

Supplemental Table 1 Model organism <i>ETS</i> genes			
<i>C. elegans</i> gene ^a (References)	Other name	Subfamily	Protein(s)
ast-1 (neural fate; axon guidance) (1)	T08H4.3	ERG	CE19576, AST-1
ets-5	C42D8.4	ERG	CE04205, ETS-5
lin-1 (vulval cell fate) (2-4)	C37F5.1	TCF	CE31440; LIN-1
ets-4 (intestine, seam cells) (5)	F22A3.1	SPDEF ^b	CE34001, CE41797, ETS-4
C24A1.2 (n.d.)		ELF	CE27722, CE38587
F19F10.5 (n.d.)		Unknown ^c	CE43542
C33A11.4 (n.d.)	tag97	ESE	CE31678
C50A2.4 (n.d.)		Unknown ^c	CE17582
C52B9.2 (n.d.)		Unknown ^c	CE04253, CE30261
F19F10.1 (n.d.)		Unknown ^c	CE09481
<i>D. melanogaster</i> gene ^d	Flybase symbol	Subfamily	Protein(s)
Pointed (nervous system; oogenesis; eye development) (6-8)	pnt	ETS	D-ETS-2, ETS2, Ets58AB, Pnt-P2
ETS at 65A (n.d.)	Ets65A	ERG	D-ETS-3, ETS3
ETS at 21 (n.d.)	Ets21C	ERG	LP04687p, D-ETS-6, ETS-6
Ets at 96B (n.d.)	Ets96B	n.d. ^e	
ETS at 97D (female germline)	Ets97D	GABPA ^b	D-elg, Elg
Ecdysone-induced protein 74EF (salivary gland) (9)	Eip74EF	ELF	Eip74EF
Anterior open (nervous system; eye development; hemocyte) (10-13)	aop	TEL	Yan, Pok
Ets at 98B (n.d.)	Ets98B	SPDEF ^b	FI03841p, MIP16944p, D-ETS-4, ETS-4

^aAll *C. elegans* gene/protein names from <http://www.wormbase.org>. Additional genetic studies and phenotypic information can be found at this site and reviewed (14). Tissue characterized phenotypes in italics. No phenotypic information (n.d.). Subfamily (Figure 2) and (5).

^bAligns closest to single gene, not a subfamily.

^cNo apparent vertebrate ortholog, but clustered on dendrogram as a *C. elegans* subfamily.

^d*Drosophila melanogaster* gene/protein names from <http://flybase.org>. Additional genetic studies and phenotypic information can be found at this site and reviewed (15). Tissue characterized phenotypes in italics. No phenotypic information (n.d.). Subfamily (Figure 2) and assigned as in (16).

^eNot determined.

