Molecular Biology 2016 vol.50 N3, pages 442-451

Molecular dynamics of immune complex of photoadduct-containing DNA with Fab-Anti-DNA antibody fragment

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Abstract

© 2016, Pleiades Publishing, Inc.Antibodies to DNA play an important role in the pathogenesis of autoimmune diseases. The elucidation of structural mechanisms of both the antigen recognition and the interaction of anti-DNA antibodies with DNA will help to understand the role of DNA-containing immune complexes in various pathologies and can provide a basis for new treatment modalities. Moreover, the DNA-antibody complex is an analog of specific intracellular DNA-protein interactions. In this work, we used in silico molecular dynamic simulations of bimolecular complexes of the dsDNA segment containing the Fab fragment of an anti-DNA antibody to obtain the detailed thermodynamic and structural characteristics of dynamic intermolecular interactions. Using computationally modified crystal structure of the Fab-DNA complex (PDB ID: 3VW3), we studied the equilibrium molecular dynamics of the 64M-5 antibody Fab fragment associated with the dsDNA fragment containing the thymine dimer, the product of DNA photodamage. Amino acid residues that constitute paratopes and the complementary nucleotide epitopes for the Fab-DNA construct were identified. Stacking and electrostatic interactions were found to play the main role in mediating the most specific antibodydsDNA contacts, while hydrogen bonds were less significant. These findings may shed light on the formation and properties of pathogenic anti-DNA antibodies in autoimmune diseases, such as systemic lupus erythematosus associated with skin photosensitivity and DNA photodamage.

http://dx.doi.org/10.1134/S0026893316020023

Keywords

3D structure of the Fab-dsDNA immune complex, molecular dynamics, thymine dimers