YebC Modulates OspC and VlsE Inverse Regulation and VlsE Expression in Persistent Lyme Disease

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Background & Hypothesis: Lyme disease, caused by the bacterium *Borrelia burgdorferi*, is the most common vector-borne infectious disease in the United States. Although easily treated with antibiotics, undiagnosed cases may develop into persistent infections with complications including Lyme carditis, neuroborreliosis, & arthritis. VlsE antigen variation is one of the major mechanisms employed by *B. burgdorferi* to establish persistent infection. We hypothesize that YebC modulates VlsE expression and antigen variation, enabling the shift from acute to persistent infection.

Materials & Methods: C3H/HeN or C3H/SCID mice were infected with the *B. burgdorferi* strain 5A4NP1, *yebC* mutant, and *yebC* complement at a dose of 10^5 or 10^6 spirochetes. Mice were sacrificed at days 7, 30, 60, and 90 post-infection and tissue samples were subjected to RNA and DNA extraction.

Results: YebC levels were closely associated with the upregulation of vlsE and the downregulation of *ospC in vitro* and *in vivo*. The *yebC* mutant displayed loss of infectivity in C3H/HeN mice, and reduced VlsE antigen variation.

Conclusion & Impact: This data demonstrates that YebC of B burgdorferi can regulate the frequency of *vlsE* recombination and modulates the inverse regulation of OspC and VlsE. This new factor may serve as an avenue for developing drugs which can target *vlsE* recombination to combat complications of persistent Lyme disease.