYFR
MmTgfb3	119	ELAVC---PK-----		
CeC53D6.2	53	-LTE--HMKNLYENFIDEDSNEDGNLVRAIEPAVGKFEGQEVLV		FDVEG-FDSHESIMRA
CeDAF-7	103			PSQLVAKSDVTN-DLERSDILQA
MmBmp3	104	-GTP--QTKG-----		LHTENLTS-LTKSENILSA
MmGdf10	104	-MI---DQKP-----		VYFENLTS-MQDSEMILTA
MmInhba	101	VEIE--DDIGRRA-----		EMNELMEQTSEIITAEAG--T--ARK
MmInhbb	125	VEIP--HLDGHAS-----		PGADGQERVSEIISAEETD-GLAS--SRV
MmInhbc	87	-LLE--H-----		DQRQEEYEIISADTD-LSSI--NQT
MmInhbe	86	--P-----		GN--REKVISATII-DKST-STYRS
DmActivin-beta	613	IEYE--NQKGHHESFADDHEN-----		IDHEDFFGNTQEIITAEAG-TQYR--QYR
MmLefty1	96			TH-----
MmLefty2	96			TH-----
DmDawdle	330			SM-----
MmGdf15				
MmGdnf				
MmAmh				

Fig. S6. Page1

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		bowtie-- β 9--	no- β 9'-	-- β 10--	-- α 5--
DmMaverick	520	DFSPSTPPR-----	STASSDEHLNMPVNIIGHGTLN---		
DmMyoglianin	463	-----SLVVTTD-----	NTSKNELTHIEIG-----		
MmGdf11	269	-----VTSLGP-----	GAEGLHPFMEIRVLE-----		
MmMstn	240	-----VTFPGP-----	GEDGLNPFLERKVTD-----		
CeTIG-3	135	-----	-----		
MmTgfb1	232	----- <u>LHVEING</u> -----	ISPKRRG-DLGTIH-----	DMNRPFLLMATPLERAQ---	
MmTgfb2	269	NKSEELEARFAGID--	GTSTYASG-DQKTIKSTRKKTSGKTEHLLMLLPSYRLE---		
MmTgfb3	241	NVHEVMEIKFKGVD--	NEDDHGRG-DLGRLK---	KQKDHNNPHLIIMMIPPHRLD---	
CeUNC-129	191	-----	RPYA-----	EMIRKSTPFLVYISKVNHTLDTVSV	
CeDAF-7	216	-----	-----	VDNRLQLSTRPK---	
MmBmp3	229	-----LFFPEPYI---	LVYANDAAISEPESVSSLQRHDETAGTG-----	PR----	
MmGdf10	233	-----PSSHMPYI---	LVYANDLAISEPNSVAVSLQRYDPFPAGDFEPGAAPN---		
MmInhba	254	-----LVLLGKKKKKEVDGDGKKKDGSDGGLLEEKEQSHRPFLMIQARQS-----			
MmInhbb	266	-----PVFVD-----	PGEESHRRPFVVVQARLG-----		
MmInhbc	207	-----	HSSL-ILGWFSHRPFVAAQVRVE-----		
MmInhbe	204	-----	LPRLLLDTAGQRPFLERKIRAN-----		
DmActivin-beta	794	-----HLFQTSKLRGN-----	SSDYLSTNPNRPFVLHTESS-----		
MmLefty1	195	-----	-----	QPLLI-QVSVQ-----	
MmLefty2	195	-----	-----	QPLLI-QVSVQ-----	
MmInha	213	-----	-----	TPFLVAHTRAR-----	
DmDawdle	445	-----EIIS-----	VDKDYRPFIVDMQNR-----		
MmGdf15		-----	-----		
MmGdnf		-----	-----		
MmAmh		-----	-----		

Fig. S6. Expanded Activin+TGF- β subfamily prodomain alignment indicating structural conservation. Sequences from Fig. 6 including underlining and presented as in Fig. S4.

