May 20th, 12:30 PM

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Structural and Molecular Analysis of a Protective Epitope of Lyme Disease Antigen OspA and Antibody Interactions

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Abstract

The murine monoclonal antibody LA-2 recognizes a clinically protective epitope on outer surface protein (OspA) of Borrelia burgdorferi, the causative agent of Lyme disease in North America. Human antibody equivalence to LA-2 is the best serologic correlate of protective antibody responses following OspA vaccination. Understanding the structural and functional basis of the LA-2 protective epitope is important for developing OspA-based vaccines and discovering prophylactic antibodies against Lyme disease.

Here, we present a detailed structure-based analysis of the LA-2/OspA interaction interface and identification of residues mediating antibody recognition. Mutations were introduced into both OspA and LA-2 based on computational predictions on the crystal structure of the complex, and experimentally tested for in-vitro binding and borreliacidal activity. We find that Y32 and H49 on the LA-2 light chain, N52 on the LA-2 heavy chain and residues A208, N228 and N251 on OspA were the key constituents of OspA/LA-2 interface. These results reveal specific residues that may be exploited to modulate recognition of the protective epitope of OspA and have implications for design of vaccines against Lyme disease.

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