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Nanodynamics of MHC/peptide complexes and its dependence on MHC polymorphism (Weiterführung)

Initiative: Konformationelle Kontrolle biomolekularer Funktionen (beendet)

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The causative role of the human major histocompatibility gene HLA-B27 in spondyloarthropathies, a common group of chronic inflammatory rheumatic diseases, is not understood, but the HLA-B27 molecule itself appears as the strongest predisposing factor for pathogenesis. It seems that the study of HLA-B27 subtypes differing at only one amino acid position might provide a clue to pathogenesis. It is proposed to investigate the peptide dynamics and conformational changes in a comparative study with the two differentially disease associated subtypes B*2705 and B*2709, complexed with three self-peptides, a sequence-related foreign peptide of viral origin, and various modeled peptides with predicted similar binding characteristics. New developments in molecular dynamics simulations and peptide synthesis shall be combined with real-time fluorescence depolarization and fluorescence correlation measurements as well as cellular immunological assays to address the question whether differential peptide dynamics related to HLA-B27 polymorphism can be linked to the biological response in terms of T cell activity. Photocontrol of differential peptide dynamics by means of photoswitchable peptide analogs will provide additional insight into the peptide dynamics of HLA/peptide complexes and its dependence on HLA polymorphism.

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