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## Metabolic control of virulence potential of the agent of Lyme disease

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Lyme disease is the most-prevalent arthropod-borne disease in the US and is caused by a spirochetal pathogen, *Borrelia burgdorferi*. The agent of lyme disease is transmitted to humans and other domestic animals by the bite of infected *Ixodes* spp. ticks. The genome of *B. burgdorferi* is very compact and encodes for limited metabolic capabilities suggesting the dependence of this pathogen on host-derived nutrients for its survival in the tick vector or the vertebrate hosts. We have identified two regulators (*Borrelia* host-adaptation Regulator – BadR and Carbon storage regulator A – CsrA<sub>Bb</sub>) of gene expression that contribute to the adaptation of Lyme spirochetes in the arthropod vector or vertebrate host, respectively. These regulators alter metabolic pathways critical for generation of key activating factors or for enzymes that are rate limiting for cell biogenesis and in turn, the viability of the spirochetes. Notably, these regulators also control the levels of expression of key transporters that result in influx of critical nutrients that contribute to activation of regulatory networks that favor adaption to respective hosts. Multiple metabolic pathways are also activated or dampened by these regulators indicating that the host-specific survival and virulence of *B. burgdorferi* is modulated by basic metabolic processes of the pathogen and availability of host-derived nutrients in different microenvironments of its highly disparate hosts. By employing transcriptional (RNA-Seq analysis) proteomic and metabolomic analysis of *B. burgdorferi* under *in vitro* and *in vivo* growth conditions of the tick or the vertebrate hosts, we have identified that the regulatory networks are remarkably plastic allowing the spirochetes adaptive advantages when transitioning between ticks and vertebrate hosts. These studies will potentially lead to development of strategies to alter host-derived nutrient concentrations to either reduce or eliminate the ability of Lyme spirochetes to colonize the transmission vector or the reservoir hosts leading to a reduction in the incidence of Lyme disease in endemic areas.

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