

Letters to the Editor

TIMP-1 enhancer sequence – real or bacterial?

IM Clark^{*,1}, DA Young¹ and DR Edwards¹¹School of Biological Sciences, University of East Anglia, Norwich NR4 7TJ, UKBritish Journal of Cancer (2003) 89, 1812. doi:10.1038/sj.bjc.6601353 www.bjcancer.com
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Sir,

We have read with interest the recent paper in the *British Journal of Cancer* (Wang *et al*, 2003). Our groups have worked on TIMP-1 gene regulation for a number of years, including a dissection of the gene promoter in both human and mouse.

The 18 bp HTE-1 enhancer element used in this paper (and others referenced therein) is described to be in intron 1 of the human TIMP-1 gene. However, a search of sequences from our own human and mouse TIMP-1 genomic clones, or indeed a BLAST into the human genomic sequence databases, including the X-chromosome sequences containing the TIMP-1 gene, do not reveal a perfect match for HTE-1. The best match in the human

genome, for the first 16 base pairs of HTE-1, is in chromosome 17 (though outside of the TIMP-2 gene which lies on this chromosome). It is with some concern that we note that the HTE-1 sequence is matched in its entirety within the *E. coli* genome.

The authors have cloned an IL-10-responsive DNA-binding protein on the basis of its binding to the HTE-1 sequence, and explored its function. However, the interpretation of the data demonstrating that overexpression of the HTE-1-binding protein induces TIMP-1 expression (Figure 11) is made more difficult if the HTE-1 sequence is not within the TIMP-1 gene.

We would very much welcome the authors' input on these matters.

REFERENCE

Wang M, Hu Y, Stearns ME (2003) A novel IL-10 signalling mechanism regulates TIMP-1 expression in human prostate tumour cells. *Br J Cancer* 88: 1605–1614

Reply: TIMP-1 enhancer sequence – real or bacterial?

ME Stearns^{*,1}, Y Hu¹ and M Wang¹¹Department of Pathology and Laboratory Medicine, Drexel University College of Medicine, Mail Stop 435, 15th and Vine Sts, Philadelphia, PA 19102-1192, USABritish Journal of Cancer (2003) 89, 1812–1813. doi:10.1038/sj.bjc.6601354 www.bjcancer.com
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Sir,

The characterisation of the TIMP-1 gene was published in Wang *et al* (1998). The TIMP-1 gene was cloned from PC-3 ML genomic

DNA. The *Pst1-Xba1* fragment at the 5' end of the *Pst1* 4.0-kilobase TIMP-1 genomic clone was subcloned into plasmid PUC 19. This fragment was sequenced from both ends on opposite strands with the Sequenase Virgin 2.0 sequencing system (US Biochemical). Each strand was sequenced with both the Klenow fragment and reverse transcriptase by standard dideoxy procedures. Blast analysis of the 5' promoter region revealed a 97%

*Correspondence: Dr IM Clark; E-mail: i.clark@uea.ac.uk

*Correspondence: Dr ME Stearns; E-mail: Stearnsm1@aol.com



homology with *Homo sapiens* TIMP-1 promoter region (chromosome X genomic contig, NT 011568). Blast analysis of the coding region revealed a 97% homology with human TIMP-1 (Docherty

et al, 1985) and 96% homology with the coding region of the *E. coli* TIMP-1.

REFERENCES

Docherty AJ, Lyons A, Smith BJ, Wright EM, Stephens PE, Harris TJ, Murphy G, Reynolds JJ (1985) Sequence of human tissue inhibitor of metalloproteinases and its identity to erythroid-potentiating activity. *Nature* **318**: 666–669

Wang M, Hu Y, Shima I, Stearns ME (1998) Identification of positive and negative regulator elements for the tissue inhibitor of metalloproteinase 1 gene. *Oncol Res* **10**: 219–233