

Flexibility of Amino Acid Residues at Position Four of Nonapeptides Enhances Their Binding to Human Leucocyte Antigen (HLA) Molecules

Alberto Chersi*, Francesca di Modugno and Laura Rosano

Istituto Regina Elena for Cancer Research, Laboratory of Biochemistry, CRS, Viale Messi d' oro 156, 00158 Roma, Italy. Fax: 039-06-49852505. E-mail: biochimica@crs.ifo.it

* Author for correspondence and reprint requests

Z. Naturforsch. **55c**, 109-114 (2000); received August 2/September 21, 1999

Human Leucocyte Antigen (HLA), Peptide Binding, Secondary Interactions

The binding affinity of synthetic nonapeptides to human leucocyte antigens (HLA) molecules of the A0201 allotype, the most common in Caucasian, is enhanced or reduced by suitable amino acid substitutions at position 4, as a result of increased or decreased chain flexibility. A higher flexibility of the bond at this position correlates with an easier accommodation of the fragment into the HLA groove, while rigidity of the peptide chain appears to interfere. These data are based on two lines of evidence: a) most natural high affinity ligands for HLA-A0201 possess, at position 4, flexible residues b) substitutions of such residues by rigid amino acids results in a decrease of binding affinity.