

Identification of an HLA-A2 restricted Cyclin B1 derived CTL epitope

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Cytotoxic T lymphocytes (CTLs) recognize peptides derived from tumor associated antigens (TAAs) in context of HLA molecules. TAA derived peptides can be used in therapeutic cancer vaccines, and clinical trials with cancer patients have in some cases been promising. Cyclin B1 is a cell cycle checkpoint protein that regulates the transition from G2 to M phase of the cell cycle. Cyclin B1 is over expressed in many cancers and as a result, the cell cycle is deregulated. This allows uncontrolled growth of cancer cells.

In 2001 Cyclin B1 was identified as a TAA, and eight low affinity peptides were described. In the present study a high affinity CTL epitope is described.

To identify Cyclin B1 derived peptides with high affinity for HLA-A2, three *in silico* prediction algorithms were used. One peptide scored highest in all three algorithms, and the high HLA-A2 binding affinity of this peptide was verified in an assembly assay. Subsequently, a CTL clone was established, which was able to kill two breast cancer cell lines in an HLA-A2 dependent and peptide specific manner. This indicated presentation of the epitope on cancer cells.

Furthermore, spontaneous reactivity against the peptide was investigated in an IFN- γ ELISPOT assay, which showed that a high number of patients with breast cancer, melanoma or renal cell carcinoma hosted powerful T cell responses against the peptide. However, when blood from healthy donors was tested, powerful and frequent responses were also observed. The T cells responsible for the responses in both cancer patients and healthy donors will be analyzed further with regard to phenotype.