			-----α1-----	-LatencyLasso-----	
DmSCW	30	-----	IYQKRPLSEQME	ITIDILDLGDRPRRQAEP	-----
DmGBB	56	-----	LSEDDKLDVSYETIE	FLGLTAERTHLSSHQL	-----
MmBmp8a	35	-----	LGARERRDMQREITL	AVLGLPGRPRRAQAAA	-----
MmBmp8b	35	-----	LGVREPRDMQREIRE	VLGLPGRPRRAPVGAA	-----
MmBmp6	68	-----	LKTHEKREMQKETIS	VLGLPHRPRPLHGLQQPQPPVLPFQQQQQQQQQQ	-----
MmBmp5	43	-----	LRNHERREIQREIT	LSILGLPHRPRPFSPG	-----
MmBmp7	46	-----	LRSQERREMQREIT	LSILGLPHRPRHLQG	-----
CeDBL-1	42	-----	ADQHASHATRRGLR	KLKGLHVE--V--QT	-----
MmBmp10	50	-----	DFNTLLQSMKNEFT	KTTLNLSDF--V--QD	-----
MmGdf2	53	-----	DLQMFLNMKVDFIR	SLNLSGIE--S--QD	-----
CeTIG-2	38	-----	G--QATDK--IGE	QIRELFNIDINE--NGPAV	-----
MmGdnf	61	-----	PAED-----	HSGLHRRVP--F--AL	-----
DmDPP	213	-KD--KLK--PDPSTLVEIEKS	LSLNFNKRFP--K--ID	-----	-----
MmBmp2	41	-----	LSR--PSEDVLSEFELRL	SMFGLKQRP--T--PS	-----
MmBmp4	43	GGR--RSG--QSHELLRDFEAT	LLQMFGLRRR--Q--PS	-----	-----
MmBmp15	35	---	LADDP	TLPSILDLAKEA---PG-----KEMKQ	-----
MmGdf9	55	---	GTD	RSGLPPLFKVLSDR---RG-----ETPKL	-----
MmGdf1	25	PAPASMG---	PAAALLQV-----	LGLPEAFRSVPTHR	-----
MmGDF3	20	-GQTSEF---	QSDLLQF-----	LGLEKAPSP-HRFQ	-----
MmNodal	13	-----	ACWALLHPR---	APTAAALPL--WTRGQ	-----
MmGdf5	124	GKGASSKAGSAPSSFLKKTR	---	EP-GTPRE--KEPFR	-----
MmGdf6	81	G-----	QH-QGQEPF--G--R	-----	-----
MmGdf7	65	G-----	PR-AVRRAA--GSGFR	-----	-----
			-----α2-----		
DmSCW	59	-----	NLHNSASKF	ILEVYNETSEDQEPKEVLHQR	-----
DmGBB	87	-----	SLRKSAPKF	ILDVYHRTIAEEGLSDQDEDDDYERGHRS	-----
MmBmp8a	67	-----	RQPASAP	LEMLDLYHAMTDDDDGGFP	-----
MmBmp8b	67	-----	QQPASAP	LEMLDLYHAMTDDSGGTP	-----
MmBmp6	117	TAREEPPPGRLKSAP	LEMLDLYNALNSDDEEDGASEGVGQEPGSHGGASSQLRQPSPGA		
MmBmp5	72	-----	KQASSAP	LEMLDLYNAMASEDNPEESEYLVRVSLAGEAKETRKGYPASPNGY	-----
MmBmp7	75	-----	KH-NSAP	MEMLDLYNAMAVEESGPDG	-----
CeDBL-1	68	-----	GPSIDVPEQH	MDIYDDNDVD	-----
MmBmp10	76	-----	TGRVDPPEY	MLELYNKFATDRT	-----
MmGdf2	79	-----	KTRAEP	PEYMLDLYNRYTTDKS	-----
CeTIG-2	64	-----	KANNYVSTYMKRLY	KOLENYEHGENHNEE-EVN	-----
MmGdnf	77	-----	TSDSNMEEDY	PEQEDDVMDFIQATIKRLKRSPDK	-----Q
DmDPP	244	-----	RSKIIIEPEPMKKLYAE	IMGHELD--SVNI	-----
MmBmp2	70	-----	KD-VVVP	PEYMLDLYRRHSQGPGA--PAPD	-----
MmBmp4	75	-----	KS-AVIE	PYMRDLYRLQSGEEEE--EEQS	-----Q
MmBmp15	59	-----	WPQGYPLRYMLKLY	HSAD-PHGHPRE	-----
MmGdf9	80	-----	QPSDRALYIMKKLY	KTYAT-KEGVKPK	-----
MmGdf1	54	-----	PVPP--VMWRL	ERRRDQEARVGRPL	-----
MmGDF3	47	-----	PVPR--VLRKI	IRAREA-AAASGASQ	-----
MmNodal	36	-----	PSSPSPLAYMLSLY	RDPLP-RA	-----
MmGdf5	158	-----	PPPITPHEYMLSLY	RTISD-ADRKGGNS	-----
MmGdf6	92	-----	GLRVVPHEYMLSTY	KTYYSI-AEKLGINA	-----
MmGdf7	79	-----	NGSVVPHHEMMSLY	RSLAG-RAPVAAA	-----
			end straitjacket--β1---	-β1'--	
DmSCW	89	---H---	KRSLDDILISNEDRQEIASCNS	ILTFSSRLKPE---QL---DNELD	
DmGBB	125	---	RRSADLEEDEGEQQKNFITDLDKRAIDES	DTIMIFLNKRHHNVDEL---RHEHG	
MmBmp8a	93	-----	QAHLGRAD	LVMSFVNIVERDRTLG---QEPHW	
MmBmp8b	93	-----	QPHLDRA	LVMSFVNIVERDRTLG---QEPHW	
MmBmp6	177	AHSLNRKSLAPGPGGGASPLTSAQDSAFLNAD	VMSEFVNIVEYDKEFSP---HQRHH		
MmBmp5	124	AHRLHLP--PRTPLTTQSPPLASLHDTNFLNAD	VMSEFVNIVERDKEFSP---QRRHY		
MmBmp7	100	-QGFSYP--YKAVFSTQGPPLASLQDSHFLTD	ADVMSEFVNIVEHDKFFH---PRYHH		
CeDBL-1	89	-----	WVRHMYPKEI	IDNEG--F-----	
MmBmp10	98	-----	SMPSAN	LIRSFKNEDLFSQPVT---F-NGLRK	
MmGdf2	101	-----	STPASN	LVRSFVEDAISTAAT---EDFPFQK	
CeTIG-2	96	-----	AWLSAD	RLVSHMAQEV---H--R-LDDGS	
MmGdnf	112	AAALPRR-----	ER-----		
DmDPP	271	---PKP---	GLLTKSANT	VRSFTHKDSKID-DR---F-PHHHR	
MmBmp2	96	---HRL---	ERASRANT	VRSFHHEEAVEELPE---M-SGKTA	
MmBmp4	102	GTGLEYP-----	ERPASRANT	VRSFHHEEHLNIPG--T-SESSA	
MmBmp15	85	-----	NRTIGAK	MVLVKPSANTVVRPPR-GSW---HV	
MmGdf9	106	-----	SRSHLYNT	VRLFSPCAQQEQAPS-NQVTGPLPM	
MmGdf1	78	--RPCHV-----	EELGVA	ENVIRHIPDGLSSRPAQPARTSGLCPE	
MmGDF3	70	--DLCYV-----	KELGVR	NLQLLPDQGFFLNTQKPF-QDGSCLQ	
MmNodal	57	-----	DIIRSLQAQDVD	-----VTGQN	
MmGdf5	185	---SV---	KLEAGLANT	ITSFIDKQDVRG---PAVRK	
MmGdf6	119	---SF---	FQSSKSANT	ITSFVDRGLDLSH---TPLRR	
MmGdf7	105	-----	SGHGRVDT	ITGFTDQATQETA---AAEPG	

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		β 10-	no- α 5-	
DmSCW	251	IVGYFNGPELLV	KIQKLRFKR	-----
DmGBB	302	MTGFERGPELIK	ATAHSSHRSKR	-----
MmBmp8a	245	MVTFFRASQSPV	RAPR	-----
MmBmp8b	245	MVGFFRANQSPV	RAPRTAR	-----
MmBmp6	356	MVAFKVKSEVHV	RTTR	-----
MmBmp5	301	MVAFKASEVLLR	SVR	-----
MmBmp7	276	MVAFKATEVHLR	SIR	-----
CeDBL-1	219	PLIVFSDLSEPSS	VRRK-R	-----
MmBmp10	252	LLVVFSDDQSN	DK--EQ-KEELNELITHEQDL	LDSDA---FF-SGPD--EEALLQMR
MmGdf2	252	FFVVFSDNDRS	NGTK-ET-RLELKEMIGHEQETMLV	KTNAYQVAGESQEEEGLDGY---
CeTIG-2	214	LVIALKDE	DAGPPKKRSRRSASTTPI	SAPPMRQKVKRSESAYFEK-PNENERCQ----
MmGdnf				-----
DmDPP	440	LLFTVTDDGRH	KA--RSIRDVSGGEGGGKGG	-----RNKR-----
MmBmp2	261	LLVTFGH	DGKGHP--LHKREKR	-----
MmBmp4	272	LLVTFGH	DGRGHT--LTRRRAKR	-----
MmBmp15	231	LLLYENDTDDR	VQGK-----L-----	-----LARGQEELTDR
MmGdf9	253	LLLYLNDTSTQ	AYHS-----W-----	-----QSLQSTW---RPLQHPGQAGVAAR
MmGdf1	220	LLVTLDPRL	CP-----	-----
MmGDF3	234	LLVVTLNPKH	CH-----	-----
MmNodal	198	LMLYSNRPQEQ	RQL-----GGATLLWEAESSW	---RAQE--GQL----
MmGdf5	335	LLVFGRTKKR	DLFFNE-----IKARSGQDDKT	VYEY-----
MmGdf6	280	LLVVFTR	SQRKN-LFTE-----MHEQLGSAEAAGAEGSW	---PAPS--GSP----
MmGdf7	263	LLVISSRTQR	KESLFRE-----IRAQARALRAA	---AE-----PPPD--PGP----

Fig. S7. Expanded BMP subfamily prodomain alignment indicating structural conservation.

Sequences from Fig. 8 including underlining presented as in Fig. S4.

