NMR spectroscopic investigation of micropolymorphism-dependent dynamics of human major histocompatibility antigens

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Major histocompatibility complexes (MHCs) play a central role in the immune response. In case of the human leukocyte antigens (HLA) class I molecules small peptide fragments of 8 to 12 amino acids are presented to T lymphocytes and selectively recognized by T-cell receptors (TCRs). Detailed functional and structural studies have been carried out with two HLA-B27 subtypes (HLA-B2705 and HLA-B2709), one of which (B2705) is associated with the autoimmune disease ankylosing spondylitis while the other (B2709) is not. While a lot of structural information on MHC-peptide complexes has become available, the static picture resulting from mainly X-ray crystallography has not been able to fully explain the selectivity and subtype-specificity in immune response and disease association.

It has been shown that the dynamic behavior of binding partners can be of great importance in protein-protein interactions. We use heteronuclear NMR spectroscopy in conjunction with extensive labeling to investigate two different HLA-B27 subtypes and two peptides (four HLA molecules in total) to obtain dynamic information on the HLA molecules at physiological temperature. We hope to be able to correlate the dynamic behavior of the loaded MHCs with their recognition by TCRs.

First results using a complete resonance assignment for a qualitative analysis of the line width of all three components of the complex will be presented and some practical aspects will be discussed.

M. Beerbaum; M. Ballaschk; N. Erdmann; C. Schnick; A. Diehl; B. Uchanska-Ziegler; A. Ziegler; P. Schmieder; "NMR spectroscopy reveals unexpected structural variation at the protein–protein interface in MHC class I molecules"; \textit{J. Biomol. NMR} \textbf{57}, 167-178 (2013)