

# Targeting Tick-Borne Diseases

R. W. Stich

University of Missouri

Department of Veterinary Pathobiology

Ticks transmit the majority of vector-borne diseases of human beings in the USA and of domestic animals worldwide. Among these, tick-borne rickettsial pathogens cause at least four important tick-borne zoonoses in the USA, and two of the five major vector-borne diseases of cattle worldwide. Notably, five of the aforementioned zoonotic and bovine diseases are endemic to Missouri. Tick-borne diseases of humans are zoonotic, and dogs are also naturally exposed to most of the etiologic agents of such maladies, suggesting potential roles of canine sentinels, reservoirs and models for tick-borne zoonoses. Our group utilizes canine ehrlichiosis (*Ehrlichia canis* and *E. chaffeensis*) and bovine anaplasmosis (*Anaplasma marginale*) models to better understand mechanisms of rickettsial infection of both acarine and mammalian hosts. Ticks used for these projects include *Rhipicephalus sanguineus*, *Dermacentor variabilis*, *D. andersoni*, *Amblyomma americanum*, *A. maculatum* and *Ixodes scapularis*. Projects currently underway include mechanisms responsible for rickettsial manipulation of host cell actin, and strategies that could lead to interference with tick acquisition and transmission of infections. In addition to the infectious cycles of these agents, we are also interested in pathogen interactions with the mammalian host, including the immunology and pathology of anaplasmosis and ehrlichiosis. These studies are expected to lead to better understanding of immune responses associated with different phases of ehrlichiosis, influence of vector feeding on biological and clinical outcomes of infection, immunoprophylaxis, and risk factors for exacerbation of clinical disease. The University of Missouri provides an optimal environment for this work, because i) MU has Veterinary, Medical and Agricultural colleges on the same campus; ii) MU has outstanding nucleic acid, proteomics, flow cytometry and microscopy (both fluorescence and electron) core facilities; iii) almost every tick-borne disease enzootic to the USA is in Missouri, thus allowing local access to diagnostic specimens from naturally infected hosts; iv) MU has established graduate programs in infectious disease research, pathobiology and comparative medicine; v) MU has BSL2 facilities to investigate tick-borne infections of dogs and cattle, which will soon be expanded with construction of a new Animal Resource Center; and vi) MU is home to the Missouri Regional Biocontainment Laboratory, for which an expansion of facilities is anticipated for investigation of tick-transmission of zoonotic BSL3 agents among dogs (e.g., *Rickettsia rickettsii*, *Coxiella burnetii* and *Francisella tularensis*). Our current capabilities center on large animal transmission, infection and disease models for anaplasmosis and ehrlichiosis. Mouse, guinea pig and rabbit models are also possible for certain tick and pathogen species. Technical skills include tick infestation of dogs and cattle, qualitative and quantitative PCR assay development and implementation, monitoring of clinical and hematologic parameters, and characterization of protective and pathogenic mechanisms with immunological and molecular methods. We are interested in opportunities to test new products designed to interfere with tick-pathogen-host interactions, and opportunities to investigate novel approaches for diagnosis or alleviation of ehrlichiosis and anaplasmosis