		Association	-----a1-----	-----LatencyLasso-----	
MmBmp15	35				LADDP
MmGdf9	55				GDRSG
MmNodal	1				SAHSRLILQ
MmGdf5	92				PPRSGGPETKPGPSSQTR--QAAAR--TTFKGLGGKASSKAG
MmGdf7	50				ARAPGP--SALQA--AAVPG
MmGdf6	53				QRTPQESAEGR--TPEHGLRQKDRRRPFG
DmActivin-beta	314				SHKGCTLCHESGKPNYTKDNPHDYASDEVRLSHKROLTKGGLSH-KEN--VSHPL
CeTIG-3	1				MS
DmSCW	17				TTYVTT--N--NHIE--M--PIYQKRPLSEQMEYDIDIDLDG-RFR--RQAEF
DmGBB	40				GIYIDN--GKDQTIMH--R--VLSEDDKLDVSYELFEFGHAE-RPT--HLSSH
MmBmp8a	19				GGGHGP--RPPHTCPQ--R--RLGARERRDYQREHLAVGCLPG-RFR--PRAQP
MmBmp8b	19				GGGHLN--HPPHVFPQ--R--RLGVREPRDYQREHREVGLPG-RFR--SRAPV
MmBmp6	52				EQPPFQ--SSSSGFLY--R--RLKTHEKREYQREHLSVGLPH-RFR--PLHGL
MmBmp7	30				DFSLDN--EVHSSFIH--R--RLRSQERREYQREHLSIGLPH-RFR--PHLQG
MmBmp5	27				GGLDN--HVHSSFIY--R--RLRNHERREYQREHLSIGLPH-RFR--PFSFG
MmBmp3	4				ARGLLCLWLGYFCLNLAQGR-PNHLPLGLRETEES--DRATG
MmGdf10	17				MVPLLLLLRGAGCGHRGPSWSSLPSSAAGLQGRDS--QQSPG
DmMyoglianin	175				SRVQSVSLYRNTLINIESMLQRLREKAKVDSIESHKMHLMRNLKKL-PN--ITKP-
MmMstn	35				KEGLCNACAWRQ--NTRYRIEAKIKQLSKRLKETA-PN--ISKD-
MmGdf11	56				EPDGPFCVVRQ--HSRELRLSHKQQLSKRLKEA-PN--ISRE-
MmTgfb1	29				GLSTCKTID--MELVKRRRIEARGQLSKRLKASP-PS--QG-E-
MmTgfb2	20				SLSTCSTLD--MDQFMKRRIEARGQLSKRLKASP-PS--DY--
MmTgfb3	23				SLSTCTTLD--FGHIKKRVEARGQLSKRLKASP-PS--PS--
MmInha	21				CGG--PELV-R--ELVLAKVKAFLDALGPPAM-DG--EGGD-
MmGdf15	33				SQG--DALA-MP--EQRPSGPESQNA--DE--LR--
MmGdf1	22				TLA--PAP--ASMGPAAALQVGLPEA-RF--SV--
MmGDF3	20				GQ--TSEFQDSDLQFGLPEA-PS--P--
CeUNC-129	2				RRLPVILLV--F--SIANCAKVDVLDINETHRLDHFHSSDPN--VTSF-
CeDAF-7	30				CIEKMKQHR--TEYIKNEHLDQNMKE-APK--GLKP-
DmMaverick	249				DETRIKHLVLKGGGKK-LPD--MRKV-
MmInhba	44				PDCPSCALATL--PKDGPNSQPEMVEAKKHHLNMHKK-RED--VTQP-
MmInhbb	68				DTCTSCGGGG--PEELGRVDGDFLEAKKHHLNRQLRG-RFN--ITHA-
MmInhbc	39				GPCPCWGAIF--QRELLDLAKSHLDKHLKQ-RFI--LSRP-
MmInhbe	39				SACPCGGPTL--ERALVLELAKQQLLEGHLS-RFR--ITRP-
CeDBL-1	24				SAILHLFLIS--FTPMSAAADQHASHATRRGLRKGLDEH-VFV--Q-
MmGdf2	56				M--FLENKVDPLRSNLSG-IPS--Q-
MmBmp10	53				T--LLQSKNEFKTNLSD-IFV--Q-
CeTIG-2	42				DKGGEQRELFNHI-NEN--GP-
DmDawdle	226				SAGGCPKCESNRQ-VEHITE--EQLTH-LRIEFYKQHLKELKE-SPK--
MmLefty1	27				IL--GSELQQLDQ-PEV--LDKA-
MmLefty2	27				VL--SSELQQLDQ-ATF--LDSA-
MmAmh	191				RYLV--L--TVDFP--AGAWSGSGIL-TLQ--P-
MmGdnf	65				HSLSHRR-VFV--A-
DmDPP	223				LVEIE-KSLSLFNKKR-PEK--I-
MmBmp2	49				LSEFE-LRLSLMFGLKQ-RPT--P-
MmBmp4	54				LRDFE-ATLQMFGLRR-REQ--P-
MmBmp15	53				GKEMKQWPQGYPLRYLKLHRSADPHGHPRE-
MmGdf9	74				GETPKLQPDSTRALYYKKYKTYATKEGVKPK-
MmNodal	30				LWTRGPSSPSPLAYLSLYRDPLPRA--
MmGdf5	152				PKEPFRPPPIITPHEYLSTYRTLSADRRKGNS
MmGdf7	73				AGSGFRNGSVVPHFMSLYRSLAGRAPVAAA-
MmGdf6	89				PG--RGLRVVPEHYLSYKTYISIAEKLGINA
DmActivin-beta	515				MPIELKSHHNSSPKELKSGAVRKVNGINGTQMNEALNKKSTYPMHNHSDNKTHTGNG
CeTIG-3	3				TSRKHDVGGVL--
DmSCW	65				SKFLVYNEISEDQEPKEV--
DmGBB	93				PKFLDVVHRITAEGLSDQ--
MmBmp8a	73				PLFVLDYHAMTDDDDGGPP--
MmBmp8b	73				PLFVLDYRAMTDDSGGGTP--
MmBmp6	131				PLFVLDYNALSDDEEDGA--
MmBmp7	80				PMFLDYNAMAVEESGPDG--
MmBmp5	78				PLFVLDYNAMASEDNPEES--
MmBmp3	56				VSEHYLDYD-RYSGSSRVQAT--
MmGdf10	71				VAIHRLRYE-KYNRRG--
DmMyoglianin	235				NIDNRYRDYNASSKTTVM--
MmMstn	87				PLREHDDQVQRDSS-S-DGS
MmGdf11	107				PLQQLDHDHFGDALQP-EDF--
MmTgfb1	76				AVLAINSTRDRVAG-ESA--
MmTgfb2	66				EVSTYNSTRDLLQE-KAS--
MmTgfb3	68				QVLAUNSTRELLEE-MHG--
MmInha	63				RHAGGFMHRTSEPEEE-DVS--
MmGdf15	65				SRLHANQSRDSS-NSE--
MmGdf1	58				VWRFLRRRDPQEA-RVG--
MmGDF3	51				LRKIIRAREA-AA-ASG--
CeUNC-129	53				LTEHKNYENFIDEESN-EDG--
CeDAF-7	66				MKSVYELRDLEKDEQ-DMG--
DmMaverick	279				YSSKYHEYLSRLSNQEK-GNS--
MmInhba	79				PKAATNAIRKLHVGVG-ENG--
MmInhbb	103				PKAATNALRKLHAGKVR-EDG--
MmInhbc	68				SRGAKTALQRLRGPRRE-T--
MmInhbe	68				PQAAATRALRRLQPKSMV--
CeDBL-1	73				VPQHWDIQDDNDVDW--
MmGdf2	84				PQYVLDLNNRYTTDK--
MmBmp10	81				PPEYVLDLNNKFATDR--
CeTIG-2	65				ANN--
DmDawdle	276				LKPFDFGMTLSHPDST-KNK--
MmLefty1	53				IPSHORTQVALLQSHA--
MmLefty2	53				IPTHRSQVALLQSHA--
MmAmh	222				LSIDQ--AFLFGSDSR--
MmGdnf	82				MPEDYPDQDDVMDFIQA--
DmDPP	249				IPFPKKHAEIMGHELD--
MmBmp2	74				VPPYVLDLRRHSGQPGA--
MmBmp4	79				TPDYRDLRLQSGEEEE--

