Progression of Lyme Disease to Later Stages Is Associated with Antibody Response Towards the Membrane-Proximal Domain of the VlsE Protein of Borrelia burgdorferi

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Methods:

Preparation of peptides representing the VlsE epitopes. Biotin-labeled peptides representing sequences of the three major epitopes of VlsE were synthesized by utilizing Fmoc chemistry (Sigma-Aldrich). These sequences were 1) VlsE N (amino acids 274-288, representing the IR6 epitope: MKIDQDVAAALGIAKDKDD)FVK), 2) VlsE C (aa 21-44, representing the N-terminal epitope: SQAVDHDINTFNYKQVSQOLIGDF), and 3) VlsE M (aa 336-349, representing the C-terminal epitope: LKRVGDIVKVAIKSK). Peptide notation was based on the amino acid number of the first residue of each peptide in the protein sequence for B. burgdorferi B31 VlsE protein (NCBI AAC45733). NCBI's 3D-structure database coordinate, based on the published crystal structure of VlsE [1], were used to visualize the spatial location of the three epitopes. Images were rendered with the VMD molecular graphics program. Preparation of recombinant VlsE protein representing the membrane-proximal region (VlsE336)349 in post-Lyme disease syndrome. Clinical immunology

Results:

1. The 3D structural model of the protein indicates that the VlsE N- and VlsE M-epitopes of the invariant variable domain are sequentially distant, but are spatially adjacent to one another and are located in the membrane-proximal region.

2. While antibody reactivity to the IR6 region is generated early on and remains highly elevated following the dissemination of Lyme disease, antibody reactivity towards the membrane-proximal epitopes in the N- and C-terminal invariant domains of VlsE, and VlsE M-epitope, are largely absent in the early stages and sharply increase when infection progresses to later stages.

Conclusions:

- There is a highly divergent antibody response towards the central IR6 and terminal VlsE N- and C-terminal epitopes of VlsE during the course of Lyme Disease.
- Differential humoral response towards the immunodominant epitopes of VlsE at various stages of infection may offer novel clues about protein’s role in B. burgdorferi immune evasion strategy.
- Assessment of antibody reactivity against the membrane proximal epitopes of VlsE may be useful in aiding the determination of the stage of active infection and/or identifying patients at increased risk for developing persistent symptoms following therapy.

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