Immunogenicity of HLA Class I and II Double Restricted Influenza A-Derived Peptides

The aim of the present study was to identify influenza A-derived peptides which bind to both HLA class I and II molecules and by immunization lead to both HLA class I and class II restricted immune responses. Eight influenza A-derived 9-11mer peptides with simultaneous binding to both HLA-A*02:01 and HLA-DRB1*01:01 molecules were identified by bioinformatics and biochemical technology. Immunization of transgenic HLA-A*02:01/HLA-DRB1*01:01 mice with four of these double binding peptides gave rise to both HLA class I and class II restricted responses by CD8 and CD4 T cells, respectively, whereas four of the double binding peptides did result in HLA-A*02:01 restricted responses only. According to their cytokine profile, the CD4 T cell responses were of the Th2 type. In influenza infected mice, we were unable to detect natural processing in vivo of the double restricted peptides and in line with this, peptide vaccination did not decrease virus titres in the lungs of intranasally influenza challenged mice. Our data show that HLA class I and class II double binding peptides can be identified by bioinformatics and biochemical technology. By immunization, double binding peptides can give rise to both HLA class I and class I restricted responses, a quality which might be of potential interest for peptide-based vaccine development.