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			end straitjacket TGFβ--β1---	
MmBmp15	85	-----	-----	-----
MmGdf9	106	-----	-----	-----
MmNodal	57	-----	-----	-----
MmGdf5	185	SVK-----	-----	-----
MmGdf7	105	-----	-----	-----
MmGdf6	119	SFF-----	-----	-----
DmActivin-beta	575	EMSHN-D-----	YEYFNDYSVQTHDKNR-YHEGRSSSIGYPANHNI-EYENQ-KG----	-----
CeTIG-3	15	-----	-----	-----
DmSCW	85	-----	LHQR-----H-----KRSL-----	-----
DmGBB	113	-----	DEDDDYERGHRS-----RRSADLEEDEGE-----	-----
MmBmp8a	93	-----	-----	-----
MmBmp8b	93	-----	-----	-----
MmBmp6	151	-----	SEGVGQEPGSHGGASSSQLRQPSGAAHSLNRKSLLAGPGGG-----	-----
MmBmp7	100	-----	-----QGFSYP--YKAVFST-----	-----
MmBmp5	98	-----	EYLVVRVSLAGEAKETRKGPASPNGYAHLRLHP--PRTPLTT-----	-----
MmBmp3	77	R-----	TPGSQL-----PGP--QPLRGG-----NTVRSFRAAAAGTP--	-----
MmGdf10	87	-----	APPGGG-----NTVRSFRARLEMI-----	-----
DmMyoglianin	254	NRMESIDESHLSINDTYGDHIMTDFDESSSSQMQGDDA----	NTVNEFLIDLKNQ----	-----
MmMstn	107	-----	LEDDDY-----HATTETIITMPT-----	-----
MmGdf11	128	-----	LEEDEY-----HATTETVISMQAQ-----	-----
MmTgfb1	94	D-----	PEPEPEADY-----YAKEVTRVLMVDRN----	-----
MmTgfb2	84	R-----	RA-----AACERERSDEEY-----YAKEVYKIDMPSHL----	-----
MmTgfb3	86	E-----	RE-----EGCTQETSESEY-----YAKEIHKFDMIQGL----	-----
MmInha	83	Q-----	AILFPATGATCEDQP-AA-----RG--LAQE-----	-----
MmGdf15	81	-----	PSPDPAVRILSPEVRLGS-----HGQLLLRV-----	-----
MmGdf1	75	-----	RPLR-----PCHVEELGV-----AGNIVRHI-----	-----
MmGDF3	67	-----	ASQD-----LCYVKELGV-----RGNLLQLL-----	-----
CeUNC-129	74	NL-----	-----	-----
CeDAF-7	87	VEM-----	SFY-----TAKDP-----	-----
DmMaverick	300	YFN-----	NFMGASFTRDH----FLSITTNGF----NDISNKRRLHRRSLKKI	-----
MmInhba	100	YV-----	-----EIEDDIGRRA-----	-----
MmInhbb	124	RV-----	-----EIPHLDGHAS-----	-----
MmInhbc	87	-----	-----LLEH-----	-----
MmInhbe	86	-----	-----P-----	-----
CeDBL-1	90	-V-----	-----RHY-----	-----
MmGdf2	100	-----	-----	-----
MmBmp10	97	-----	-----	-----
CeTIG-2	68	YV-----	-----STYMKRLYQLENY	-----
DmDawdle	297	EL-----	-----DDYARTSKKFILL	-----
MmLefty1	71	-----	-----SRSG-----	-----
MmLefty2	71	-----	-----DRSG-----	-----
MmAmh	238	-----	-----CFTRMTPTLVVL	-----
MmGdnf	100	-----	-----TIKRLKRSPPKQ	-----
DmDPP	267	-----	-----SVNI-----	-----
MmBmp2	92	-----	-----PAPD-----	-----
MmBmp4	97	-----	-----EEQSQ	-----
			end straitjacket Activin+BMP--β1---	
MmBmp15	85	-----	NRTIGAKMRLVKPSANTVRPPRG-----S--W---H	-----
MmGdf9	106	-----	SRSHLYNTGRLSPCAQQEQAPSN-----Q---VTGPLP	-----
MmNodal	57	-----	DIHRSQAQDQD-----VTGQ	-----
MmGdf5	188	-----	LEAGLANHTSIDKGQDDR-----G-PAVR	-----
MmGdf7	105	-----	SGHGRVDTTGTDQATQDE-----TAAAEF	-----
MmGdf6	122	-----	QSSKSANTTSVDRGLDDL-----SHTPLR	-----
DmActivin-beta	621	---HHESFADDHENI--DHEDFFGNTQENITAEEGTQ-----	YRQYR-----	-----
CeTIG-3	15	-----	D-----KI--TLEPNRKSWTCLTPESLV	-----
DmSCW	94	---DDDILIS--N--EDRQEIASCNSLTSRRLKPE-----	QLDNELD-----	-----
DmGBB	137	---QKNFIT--D--LDKRAIDESDHTLNKRHHNV--DEL-RHEHG	-----	-----
MmBmp8a	93	-----	QHLGRADLMSVNMVERDR--TLGYQEPHW	-----
MmBmp8b	93	-----	QPHLRADLMSVNIIVERDR--TLGYQEPHW	-----
MmBmp6	193	---GASPLTS--A--QDSAFLNADMMMSVNLVEYDK--EFSPHQRHH	-----	-----
MmBmp7	113	---QGPLAS--L--QDSHFLTDADMMMSVNLVEHDK--EFFHPRYHH	-----	-----
MmBmp5	138	---QSPPLAS--L--HDTNFLNADMMMSVNLVERDK--DFSHQRRHY	-----	-----
MmBmp3	107	Q-----	T-----	-----
MmGdf10	106	D-----	Q-----	-----
DmMyoglianin	307	AKKSDIPINTNDEEYESILS----	HISSEYIPPEEIOPH--V--RHNK-----	-----
MmMstn	125	---ESDFLMQADGKP-----	K-----	-----
MmGdf11	146	---ETDPAVQTDGSP-----	L-----	-----
MmTgfb1	118	NAIYEK-----T-----	K-----	-----
MmTgfb2	113	PSETVCVVVTF-----	S-----	-----
MmTgfb3	115	AEHNELAVC--P-----	K-----	-----
MmInha	107	AEGLF-----	-----	-----
MmGdf15	107	NRASLS-----	-----	-----
MmGdf1	96	PDSGLS-----	-----	-----
MmGDF3	88	PDQGF-----	-----	-----
CeUNC-129	76	-----	RAIEPAV-----GK--FE--G-----	-----
CeDAF-7	98	-----	SYGE-----NPSQLAKQDVTNDLER-----	-----
DmMaverick	341	NRLNQNPKK--HQNYGDLLRGEQDTMNIHLHPLTNAQD--A-----	-----	-----
MmInhba	112	-----	E-MNELMEQTSEHITSAES-----G--T--A-----	-----
MmInhbb	136	-----	P-GADGQERVSEHITSAET-----DG-LAS--S-----	-----
MmInhbc	91	-----	DQRQEYEHISADT-----DL-SSI--N-----	-----
MmInhbe	87	-----	GN--REKHSATI-----ID-KSTSTY-----	-----
CeDBL-1	95	-----	-----PKEIIDNEGFLLS-----	-----
MmGdf2	100	-----	SSTPAS--NIRSRSSVEDAISTAATE-DFPFQ-----	-----
MmBmp10	97	-----	TSMPSA--NIRSRSKNEDLFSQPVTF--NGLR-----	-----
CeTIG-2	84	EHGE--N-----	H--NEEVNNAW--LS-----	-----
DmDawdle	313	NREE--V-----	ECNR-ARDGKS--NPSMCKTFKIDDADEG--FD-----	-----
MmLefty1	76	-----	-----KRSSQNLREVA-GRFLVSETS-----	-----
MmLefty2	76	-----	-----KRSSQNFREVA-GRFLMSETS-----	-----
MmAmh	250	PP-A--E--	PSPQ-PAHGQL--DT-MFPQPGLSLE-PE--ALPHS-----	-----
MmGdnf	112	AA-A--L--	PRRE-R-----	-----
DmDPP	271	-----	PKPG-LLTKSA--NTVRSRTHKDSKID-DR--FPHHH-----	-----
MmBmp2	96	-----	HRLE-RAASRA--NTVRSRHHEAVEELPE--MSGKT-----	-----
MmBmp4	102	GT-G--L--	EYPE-RPASRA--NTVRSRHHEEHLENIPG--TSESS-----	-----

