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LETTER TO THE EDITORS

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Immunogenicity of WT-1 peptides

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It has recently come to our attention that there is some confusion concerning the nomenclature of a peptide described in our recent paper in this journal, entitled ''Prediction of an HLA-DR-binding peptide derived from Wilms' tumour 1 protein and demonstration of in vitro immunogenicity of WT1 (124–138)-pulsed dendritic cells generated according to an optimised protocol'' [1]. Our designation for the peptide [i.e. WT1 (124–138)] was based on the amino acid positions for the product of the WT1 gene, representing a product originally predicted by Bruns [2]. This latter paper describes a 575-amino-acid protein that was identified to be encoded by the WT1 gene and was entered into the NCBI Entrez protein database (accession no. CAA35956) as a krueppel-like zinc-finger protein. Utilising this whole protein sequence, encoded by the WT1 gene, we predicted the binding of a 15-mer peptide to the MHC class II molecule DRB1*0401 using the SYFPEITHI computer algorithm.

However, this peptide in fact represents positions 124–138 of the krueppel-like zinc-finger protein, and not of the actual WT1 protein as described by Housman [3] (NCBI Entrez protein database accession no. P19544). Nonetheless, the krueppel-like protein described by Bruns[2], contains the entire sequence of the WT1 protein described by Housman[3], though with an additional 126 amino acids at the N-terminus originating from an apparently untranslated region of the gene. Our predicted peptide therefore still comprises the first 12 amino acids of the Housman WT1 protein (MGSDVRDLNALL) [3], with an additional 3 amino acids preceding these (PQQMGSDVRDLNALL) from the Bruns [2] predicted protein. In retrospect, a more appropriate name for our predicted DR4 binding peptide representing the first 12 positions of the WT1 protein would be WT 12e, where ''e'' represents the extended nature of the peptide.

Interestingly, it should be noted that based on the SYFPEITHI prediction software, the first 15 amino acids of the WT1 protein (MGSDVRDLNALLPAV) are predicted to bind to DRB1*0401 with a score of 18, whereas by taking the first 12 amino acids of the WT1 protein and adding the sequence PQQ to the start of the peptide, as with our predicted peptide, the score is increased to 26, i.e. an improvement over the ''natural'' peptide. Finally, we would like to emphasise that the main focus of this paper was to demonstrate the use of a theoretically predicted peptide and an optimised sensitisation protocol to establish immunogenicity, and to ascertain a potential target for use in cancer vaccination protocols. This objective and the data presented in the paper are by no means compromised by the above.

We would like to apologise for any difficulties caused by this confusing nomenclature.

References

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