Novel glycosylation based diagnostic and prognostic for lyme disease

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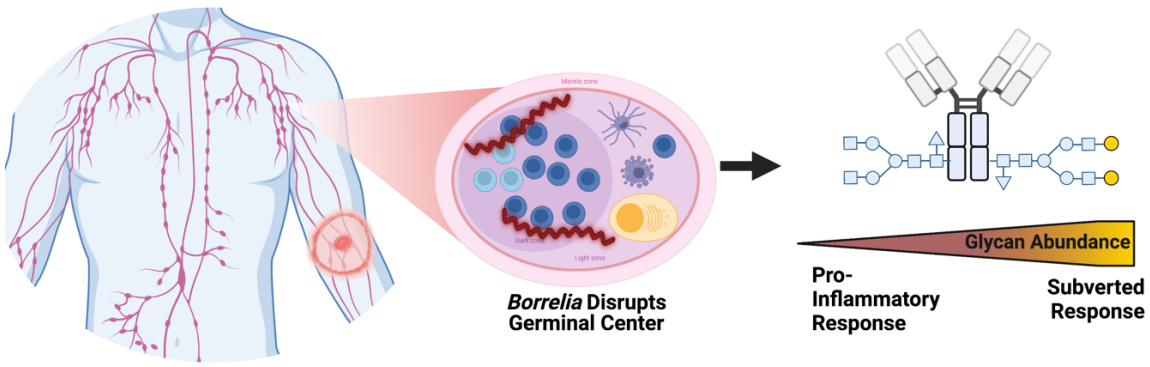
Current diagnostics for acute Lyme disease (LD) suffer from low sensitivity. As a result, patients with undetected cases of Lyme disease delay antibiotic treatment and risk bacterial dissemination to their brain, joints, and heart and causing irreversible damage. We present evidence that infection with the *Borrelia burgdorferi* spirochete alters the glycosylation of serum IgG and IgM in a manner specific to acute Lyme disease.

While inflammatory diseases canonically induce global IgG with increased agalactose content, we detect a marked decrease of agalactose during acute Lyme disease – below that of healthy control levels. Agalactosylated species are known to promote FcgR IIIA signaling on circulating lymphocytes to promote inflammation. Yet the IgG Fc fragment exhibits increased galactose and sialic acid content during acute Lyme disease. This finding suggests a novel immuno-modulation induced by acute *Borrelia burgdorferi* infection that permits evasion of adaptive immunity.

Moreover, we have detected acute LD-specific alterations of mannosylated and complex-type N-glycans in IgM. Recent reports suggest that rates of complement deposition and T-cell activation are partly controlled by the IgM glycosylation profile. Using machine learning, we determined our IgG and IgM N-glycan-based approach to be 72% sensitive and 100% specific for acute LD. In addition, the global IgG and IgM N-glycome were able to differentiate acute LD patients from diseases that present similarly. Our research indicates that glycosylation of IgG and IgM are useful biomarkers for acute Lyme disease and have diagnostic and prognostic potential.



Borrelia burgdorferi invasion of the lymph node can affect immunoglobulin glycosylation.