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	begin	arm--β2----	----β3-----	TGF-β---α3--	TGF-β-β3-----
MmBmp15	112	VQTLDE-PLASNQVAYE	IRATVYRQHLHL-VNYHL	---SCHVETWVPKCRTH	----
MmGdf9	137	MVDLLE-NLDRVTAMEH	ILKSVLTYLTNNSASSSTV	---TCMCDLVV	----
MmNodal	73	NWTFTE-DFSFLSQEED	VWAEELRLQLPGMDIPT	EGPLTIDIFHQAKGD	-----
MmGdf5	213	KQRYVE-DISAL-EKDGL	LCAEELRLRKPKPLDVAK	PAVPSSGRVQKLKSSC	-----
MmGdf7	131	QGSFLD-DVSSLSEADE	VNAEELRLVLRSSPEPD	---RDSATLLPRLLSTC	-----
MmGdf6	148	RQKYLE-DVSTLSDKEE	VGAEELRLRQAPPTPW	---GLPARPLHLQ-LFPC	-----
DmActivin-beta	659	ILEFSAQNRRVPSQKLS	RSQAQIHRIKDPHSLWIEKAKSL	---PE-----KHLL	---N
CeTIG-3	36	KDCFQHSINSINHE	---LSASLTH	-----DP	-----
DmSCW	131	-MHITENTNDVPVD	-LSVQAMRLRYKQPSLVD	-----	-----
DmGBB	176	-RRLWSDVSNVPND	-NYVMAELRYQANEGKWL	-----	-----
MmBmp8a	123	-KEFHEDLTQIPAG	-EATTAEPRIYKEPSTHPL	-----	-----
MmBmp8b	123	-KEFHEDLTQIPAG	-EATTAEPRIYKEPSTHPL	-----	-----
MmBmp6	233	-KEFKENLSQIPEG	-EATTAEPRIYKDCVVGVSF	-----	-----
MmBmp7	153	-REFREDLSKIPEG	-EATTAEPRIYKDYIRERF	-----	-----
MmBmp5	178	-KEFREDLTQIPHG	-EATTAEPRIYKDKGNHRF	-----	-----
MmBmp3	109	KGLHTE-NLTSLTKESEN	LSATLYFVVGELVNI	---SLSCP-E--PQCSHHTQR	---
MmGdf10	108	KPVYFE-NLTSMDQSEM	LTAAEFHSEPPRPW	---RAREVFCKPRAKNASCRLLTPG	---
DmMyoglianin	348	VDVFRS-QIDSSYSDL	S---YATLHLYLRGWDWI	---SAHQPGLLIEIKKQP	---
MmMstn	138	CCFFKQ-SSKI	-----QYNKVVAQLWI	---YLRPVKT	---PTTVFVQILLR
MmGdf11	159	CCHFHQ-SPKV	-----MFTKVLKAQLWV	---YLRPVPR	---PATVYLQILLR
MmTgfb1	126	-----DISH	---SIY	---MFFNTSDIREAVPEPPLLSRAELR	---
MmTgfb2	126	GSLGSE-CSRQSQVLCGYL	DAIPPTTYRPFYRI	---VRFDVST	---MEKNASNLVKAEFR
MmTgfb3	126	-----	---GITSKV	---FRFNVSS	---VEKNGTNLFAEFR
MmInha	113	--TYVE-RPSQHIRSHQ	---MT	---SAQLWF	---HTG-LGRKS
MmGdf15	113	--QGL---PEAYRVHRALL	LLTP---TARFWD	---ITRPLKRALS	---LRGPAPALRLR
MmGdf1	102	--SRP---AQPARTSG	-----LCPEWT	---VVFDSLNVEP	---TERPTRARLELR
MmGDF3	94	--LNT---QKPF-QDG	-----SCLQKV	---LYFNLSAIKE	---KAKLTMAQLTLTD
CeUNC-129	89	QEVLVG-DVEGFDSHES	MRRELHFLRRRDSFARRSRQIRAKSV	-----	-----
CeDAF-7	119	-----SDILCATL	THSIEIP	---A---KDSG	-----
DmMaverick	379	-----NFHDKHDEANVR	MLLYSSSLATNFRRGPGSRKN	---KISQISGNDN	---
MmInhba	133	RKTLHEISKEGSDLSV	VERAEVWLKVP	---KAN---R---T---R	-----
MmInhbb	160	RVRLYEFVSNEGNQNL	FVCAEWLKLKLL	---PYVLEKG	---S---R
MmInhbc	112	QTRLESHFSGRMASGME	VRQTRFMFVQFP	---HNATQT	-----
MmInhbe	107	RSMLTQLSPLWSHH	---LYHAR	---LWLHVP	---PSFPGT
CeDBL-1	109	-YNL--SLAARNAHNEE	TKATLKLRLRRN	---NKARRS	-----
MmGdf2	129	KHILIS--NISIPRHEQ	TRAEELRLVW	---S---CQNDVD	-----
MmBmp10	125	KYPLIE--NVSIPHHEE	VMAELRLHT	---L---VQRDRM	-----
CeTIG-2	100	ADRIVSHMAQEVSHRL	DDGSYSIRFAK	---E---HVPKEGQSIV	---R
DmDawdle	347	-----	---MSTAVWLEK	---N---KQNRDTASVN	---S
MmLefty1	96	THLLVGEQRLPPNSEI	VCAVRLRQ	---E---FVPRTA	---LRR
MmLefty2	96	THLLVGEQRLPPNSEI	VCAVRLRQ	---E---FVPRTA	---LRR
MmAmh	284	ADPFLE-TLTRLVR	-ALRGPLTQASN	-T---QLALDPGALAS	-F-----PQ
MmGdnf					
DmDPP	302	RFRLEH-DVKSIPADEK	KAAEELQTR	-D---ALSQQVVASRS	-S-----AN
MmBmp2	128	ARRFFE-NLSSVPSDEF	TSAEELRIR	-E---QIQEALGNSSF	-Q-----HR
MmBmp4	138	AFRFLD-NLSSIPENEV	SSAEELRLR	-E---QVDQGPDWEQG	-F-----HR
		Activin+BMP-α3	--β4----		
MmBmp15	162	-----	---LPS	-----SKSGSSKP	---
MmGdf9	181	-----	---KEA	-----MSSGRAPP	---
MmNodal	122	-----	---	---PERDPADCLE	---
MmGdf5	263	-----	---	---PSGRQPAALLD	---
MmGdf7	179	-----	---	---PDEAGTAHLH	---
MmGdf6	195	-----	---	---LS	---PLLLD
DmActivin-beta	707	--TK-----RKWGA	NKPHHRIKMTFQLSTSIN	---I---T---EKGIDKAI	---
CeTIG-3	60	-----	---KDTNISVVEVDE	---L---FG	---ELQ
DmSCW	162	-----	---RRANFTVSRKLD	---N---RQ	---DFSYR
DmGBB	210	-----	---ANREFTITVAIGT	---G---TLGQH-TME	---
MmBmp8a	155	-----	---NTTLHHSMEVVQ	---E---HSNRESDLF	---
MmBmp8b	155	-----	---NTTLHHSMEVVQ	---E---HSNRESDLF	---
MmBmp6	265	-----	---KNQTFLESYQVLQ	---E---HQHRDSDLF	---
MmBmp7	185	-----	---DNETFQITVQVLQ	---E---HSGRESDLF	---
MmBmp5	210	-----	---ENETIKSSEIPIK	---E---YTNRDADLF	---
MmBmp3	157	-----	---QHIQIDSAAILKS	---	---NQSQLLG
MmGdf10	162	-----	---LPARLHIFRSLS	---	---QNTATQG
DmMyoglianin	393	--RK-----DIVVTI	HRAIRANNT	---	---SFNPKVKMF
MmMstn	177	LIKPMKD	-----	---	---GTRYT
MmGdf11	198	LKPLTGEGTAGGG	-----	---	---GGGRRHI
MmTgfb1	157	LQRL-----KS	---SVEQHMEVYQYS	-----	---NNSWRYL
MmTgfb2	179	VFRL-----QNP	K---ARVAEQRELYQILKSK	-----D	---LTSPTQRYI
MmTgfb3	153	VLRV-----PNPS	---SKRTEQRDELQILRPD	-----E	---H-IAKQRYI
MmInha	149	SAPLLDLLVLSGG	PMAVPVS LGQGPRAVLH	---	---LAASAFP
MmGdf15	159	LTPPPDLAMLPSGGT	QLELRLRVAAGRGR	---	---
MmGdf1	141	LEAESE---DTGGWEL	---SVALWADAE	---	---HPGPELL
MmGDF3	132	LGPRSY---YNLRPELV	VALSVQDRGVGRSH	---	---PKVGRLL
CeUNC-129	134	-----	---CNEYCR	-----	---
CeDAF-7	139	-----	---MLQDVQVQTEKNEDG	---SMGEMVTSG	---IFATKGSER
DmMaverick	424	IERHCNFGDVNLN	---QSNKNSSQLTETKQQLLSAN	---	---RRR
MmInhba	169	-----	---TKVTIRLHQQKHFPQGLD	TGDEAEEMGLKGRSEL	---
MmInhbb	199	-----	---RKVRVQVQFE	---	---QGHGDRW
MmInhbc	148	-----	---MNRRLVLRP	---	---YDTNLT
MmInhbe	139	-----	---LYRDERCGT	---	---TRCRGF
CeDBL-1	142	-----	---GNISSEYFF	---	---EDDINNDRF
MmGdf2	161	-----	---STHGLEGSVVVDVLEDS	---ET	---WDQATGTKT
MmBmp10	157	-----	---MYDGVDRKTHSEVLESA	---DG	---SEERSM-L
CeTIG-2	140	-----	---AQLRHQHGIVSPV	---FF	---Y---IEDTNL
DmDawdle	371	-----	---SAQQTIVSEV	---E	---VDQQKDSKY
MmLefty1	136	L-----	---SPHSARARVTH	---EWL	---RF---RDDGSNRTA
MmLefty2	136	L-----	---SPHSARARVTH	---EWL	---RV---REDGSNRTA
MmAmh	323	-----	---GLNLSDPALG	---RL	---LDWEEPILL
MmGdnf					
DmDPP	343	-----	---RTRYQNLWDITRVG	---VR	---GQREPSYL
MmBmp2	169	-----	---DNDEIIPKA	---AA	---NL-KFPVTR
MmBmp4	179	-----	---DNDEIIPKA	---AE	---MVPGHLLTR

