The human TTP protein: sequence, alignment with related proteins, and chromosomal localization of the mouse and human genes

Gregory A.Taylor, Wi S.Lai, Rebecca J.Oakey[1], Michael F.Seldin[1], Thomas B.Shows[2], Roger L.Eddy,Jr[2] and Perry J.Blackshear
Howard Hughes Medical Institute Laboratories and the Section of Diabetes and Metabolism, Division of Endocrinology, Metabolism, and Genetics, Departments of Medicine and Biochemistry and [1]Departments of Medicine and Microbiology, Duke University Medical Center, Durham, NC 27710 and [2]Department of Human Genetics, Reswell Park Memorial Institute, Buffalo, NY 14263, USA

Submitted April 29, 1991

GenBank accession no. M63625

The mouse tristetraprolin (TTP) protein is a basic proline-rich protein of M_r 33,600 that contains three PPPPG repeats (1). Its mRNA levels increase dramatically after stimulation with various mitogens. Also called Nup 475 (2) and TISII (3), it has been localised to the cell nucleus and is thought to contain an unusual zinc-finger structure (2). A distinct protein (cMG1) with an analogous zinc-finger structure was cloned recently (4). We report here the sequence of human TTP, which is 87% identical to the mouse protein; the putative zinc-finger structure is conserved among human and mouse TTP and rat cMG1 (Figure 1).

The human gene encoding TTP was localized to chromosome 19 using panels of rodent/human hybrid cell lines (5, 6). The mouse gene was localized to chromosome 7 using an interspecific cross; in 114 out of 114 meiotic events, it cosegregated with the *D19F11S1h* locus, which maps approximately 6.0 cM from the proximal end of mouse chromosome 7 (7). This is in the middle of a linkage group conserved with a segment of human chromosome 19 (7); the mouse mapping suggests that the human gene is at band q13.1 on human chromosome 19. This was confirmed by *in situ* hybridization of the human cDNA probe to metaphase chromosome spreads.

In recognition of its probable zinc-finger structure (2), the gene encoding the mouse TTP protein has been labeled Zfp-36 by the Committee on Standardized Genetic Nomenclature for Mice. The human gene is ZFP36.

ACKNOWLEDGEMENTS

We are grateful to Dr Ken Brown for helpful discussions concerning the cMG1 clone. Supported in part by grant # R01 DK-40408 from the National Institutes of Health.

REFERENCES

1. Lai,W.S., Stumpo,D.J. and Blackshear,P.J. (1990) *J. Biol. Chem.* **265**, 16556–16563.
2. DuBois,R.N., McLane,M.W., Ryder,K., Lau,L.F. and Nathans,D. (1990) *J. Biol. Chem.* **265**, 19185–19191.
3. Varnum,B.C., Ma,Q., Chi,T., Fletcher,B. and Herschman,M.R. (1991) *Mol. Cell. Biol.* **11**, 1754–1758.
4. Gomperts,M., Pascall,J.C., and Brown,K.D. (1990) *Oncogene* **5**, 1081–1083.
5. Shows,T.B., Sakaguchi,A.Y. and Naylor,S.L. (1982) *Advances in Human Genetics*, **12**, 341–452.
6. Shows,T.B., Eddy,R., Haley,L., Byers,M., Henry,M., Fujita,T., Matsui,H. and Taniguchi,T. (1984) *Somat. Cell Mol. Gen.* **10**, 315–318.
7. Saunders,A.M. and Seldin,M.F. (1990) *Genomics* **8**, 324–332.
8. Higgins,D.G. and Sharp,P.M. (1988) *Gene* **73**, 237–244.

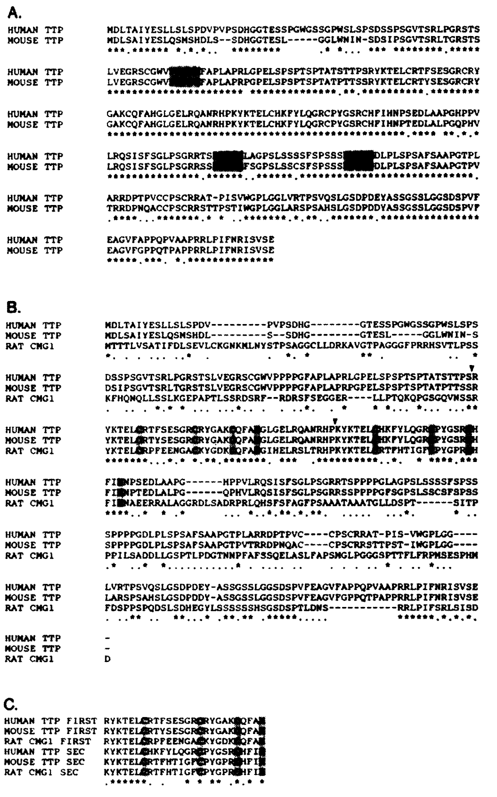

Figure 1. Alignment of the protein sequences of human and mouse TTP (A), both TTP sequences and rat cMG1 (B), and the two internal repeats from all three sequences (C); these repeats begin with the arrowheads in (B). All alignments were performed with the program Clustal (8), kindly provided by Dr D.G.Higgins. Sequence identities are indicated by an asterisk (*); conservative substitutions are indicated by a dot (·). The PPPPG motifs are highlighted in A; in B and C, the C and H residues thought to be part of the zinc-finger structure (2) are highlighted. 'First' and 'Sec' refer to first and second repeats, respectively.