

Public Abstract

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Degree: PhD

Academic Program: Molecular Microbiology and Immunology

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Title: Lipid mediators in the development and resolution of experimental Lyme arthritis

The focus of my graduate studies was to determine the contribution of members of the eicosanoid cascade, namely the cyclooxygenase enzymes, to the regulation of experimental Lyme arthritis pathology. Using COX-2-specific inhibitors and knock-out animals, it was determined that COX-2 was not required for the development of Lyme arthritis, but played a prominent role in the resolution of arthritis pathology. Regulation of arthritis resolution by COX-2 was not mediated via alterations in antibody production or an inability to clear *Borrelia* from arthritic joints. Further pharmacological and knock-out studies found that COX-1 played a regulatory role during development of arthritis by maintaining a check on the developing inflammatory response. At later time points, COX-1 mediated down-regulation of the inflammatory response. The differential contribution of the COX isozymes to arthritis pathology during infection with *B. burgdorferi* lead to the characterization of a previously unappreciated role for COX-1 in the regulation of B lymphocyte responses and pathogen-specific antibody production using isozymes-specific inhibitors and COX-1 and -2 gene knock-out animals. Finally, the role of LTB₄ in regulation of Lyme arthritis pathology was investigated using a BLT₁-specific antagonist, and it was found that LTB₄ may play a previously undescribed role in mediating the down-regulation of the inflammatory response to *B. burgdorferi*.