Fig. S8 Page 3

		-----β5-----	-----β6-----	-----α4-----	-----β7-----	TGFβ-β8
MmBmp15	173	-----SPMSKAMT-EIDTTHCI	-----CQKLWNRKGRSVPRFRM	-----CQK		
MmGdf9	192	-----RAP-----YSFTLKKHRAI-EIDTSL	-----QPLVTSSERSIHSNFT	-----CTK		
MmNodal	132	RIMETFTVI-----PSQVTFASGST-VLNAIK	-----PLSKWLKDPAEKEQVSSRAEK	-----NH		
MmGdf5	274	V-----RSV-----PGL-----DGSQME-VSDWKLF-RM	-----KNSAC	-----EAW		
MmGdf7	190	S-----RAA-----EPLG-----GARME-ADVTDAI	-----QSHRRWPASRKFV	-----RAVT		
MmGdf6	202	A-----RTL-----DPGPTQAGME-VSDWQGG-RP	-----QPKQ	-----RAAMG		
DmActivin-beta	744	-----FRASF-----QVDPKNLGMQ-KSDTDTI	-----RENYGH-TSHEKRL	-----IDCTGCCG		
CeTIG-3	80	-----YDRF-----EI-RETLDKY-HSDSHLF	-----HKMKQ-KSSDKMKI	-----EITNS		
DmSCW	184	-----IGSV-----NTSSQRGM-EIDTDTI	-----RYALHN-KGLQRNEL	-----RIS		
DmGBB	233	-----PSSV-----NTGDYVGM-ELNTEG	-----HEALVK-SKDNHG	-----GAHAV		
MmBmp8a	178	-----FDLQ-----TLRSQDEGM-VLDTAAS	-----DRLLN-HHKD	-----YVET		
MmBmp8b	178	-----FDLQ-----TLRSQDEGM-VLDTAAS	-----DRLLN-HHKD	-----YVET		
MmBmp6	289	-----LSDR-----VWASEEGM-EEDTATS	-----NLAVVT-PQHN	-----SVET		
MmBmp7	209	-----LSDR-----TIWASEEGM-VSDTATS	-----NRAVNV-PRNN	-----SVET		
MmBmp5	234	-----LSDR-----KTQALDVM-VSDTATS	-----NRAVIN-PQNN	-----CAET		
MmBmp3	178	-----HSDVD-----VRPYRDSVM-SKDTQL	-----RKAKQN-EFLGNIT	-----SRAHE		
MmGdf10	182	-----LARGAM-----ALTPPPRLGM-ANDSII	-----KAARRD-GELL	-----TGKED		
DmMyoglianin	420	-----EFR-----HSIPSGLGQV-AVDKSL	-----GNLGSN-----TCEIL	-----TKGE		
MmMstn	189	-----GIRSLK-----LDMSPGTGMQ-SIDKTV	-----QNALKQ-PESN	-----ALDEN		
MmGdf11	218	-----RIRSLK-----IELHSRSGHM-SIDKQV	-----HSMFRQ-PQSNW	-----AFDPS		
MmTgfb1	183	-----G-----NR-----LLTPTDTPM-SDDTVGV	-----RQNLQ-GDGIQGFRESAHCDSK			
MmTgfb2	214	-----D-----SK-----VVKTRAEGEM-SDDTDV	-----QRLHH-KDRNGFKISLHCPCTF			
MmTgfb3	187	-----G-----GK-----NLPTRGTAEM-SDDTDV	-----RQALLR-RESN	-----IHCPCTF		
MmInha	189	-----L-----L-----				
MmGdf15		-----				
MmGdf1	170	-----RVPPPGVLL-RAL	-----LGTA-VAANAS--VPCT	-----RAL		
MmGDF3	169	-----F-----LR-----SVPGPQQL	-----CQNLQGA-KDSSN	-----RLKND	-----HLE	-----ILVKE
CeUNC-129	141	-----QOTLKIRVG-----GDNLEEKVIA	-----PDKSFDSDHDA-KQAVFR	-----R		
CeDAF-7	173	-----ISILPI-----	-----DTVKSMTISPIOGIFVKAMLDG	-----RN	-----TAH	-----PQQT
DmMaverick	461	-----KITSRKIEFGNVGFQETRTQMI	-----EEDTKAM-RSLN	-----SHEN	-----GIE	-----IQCDKCKS
MmInhba	205	-----LSEKVVVD-----A-----RKSTM	-----IPSSSS-QRLLDQ-GKSSD	-----DAR	-----IACQCOE	
MmInhbb	217	-----NVEKKVD-----L-----KRSQAH	-----TTPTEAL-QALFER-GERRND	-----VCCSCCOE		
MmInhbc	164	-----LTSQVVVQ-----V-----NASQNY	-----QLLQPEA-QAACSQ-GHLT	-----E		-----VPES
MmInhbe	155	-----RTFLAEHQ-----T-----TSSGM	-----ALTPSSG-LRSEDS-GVVKQ	-----E		-----FRPLD
CeDBL-1	159	-----CESRSV-----DNLTETI	-----DQTAAF-LRRTNR-ISFF	-----D	-----PED	-----VEIEE
MmGdf2	190	-----F-----VS-----QDI-----RDEGM	-----TLVSSAN-KRAVRA-DSTTNK	-----N	-----K	-----LEVIV
MmBmp10	185	-----V-----VS-----TEIYGTNSEM	-----TDDTAT-RRQKS-GPSTHO	-----E	-----I	-----HIES
CeTIG-2	163	-----PGDVTLV-----SDPTVVTD	-----TMM-DRASHL-QLST	-----P	-----V	-----TAR-A
DmDawdle	392	-----LSAAKTIA-----IQSVNVQDEM	-----KIDHEWFI-KHISG-HELSHL	-----Q	-----I	-----ITCGGCOV
