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Abstract

Lyme neuroborreliosis- the role of the meninges

Lyme disease is a multisystem infection that is spread via the bite of a tick infected by the bacterium *Borrelia burgdorferi*. Individuals that do not receive a timely diagnosis and antibiotic treatment can develop neurological complications that include cranial palsies, meningitis, and radiculopathies, a condition collectively referred to as neuroborreliosis. The physiological mechanisms that underlie neuroborreliosis have been characterized based on clinical data and research conducted on non-human primates. A mouse model of neuroborreliosis would be essential in further elucidating specific mechanisms of pathogenesis pertaining to both host physiological responses and modes of microbial dissemination. Previously we have demonstrated that late stage disseminated infection in C3H mice is associated with the presence of *B. burgdorferi* spirochetes in the meninges, and T cell responses. Here we further characterize a mouse model of meningeal borreliosis by 1) determining the kinetics of meningeal infection; 2) identifying phenotypic differences in meningeal pathogen burden based on variation in inoculum dosage, and infection site; and, 3) determining the contribution of host and pathogen strain variation to meningeal pathogen burden. Our results demonstrate that meningeal infection reaches a relative maximum during the first week of infection, that C3H mice exhibit a higher pathogen burden in the meninges than C57.B6 strains, that meningeal pathogen burden is dependent on inoculum dosage, and that the site of needle inoculation influences pathogen burden in the meninges. Overall, these data establish a mouse model of meningeal

borreliosis that will be useful in understanding the host-pathogen relationship in neurologic manifestations of Lyme disease.

Bio-Summary

Dr. Catherine (Cat) Brissette received her B.S. in Zoology from Louisiana State University, her M.S. with Dr. Paula Fives-Taylor at the University of Vermont, and her Ph.D. from the University of Washington for her work with Dr. Sheila Lukehart on interactions of oral spirochetes with the gingival epithelium. She continued work with spirochetes as a postdoc with Dr. Brian Stevenson at the University of Kentucky, switching to the Lyme disease spirochete Borrelia burgdorferi. Her work with Dr. Stevenson involved studies of outer surface adhesins and regulation of virulence factors. Cat accepted a faculty position at the University of North Dakota in the Department of Microbiology and Immunology (now part of Biomedical Sciences), where she continues work with pathogenic Borrelia species. Cat's lab is particularly interested in understanding why B. burgdorferi has a tropism for the central nervous system, the function of outer surface proteins that interact with the mammalian hosts' extracellular matrix, cells, and components of the immune system, and the regulatory mechanisms controlling the expression of these infection-associated proteins.