

Isolation and nucleotide sequence of a murine cDNA homologous to human activating transcription factor 4

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Members of the Jun, Fos and ATF/CREB families constitute a super-family of b-zip DNA binding proteins capable of heterodimerization and recognition of AP-1 (TGACTCA), CRE (TGACGTCA) and related sequences (reviewed in 1 and 2). One member of this family, ATF-4, was first identified as a partial cDNA from a human λgt11 expression library based on specific recognition of an ATF (CRE) probe sequence (3). Recently, a full length cDNA encoding ATF-4 was independently isolated from a human λgt11 library by similar methods using a TAX-responsive enhancer from the LTR of Human T-Cell Leukemia Virus Type I as a probe sequence (TGACGTCT) and this gene was termed TAXREB67 (4).

In the present study, a murine nucleotide sequence homolog to human ATF-4 was isolated. A cDNA library was constructed from F9 embryonal carcinoma cells using the vector pcDPolyBN-(5). This library was screened under reduced stringency conditions using a 511 bp *Eco*RI insert from pATF-4 (3). The nucleotide sequence for one isolate, pcDmATF-4 was determined and the deduced amino acid sequence for this isolate is shown in figure 1. Figure 1 also shows the deduced amino acid sequence of TAXREB67 (4). The murine and human cDNAs are 85% homologous in nucleotide sequence in a region encompassing the open reading frames of both cDNAs (nucleotide positions 176 to 1318 in pcDmATF-4, data not shown). The cDNAs encode proteins which are 80% similar overall with 98.6% amino acid identity throughout the regions coding for the DNA binding and dimerization domains (amino acid positions 307 to 364 in murine ATF-4). Two acidic regions, similar to the acidic transcriptional activation domains present in other transcription factors (6 and 7), have previously been identified in TAXREB67 and are also present in the murine ATF-4 sequence (region II, amino acid positions 91 to 152, and region III, amino acid positions 212 to 249). However, region II is extended by 22 amino acids in the murine sequence. Additionally, a third acidic domain, which is not present in TAXREB67, is found in the murine ATF-4 sequence (region I, amino acid positions 49–70) and results from divergence in the N-terminal region of each protein. The murine protein is also slightly larger predominantly due to the presence of an additional 31 N-terminal amino acids. This divergence, and the observation that hybridization of ATF-4 to human genomic DNA at reduced stringency detects more than a single ATF-4 related sequence (2), makes it uncertain if the murine sequence isolated here is functionally analogous to the human TAXREB67 gene.

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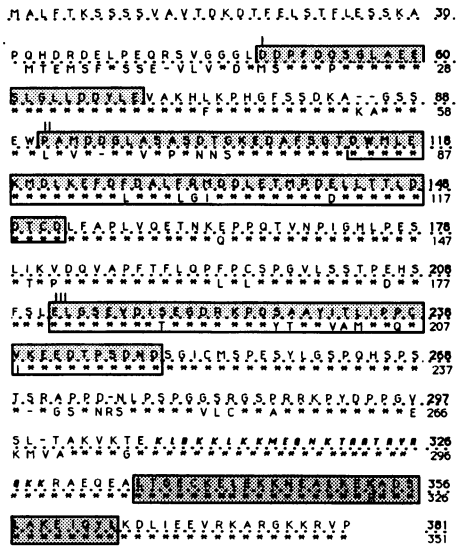

Figure 1. The deduced amino acid sequences of murine ATF-4 (upper sequence) and human TAXREB67 (lower sequence) are compared. Identical residues are indicated with an asterisk. Dashes indicate spacing allowances for alignment. The positions of acidic domains I, II, and III are indicated by lightly stippled and clear boxes in the murine ATF-4 and human TAXREB67 proteins, respectively. The DNA binding domain is represented in bold italics. Dimerization domains are indicated by the darkly stippled box where leucine residues of the heptad repeat are in bold type.

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