Lyme neuroborreliosis in children: Etiology and comparison of clinical findings of lyme neuroborreliosis caused by B. garinii and B. afzelii

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Abstract

The adaptive immune response is one of the most important systems of defense against pathogens. In this contest, the ability of the CD8+ Cytotoxic T Lymphocytes (CTLs) to recognize a wide number of foreign antigens represents a strong defense against diseases. The T cells response is regulated by T Cell Receptor (TCR) activation, which may occur following the epitope recognition (p), mediated by the Major Histocompatibility Complex (MHC). Experimental studies have suggested that conformational changes involving the constant region of the TCR α chain and of the CD3 complex are responsible for the TCR transduction signal across the plasma membrane, i.e. triggering. These conformational changes allow the phosphorylation of the CD3 complex ζ chain and the propagation of the signal downstream. By means of Molecular Dynamic simulations (MDs) we analyzed the conformational behavior of two TCRs (1G4 and ILAα1β1) interacting with the same MHC of class I (HLA-A2*01), in a lipid environment. When compared to experimental results, our data suggests a correlation between the conformations explored by the β-chain constant region and T cell activity. In particular, independently by the TCR type involved in the interaction, the TCR activation seems to be linked to a specific conformation affecting the β-chain constant region. Moreover, combining experimental and theoretical studies, we recently noted that the bound peptide can affect the conformation of the MHC of class I binding groove, suggesting a different presentation of the antigens possibly related to different CTLs responses. From Molecular Dynamics simulations of the whole pMHC/TCR complex we found that the interaction pMHC/TCR constraints the MHC binding groove in a more rigid conformation, contrary to our recent prediction where the MHC of class I (HLA -B27*) has been simulated alone.