British Journal of Cancer (2003) 89, 1812–1813

www.bjcancer.com

Letters to the Editor

TIMP-1 enhancer sequence – real or bacterial?

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British Journal of Cancer (2003) **89,** 1812. doi:10.1038/sj.bjc.6601353 www.bjcancer.com

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?

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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 *Pst*1–*Xba*1 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%

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