Cyclodimerization of immunosuppressive fragment of HLA-DR molecule : design, synthesis and ESI-MS/MS analysis.

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Streszczenie

The nonapeptide fragment of the HLA-DR molecule, located in the exposed loop of the alpha-chain (164-172), having the VPRSGEVYT sequence, suppresses the immune response. Based on the three-dimensional structure of the HLA-DR superdimer, we designed a new cyclodimeric analog in which the two parallel peptide chains of VPRSGEVYT sequence are linked through their C-termini by spacer of (Gly5)2 -Lys-NH2 and the N-termini are also linked by poly(ethylene glycol). The (VPRSGEVYTG5)2 K-resin analog was synthesized using solid-phase peptide synthesis protocols. The cyclization was achieved by cross-linking the N-terminal positions of the dimeric peptide, attached to a MBHA resin, with alpha, omega-bis (acetic acid) poly(ethylene glycol), activated by esterification with pentafluorophenol. Our results demonstrate that the cyclodimerization of VPRSGEVYT results in enhanced immunosuppressive activity of the peptide. Mass spectrometry fragmentation analysis of the obtained cyclodimeric peptide is also presented.

Słowa kluczowe

ESI-MS/MS, HLA-DR analogs, PEG linker, cyclodimer

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