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An evolutionary, structural and functional overview of the mammalian TEAD1 and TEAD2 transcription factors

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ABSTRACT

TEAD proteins constitute a family of highly conserved transcription factors, characterized by a DNA-binding domain called the TEA domain and a protein-binding domain that permits association with transcriptional co-activators. TEAD proteins are unable to induce transcription on their own. They have to interact with transcriptional cofactors to do so. Once TEADs bind their co-activators, the different complexes formed are known to regulate the expression of genes that are crucial for embryonic development, important for organ formation (heart, muscles), and involved in cell death and proliferation. In the first part of this review we describe what is known of the structure of TEAD proteins. We then focus on two members of the family: TEAD1 and TEAD2. First the different transcriptional cofactors are described. These proteins can be classified in three categories: i), cofactors regulating chromatin conformation, ii), cofactors able to bind DNA, and iii), transcriptional cofactors without DNA binding domain. Finally we discuss the recent findings that identified TEAD1 and 2 and its coactivators involved in cancer progression.

Contents

Abbreviations: DBD, DNA binding domain; IAP, Inhibitor of Apoptosis Protein; LATS, Large Tumor Suppressor; MST, Mammalian Ste20-like Protein Kinase; TEA, transcriptional enhancer activator; TEAD, TEA domain; VGLL, Vestigial like; YAP, Yes-associated protein; YBD, YAP binding domain; Yki, Yorkie.

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1. Introduction

The TEAD family of transcription factors was first identified through the purification and cloning of the first mammalian TEF factor, TEF1 (TEAD1). TEAD1 was originally shown to regulate the transcription of the early and late promoters of the simian virus 40 (SV40). Specifically TEAD1 can bind to the GT-IIC and Sph enhansons of the SV40 enhancer (Davidson et al., 1988; Xiao et al., 1991). In vertebrates the TEAD family consists of four members, TEAD1 (TEF-1, NTEF-1), TEAD2 (ETF, ETEF-1, TEF-4), TEAD3 (DTEF-1, TEF5, ETFR-1), and TEAD4 (RTEF1, TEF-3, ETFR-2, FR-19) (Table 1).

TEAD proteins share a highly conserved DNA binding domain (DBD) called the TEA domain (Andrianopoulos and Timberlake, 1991). The TEA domain (77 amino acids) is also referred to as the ATTS domain because of the 4 proteins first found to harbor this motif (*A*baA and *T*EC1 in yeast, *T*EF1/TEAD1 in vertebrates and

Table 1
Characteristics of the TEAD genes. Based on NCBI, CCDS, MGI and Ensembl databases. Values indicated in the table correspond to the principal isoform. Indicated alternative isoforms correspond to the principal isoforms (APPRIS) annoted into the Ensembl database.

Species	Gene	Aliases	Chromosome	CCDS code	Ensembl transcript principal isoform.	Ensembl transcript ID-Alternative isoforms	Pre-spliced transcript length(kb)	Spliced transcript length (nt)	Exons	Coding exons	Protein length (aa)
Human	TEAD1	TEAD-1, AA, REF1, TEF-1, TCF-13, TCF13, NTEF-1	11	7810.2	ENST00000527636.5	ENST00000526600.1; ENST00000361985.6; ENST00000334310.10;	263.44	2544	13	11	426
	TEAD2	ETF, TEF-4, TEF4, TEAD-2	19	58671.1	ENST00000377214.8	ENST00000598810.5; ENST00000601519.5; ENST00000311227.6; ENST00000593945.5;	19.84	2440	11	11	450
	TEAD3	TEAD-3, TEF-5, DTEF-1, TEF5, TEAD5, ETFR-1	6	47414.1	ENST00000338863.11	ENST00000402886.7	23.48	2983	13	12	435
	TEAD4	RTEF-1, hRTEF-1B, TCF13L1, TEF3, TEF-3, TEFR-1, EFTR-2, RTEF1	12	31729.1	ENST00000359864.6	ENST00000358409.6; ENST00000397122.6	81.26	1690	13	11	434
Mouse	Tead1	2610024B07Rik, B230114H05Rik, Gtrgeo5, mTEF-1, Tcf13, TEAD-1, TEF-1	7	52365.1	ENSMUST00000059768.16	ENSMUST00000069256.1; ENSMUST00000106638.8; ENSMUST00000084705.11; ENSMUST00000164363.7; ENSMUST00000165036.7	227.49	9964	14	13	436
	Tead2	ETF, Etdf, TEF4, TEF-4, TEAD-2	7	71957.1	ENSMUST00000097216.3	ENSMUST00000097216.3	15.71	1233	11	11	410
	Tead3	TEAD-3, TEF-5, Tcf13r2, DTEF-1, ETFR-1	17	28577.3	ENSMUST00000080572.13	ENSMUST00000114799.7; ENSMUST00000154873.7; ENSMUST00000156862.1	19.14	2616	13	12	439
	Tead4	ETFR-2a, Rtef1, TEF-3, Tef3, TEAD-4, ETFR-2, Etfr2, FR-19, Tefr1, Tcf13r1, Tefr, Tefr1a	6	39646.1	ENSMUST00000006311.12	ENSMUST00000112157.3; ENSMUST00000130454.7	73.67	3076	12	11	427
Rat	Tead1	TEF-1	1	–	ENSRNOT00000090042.1	ENSRNOT00000021020.4	137.44	1607	13	13	436
	Tead2		1	–	ENSRNOT00000028086.4	ENSRNOT00000090838.1	15.88	2135	12	11	445
	Tead3	LOC294299	20	–	ENSRNOT00000000607.6		22.70	5874	13	12	372
	Tea4		4		ENSRNOT00000050834.6		47.09	5253	11	11	361