MmLefty1	162	-----LSDRLVS-----I-----H-ESGAK	-----ADTTEAL-NPQOL-SRPROP	-----L	-----L	-----QVSV
MmLefty2	162	-----LSDRLVS-----I-----H-ESGAK	-----ADTTEAL-NPQOL-SRPROP	-----L	-----L	-----QVSV
MmAmh	346	-----LSPAA-----	-----ATEREPMLHGPA-AFAAG-LQRR	-----A	-----E	-----LQAAA
MmGdnf		-----				
DmDPP	368	-----LSDTKTVR-----L-----N-STDIV	-----SLOTPAN-DRMLAS-PQNYG	-----L	-----E	-----VEV
MmBmp2	189	-----LSDTRLVN-----Q-----N-TSCME	-----SDDTPAN-MRATTQ-GHTNHGF	-----V	-----E	-----VEV
MmBmp4	200	-----LSDTRLVH-----H-----N-VTRME	-----TQVSPAN-LRRTRE-KQPNYG	-----A	-----E	-----LEV
only TGFβ-β8---bowtie---only TGFβ-β9----- BMP only -β9'-						
MmBmp15	210	QKG-----	-----NET-----REFRWH	-----G		
MmGdf9	235	DQV-----	-----PED-----GVFSMP			
MmNodal	184	Q-----	-----PYTPPVV			
MmGdf5	312	-----	-----RGRAVDLRGLGFERT	-----A		
MmGdf7	232	-----	-----ASESSPLALRRLGFGWP	-----GGG		
MmGdf6	242	ELDAGD---TGAR-----	-----ARGPQQPPPLDLRSLGFGRR	-----V		
DmActivin-beta	787	-----	-----RYSL-----HLFQTS-KLRGN	-----SSDY		
CeTIG-3	122	-----N-----	-----TONV-----IN-ALS-VL-R			
DmSCW	225	-----IG-----	-----DSQL-----STFAAG-LVTP	-----Q		
DmGBB	276	-----NRP-----	-----DREV-----KLDDIG-LIHR	-----Q		
MmBmp8a	220	-----AD-----	-----GHSN-----DPGLAG-LLGR	-----Q		
MmBmp8b	220	-----ED-----	-----GHSI-----DPGLAG-LLGR	-----Q		
MmBmp6	331	-----RD-----	-----GLHV-----NPRAAG-LVGR	-----D		
MmBmp7	251	-----LD-----	-----GQSI-----NPKLAG-LIGR	-----H		
MmBmp5	276	-----GD-----	-----GRSI-----NVKSAG-LVGR	-----H		
MmBmp3	224	-----LPKRMFLFFPEPYILVYANDAAISEPESVVS	-----LQRH-RDFTAG-TG	-----PR		
MmGdf10	228	-----PGVPRPSSHMPYILVYANDLAISEPNSVAVSLQRY	-----DPFPAG-DFEPGA	-----APN		
DmMyoglianin	459	-----TW-----	-----MKSLVTTDNT			
MmMstn	235	-----GHD-----	-----LAVTFPGP			
MmGdf11	264	-----GTD-----	-----LAVTSLGP			
MmTgfb1	226	-----DNK-----	-----LHVEING---I-SPKRRG-DLGTI	-----H		
MmTgfb2	257	-----VPSNNYIIPNKS-----EELERFAGIDGT	-----STYASG-DQKTIK	-----STR		
MmTgfb3	230	-----QPNGD-IENVH-----	-----EVMEIKFKGVND-DHGRG-DLGRK			
MmInha	191	-----				
MmGdf15		-----				
MmGdf1	203	-----	-----SLHPG-ATAACG	-----R		
MmGDF3	210	-----DRY-----	-----SRVTQ-PENPCD	-----R		
CeUNC-129	186	-----EH-----	-----SKMRPY-----	-----A		
CeDAF-7	214	-----ADV-----	-----DNMLQ			
DmMaverick	510	-----	-----IGARIL-----SDFSPT-P-FRST	-----ASS		
MmInhba	247	-----	-----SGASLV-----LLGKK-K-KKEVDG-DGKKKDGSDGGL	-----EE		
MmInhbb	259	-----	-----LAVVPV-----FVD			
MmInhbc	204	-----QVA-----	-----	-----HSSL-I		
MmInhbe	197	-----LNS-----	-----TAAG-----	-----LPRL	-----L	
CeDBL-1	202	-----TQSSSL-----	-----SSLPYA-----			
MmGdf2	230	-----Q-----	-----SHRES-----CDT	-----L	-----DISV	
MmBmp10	227	-----RQN-----	-----QAEDTG-----RGQ	-----LEIDM		
CeTIG-2	203	-----S-----	-----	-----T		
DmDawdle	438	-----	-----SDMEEI-----	-----I		
MmLefty1	204	-----QRE-----	-----HLGPGT-----WSS	-----HK	-----LVR	
MmLefty2	204	-----QRE-----	-----HLGPGT-----WSA	-----HK	-----LVR	
MmAmh	385	-----SEL-----	-----RDLPLG-----PPTA-P-PL	-----LARLLALCPNDSR		
MmGdnf		-----				
DmDPP	408	-----RTV-----	-----RSLKPA-----PHH	-----HVRLRRSADAE	-----H	
MmBmp2	229	-----AHL-----	-----EENPGV-----SKR	-----HVRISRSLHQD	-----E	
MmBmp4	240	-----THL-----	-----HQTRTH-----CQ	-----HVRISRSLPQ	-----S	

