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T Cell Stimulatory Tumor Antigens

NZ 200 IDENTIFICATION OF THE MELANOMA ASSOCIATED ANTIGENS RECOGNIZED BY MOABS NKI-beteb AND HMB-45, G.J. Adema, A.J. de Boer, A.M. Vogel and C.G. Figdor, Department of Immunology, The Netherlands Cancer Institute, Amsterdam, The Netherlands

The glycoproteins recognized by moAbs NKI-beteb (gp 100 and gp7) and HMB-45 (gp10) are amongst the best markers for human melanoma available to date. Although moAbs directed against these antigens are very suitable for diagnostic purposes, they are less suitable for therapeutic purposes since the antigens are primarily expressed intracellularly. However, peptides derived from the antigens, if presented by MHC molecules, may well be capable of evoking cellular immune responses.

Using a rabbit polyclonal antiserum against gp100 we isolated a cDNA clone containing an insert of 2.1 kb. This cDNA detected RNA species of 2.5 kb and 4.2 kb on Northern blots containing total RNA isolated from melanoma cells and melanocytes but not from any other cell type tested. Expression of the cDNA in either cos-7 cells or gp100 negative melanoma cells resulted in NKI-beteb as well as HMB-45 immunoreactivity. This indicates that NKI-beteb and HMB-45 both recognize the protein(s) encoded by this cDNA. Biochemical characterisation of the protein recognized by NKI-beteb in transfected cos-7 cells demonstrated that the cDNA clone encodes gp100 as well as gp7.

We are currently determining the sequence of this cDNA clone. In addition, we are generating CTLs which recognize peptides derived from gp100 in an MHC restricted manner. These CTLs will be tested for anti-tumor activity in an in vivo model system.