

Dimerization of the immunosuppressive peptide fragment of HLA-DR molecule enhances its potency.

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Rok wydania

2004

Czasopismo

Peptides

Numer woluminu

25

Strony

207-215

DOI

10.1016/j.peptides.2003.12.011

Kolekcja

Naukowa

Język

Angielski

Typ publikacji

Artykuł

Streszczenie

Our previous studies revealed that the nonapeptide fragment of HLA-DR molecule, located in the beta chain 164-172 with the VPRSGEVYT sequence, suppresses the immune responses. The sequence is located on the exposed molecule loop, therefore it may be involved in the interactions with other proteins. We suggested that the loop may serve as a functional epitope on the HLA class II surface for intermolecular binding, and that possible mechanism of biological action of the synthesized peptides is associated with interfering of adhesion of HLA class II molecules to their coreceptors. It has been postulated that oligomerization of the coreceptors is required for stable binding to class II HLA. Based on the crystal dimeric structure of HLA-DR molecules, we designed, and synthesized molecules able to induce the putative coreceptors dimerization. The synthesized series of compounds consisted of two VPRSGEVYT sequences linked through their C-termini by spacers of different length: (VPRSGEVYT G_n) $2K-NH_2$ ($n = 4-6$). The results demonstrate that the dimerization of the nonapeptide fragment of HLA-DR results in enhanced immunosuppressive properties.

Adres publiczny

<https://doi.org/10.1016/j.peptides.2003.12.011>

Strona internetowa wydawcy

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