Fig. S8 Page 4

		--β10--	---α5-TGFβ only			
MmBmp15	223	-MTSLDVAF	LYFNDTDDR	-----QCK-L-----		
MmGdf9	247	---LSVFE	SLIYLNDS	TQA-----YHS-W-----QS-L-----Q-S		
MmNodal	193	---ASTNV	MLMYSNR	PQEQR-----QL-----GGAT-LLWE-A-----E-S		
MmGdf5	328	--RQVHEKA	LVFGR	TKKRD-----LFFNEI	ARSQD-DKT	V--Y-----E-Y
MmGdf7	254	GGTAAEER	ALV	ISSRTQKE-----SLFREI	SAARAL-RAA	-----
MmGdf6	273	--RPPQER	ALV	VFTRSQRKN-----LFTEM	EEQLGSA-EAAG-A	-----E-G
DmActivin-beta	809	LSTNPNR	ELV	VHTES-----SRTR	VR-----	
CeTIG-3						
DmSCW	242	ASRTSLE	EFV	GYFNGPELLV-----KIQKLR	FKR-----	
DmGBB	294	V-DDEF	CFE	VGFFRGPELIK-----ATAHSS	HRSKR-----	
MmBmp8a	237	A-PRSR	CFE	VWTFFRASQSPV-----RAPR-----		
MmBmp8b	237	A-PRSR	CFE	VWTFFRANQSPV-----RAPRTA	-----	
MmBmp6	348	G-PYDK	QCFE	VAFFKVSEVHV-----RTTR-----		
MmBmp7	268	G-PQNK	QCFE	VAFFKATEVHL-----RSIR-----		
MmBmp5	293	G-PQSK	QCFE	VAFFKASEVLL-----RSVR-----		
MmBmp3	269	L--DSHV	R-----	E-----ALSVER	KKR-----	
MmGdf10	278	SSADPR	VR-----	R-----AAQVSK	PLQDNELPGLDE-RPAPALHAQNFH	
DmMyoglianin	472	---SKNEL	TWH	IEIG-----SQKKHR	KKR-----	
MmMstn	246	-GEDGL	NFE	LEKVTD-----TPKRSR	-----	
MmGdf11	275	-GAEGL	HFE	LEVRLE-----NTKRSR	-----	
MmTgfb1	252	--DMNR	FE	LMATPLERAQ-----HLHSSR	RR-----	
MmTgfb2	300	KKTSGK	TFE	LMMLPSYRLE-----SQSSSR	KKR-----	
MmTgfb3	269	KQKDH	NFE	LMMPHRLD-----SPFGSQ	RKR-----	
MmInha	191	---THE	LV	VLLRCLCS-----CSG	PETTP-----	
MmGdf15						
MmGdf1	215	L---AEAS	HL	LVTLDPRLCP-----LPRLRR	HRTE-----	
MmGDF3	226	LLRSL	HASL	LVVTLNPKHCH-----PSS	KKR-----	
CeUNC-129	195	EMIRK	STF	FLVYSKVNHTLDTVSVMKQTEQTKRK	RDLGNE-ELREYYNYSIPLDND	
CeDAF-7	223	-----LSTR	-----	-----PKGSRKR	-----	
DmMaverick	534	DEHLN	LMF	VNIIGHGT-----LNSQH	-----GDA-D---IH--QIMLTNNR	
MmInhba	282	EKEQSH	RFE	LMQARQS-----EDHPHR	RR-----	
MmInhbb	271	PGEESH	RFE	VVQARLG-----DSRHR	IR-----	
MmInhbc	212	LGWF	SHR	FEVAAQVRVE-----GKHR	VR-----	
MmInhbe	210	DTAGQ	RFE	LEKIRAN-----EPGAGR	RR-----	
CeDBL-1	214	--RAQS	AFL	LVFSDLSE-----PSSVRR	KK-----	
MmGdf2	244	PPGSK	NIF	FFVVFSSNDR-----SNGTKET	LELKE---MI-GHEQETMLVKTA	
MmBmp10	244	SAQNKH	FE	LVFSSDDQ-----SNDK-EQ	EEELNE---LI-THEQDLDLSDA	
CeTIG-2	205	NDELK	IEA	PLVALKDE-----DAGPPK	KSRRSAS-TTPI-SAPPMRQKVKRS	
DmDawdle	448	SVDKDY	RFE	LVDMQNR-----RR-----		
MmLefty1						
MmLefty2						
MmAmh	414	SSGDPL	RAL	LVKALQG-----LRAEWH	-----GRE-G---R-----	
MmGdnf						
DmDPP	432	ERWQH	KCFE	LVFTYTDG-----RHKARS	IVDSGGE-G---G-----	
MmBmp2	253	HSWSQ	IRF	LVTFGHDG-----KGHP	LHKR	
MmBmp4	264	GDWAQ	LFE	LVTFGHDG-----RGHT	LTR	

Fig. S8. Expanded All family members prodomain alignment indicating structural conservation.

Sequences from Fig. 10 including underlining from Figs. 2, 4, 6, 8 and 10 are presented as in Fig. S4. Note that on the top half of Fig. S8 Page 1 there is an exception to the presentation of accurate numbering (shown by a double backslash). We removed a completely nonconserved stretch of 25 residues from Activin for efficiency of presentation. This allowed the unexpectedly conserved cysteines in the Association-region of ten proteins to be displayed near the structural features of the straightjacket. In the Association region unexpected cysteines conservation is underlined in red with known cysteines in TGF-β1-3 underlined in black. Accurate numbering for Activin resumes with the next alignment set below. All other numbering is accurate throughout. Also note that in the top half of Fig. S8 Page 4, the dimerization region β8 displays unexpectedly conserved cysteines in eight proteins underlined in red. Known β8 region cysteines in TGF-β1-3 are underlined in black. The features of TGF-β1 not conserved are α3, β5, β9 and α5. Features of BMP9 that are not conserved are β5 and β9’.