Supplemental Table 2 Structurally characterized ETS domains ^a				
Family member^b	Protein Data Bank file^c	DNA	Protein partner	Comments
FLI1	1fli			First reported ETS domain structure (17)
SPI1 (PU.1)	1pue	AAAAAGG <u>GGAA</u> GTGGG		First reported ETS domain / DNA complex structure. Defined <u>GGA</u> recognition by conserved R232 and R235 in H3 (18)
SPI1 (PU.1)	none	AATAAA <u>GGAA</u> GTGAAACCAA (λB element of immunoglobulin light chain λ enhancer)	IRF4	Cooperativity due to direct protein-protein interactions and DNA conformational changes (19)
SPDEF (PDEF)	1yo5	TAGCAG <u>GGAT</u> GTGT (prostate specific antigen promoter)		Preference for <u>GGAT</u> set by non-conserved S308 and Q311 in H3. Wing R326 makes water-mediated h-bonds to minor groove bp (20)
ELF3	3jtg	CAAACAG <u>GGAA</u> ACTCCT (B-site type II TGF-beta receptor promoter)		Wing R349 h-bonds to minor groove basepairs of flanking A site. Flanking, ordered C-terminal coil region contacts ETS domain (21)
GABPA (GABPα)	1awc	AATGACCC <u>GGAA</u> GTACACCGGA	GABPB1 ankyrin repeats	Ankyrin repeats of GABPB1 bind H1/H4/H5 of GABPA ETS domain, indirectly enhancing DNA affinity (22)
ELK1	1dux	TGACCC <u>GGAA</u> GTGT (E74 promoter)		Distal, non-conserved residues alter position of Tyr in H3 to establish the differential affinity of ELK1 and ELK4 for the same promoter (23)
ELK4 (SAP1)	1bc8	TACCC <u>GGAA</u> GT (E74 promoter)		Promoter discrimination due to conserved and non-conserved protein residues, as well as sequence-dependent DNA structure (24)
ELK4 (SAP1)	1bc7	GACAG <u>GGAT</u> GTG (c-fos serum response element)		(24)
ELK4 (SAP1)	1hbx	CACACCC <u>GGAA</u> GTCCATATTAGGC CAT (c-fos serum response element)	SRF MADS domain	ELK4 B-box sequence binds as 3 ₁₀ -helix/beta-strand/3 ₁₀ -helix to MADS domain upon cooperative ternary complex formation. Direct contact of recognition helices also occurs (25)
ELK4 (SAP1)	1k6o	CACAG <u>GGAT</u> GTCCATATTAGGACA (c-fos serum response element)	SRF MADS domain	As similar complex as 1hbx, except lacking the B-box (26)
ETS1	1r36			Autoinhibited ETS-1 ETS domain with HI-1/HI-2/H4/H5 folded. Defines the structural bases for an allosteric inhibitory mechanism (27)
ETS1	1md0 1gvj			Domain swapped dimer of autoinhibited ETS1 (28)
ETS1	2stt	TCGAGCC <u>GGAA</u> GTTCGA		Uninhibited ETS1 ETS domain (without HI-1/HI-2/H4/H5) bound to GGAA (29)
ETS1	1k79	TAGTGCC <u>GGAA</u> ATGT		Comparing uninhibited ETS1 ETS domain (without HI-1/HI-2) bound to high-affinity GGAA and low-affinity GGAG helps delineate specificity (30)

ETS1	1k7a	TAGTGCC GGAG ATGT		(30)
ETS1	1k78	TTGTGCC GGAG ATGGGCTCCAGT GGCC (mb-1 promoter)	PAX5 paired domain	Uninhibited ETS1 ETS domain (without HI-1/HI-2), PAX5 paired domain complex. Gln22 in β -hairpin of PAX5 alters ETS1 affinity for an otherwise sub-optimal GGAG site by repositioning Tyr395 of H3 (30)
ETS1	1mdm	TTGCC GGAG ATGGGCTCCAGTGG CCT (mb-1 promoter)	PAX5 paired domain	Autoinhibited ETS1 ETS domain, PAX5 paired domain complex. HI-1 is unfolded and distal to PAX5 (28)
ETS1	2nny	TAGAC AGGA AGCACT TCCT GGAG (stromelysin-1 promoter)	ETS1 ETS domain	Autoinhibited ETS1 ETS domain (HI-1 unfolded) dimer bound to tandem DNA site. ETS1/ ETS1 contacts involve residues in the HI-2/H1 loop and the H2-H3 turn (31)
ETV6 (TEL)	2dao			Autoinhibited ETV6 ETS domain. Although not published, structural elements were investigated for role in autoinhibition of DNA binding (32)
ELF5	1wwx			

^aIncludes all Protein Data Bank files that are publicly available along with publication reference.

^bName in parenthesis below entry is a common alternative, often the one used in the Protein Data Bank file.

