Infectious Diseases
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Spitting image: targeting tick saliva proteins by vaccination as a novel strategy to prevent Lyme borreliosis

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Lyme borreliosis is a tick-borne disease caused by Borrelia burgdorferi sensu lato, which is transmitted by Ixodes ticks. Over half a million new cases of Lyme borreliosis are diagnosed in the Northern hemisphere each year. Clinical manifestations include early and chronic skin infection as well as disseminated infection such as Lyme arthritis, neuroborreliosis, or carditis. Since there is currently no human vaccine available, we are investigating the innovative approach to prevent both Lyme borreliosis and other tick-borne diseases by targeting the tick vector, rather than targeting the pathogen itself as conventional vaccines do. The rationale behind anti-tick vaccines is based on the phenomenon designated as 'tick immunity'. Non-natural hosts repeatedly infested with ticks, or repeatedly injected with tick saliva, develop humoral immune responses to tick saliva proteins, impairing subsequent tick feeding. Interestingly, tick immune animals are also protected against various tick-borne pathogens.
Through next generation sequencing, we identified and biologically validated 20 tick salivary gland genes that were consistently and abundantly expressed during early tick feeding. To assess their role in Borrelia transmission, corresponding tick proteins were expressed recombinantly in E. coli and Drosophila expression systems. Mice were immunized with recombinant tick proteins and challenged with Borrelia-infected ticks. Mice vaccinated with recombinant proteins showed no Borrelia skin infections as skin cultures were Borrelia negative, whereas mice receiving PBS-adjuvants contained Borrelia positive skin cultures. Additionally, Borrelia qPCR loads in the bladder and heart of vaccinated mice were significantly lower compared to mice receiving PBS-adjuvants, indicating no disseminated infections. We therefore anticipate that a multivalent anti-tick vaccine can provide protection against Lyme borreliosis in experimental models. To further investigate tick immunity in humans, we are currently setting up an unique human tick-challenge model in which human volunteers will be challenged four times in two-week intervals with 25 nymphal ticks (pathogen free) per challenge, placed on the forearm and contained in a plastic eyepatch. Local skin reactions and tick-feeding parameters will be recorded. Furthermore, blister liquor and blood will be collected at several time points to investigate local and systemic cellular and humoral immune responses. Al together, this will result in a better understanding of tick-host interactions and tick immunity required for the development of a human anti-tick vaccine to prevent Lyme borreliosis.