^cThe Protein Data Bank files are from <http://www.pdb.org/pdb/home/home.do>

Supplemental Table 3 Structurally characterized PNT domains ^a			
Family member^b	Protein Data Bank file^c	Protein partner	Comments
ETV6 (TEL)	1ji7	ETV6	Core SAM/PNT domain of ETV6, formed by helices H2-H5, polymerizes. Soluble monomers due to A93D or V112E mutations (33)
ETV6 (TEL)	1lky	ETV6	Structure with an ETV6 wild type dimer interface (34)
ETV6 (TEL)	2qb1	ETV6	Engineered tandem dimer for pH-dependent polymer driven crystallization (35)
Yan	1sv4	Yan	<i>Drosophila</i> Yan Monomeric SAM/PNT domain with A86R mutation (36)
Yan	1sv0	Mae	<i>Drosophila</i> Mae/Yan heterodimer forms preferentially to the Yan homopolymer (36)
ERG	1sxe		Monomeric PNT domain (core H2-H5) (37)
FLI1	2ytu 1x66		Monomeric PNT domain (core H2-H5) (37)
ELF3	2e8p		Monomeric domain (core H2-H5) (37)
SPDEF (PDEF)	2dkx		Helix H1 appended to core PNT domain (H2-H5) (37)
GABPA (GABP α)	1sxd		Helix H1 appended to core PNT domain (H2-H5) (37)
ETS1	2jv3		Dynamic helices (H0/H1) appended to core SAM/PNT domain. Serves as docking domain for ERK2 and to bind the TAZ1 domain of CBP (38)
ETS1	2kmd		Phosphorylation of T38/S41 displaces dynamic helix H0 and increases affinity for the TAZ1 domain of CBP (38)

^aIncludes all Protein Data Bank files that are publicly available along with publication reference.

^bName in parenthesis below entry is a common alternative, often the one used in the Protein Data Bank file.

^cThe Protein Data Bank files are from the protein data bank, <http://www.pdb.org/pdb/home/home.do>

Supplemental Table 4 Genomic location studies for ETS transcription factors				
Study (Reference)	ETS protein	Cell line/type^a	Mapping method	Database location
Hollenhorst et al. 2007(39)	ETS1	Jurkat	Promoter microarray	GSE7449 ^b
	ELF1 GABPA	Jurkat Jurkat		
Gangwal et al. 2008 (40)	EWS-FLI1	A673	Promoter microarray	
Valouev et al. 2008 (41)	GABPA	Jurkat	Sequencing	http://mendel.stanford.edu/sidowlab/downloads/quest/
Guillon et al. 2009 (42)	EWS-FLI1	SK-N-MC, A673	Sequencing	
Boros et al. 2009 (43)	ELK1	HeLa	Promoter microarray	E-MEXP-1527 ^c E-MEXP-2084 ^c
Hollenhorst et al. 2009 (44)	ETS1	Jurkat	Sequencing	GSE17954 ^b
Ghisletti et al. 2010 (45)	SPI1	Mouse macrophages	Sequencing	GSE19553 ^b
Yu et al. 2010 (46)	ERG	VCaP, RWPE1-ERG, Prostate tumor	Sequencing	GSE14097 ^b
Wei et al. 2010 (47)	EWS-ERG	CADO-ES1	Sequencing	SRA014231 ^b
	EWS-FLI1	SK-N-MC		
	ELF1	Jurkat		
	ERG	VCaP		
	SPDEF	VCaP		
Kubosaki et al. 2010 (48)	SPI1	HL60		
	SPI1	THP-1	Promoter microarray	CBX43 ^d
Wilson et al. 2010 (49)	SPI1	HPC-7	Sequencing	GSE22178 ^b
	ERG	HPC-7		
Chi et al. 2010 (50)	FLI1	HPC-7		
	ETV1	GIST48	Sequencing	GSE22441 ^b GSE22852

^aSpecies is human unless indicated.

^bNCBI Gene Expression Omnibus/Sequence Read Archive

^cEMBL-EBI ArrayExpress Archive

^dCenter for Information Biology Gene Expression Database (CIBEX)

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