Post-Doctoral Requests, 2016

(as of 1/1/16)

Evaluation of the Standard Diagnostics Dengue duo Rapid Diagnostic Test

Tyler Sharp, PhD, Dengue Branch, email: iyp4@cdc.gov

The Dengue Branch Epidemiology Activity solicits a Post-Doctoral Preceptor Candidate to work on projects based on the Sentinel Enhanced Dengue Surveillance System (SEDSS). The primary project would be a prospective evaluation of the Standard Diagnostics DengueDuo rapid diagnostic test (RDT) to determine the performance and clinical utility of the RDT. Responsibilities of the Candidate will be to develop study materials, train hospital and SEDSS staff on enrollment of patients into the nested study, integrate data collection tools into the pre-existing SEDSS database, and analyze study findings. Once the protocol is developed and the staff are trained, patient enrollment will begin once dengue case detection is high, since evaluating the test during non-epidemic levels of dengue case detection is will be unlikely to produce a sufficient number of dengue patients to enable appropriate evaluation of the RDT. Therefore, during this potential period of delay, a second project for the Candidate would be to analyze pre-existing data from the first 3 years of SEDSS (May 2012–April 2015) for characteristics (e.g., signs/symptoms, diagnoses, age groups, time of enrollment) associated with patients enrolled in SEDSS that did not have a pathogen identified by diagnostic testing. This will improve our understanding of the potential etiologic agents in patients enrolled in SEDSS as well as the utility of the current diagnostic algorithm, since such an analysis may suggest other causes of illness for which diagnostic testing is not routinely performed (e.g., acute gastroenteritis, localizing source of bacterial infection) or patients with false-negative test results under in the diagnostic algorithm. Last, depending on the Candidate's availability, a potential third project would be a comparative analysis of the incidence and clinical characteristics of dengue patients with viral encephalitis that were identified by the Passive Dengue Surveillance System (PDSS) versus those identified by SEDSS.

Molecular Mechanisms of Pathogenesis of *Borrelia burgdorferi*, the Lyme disease agent

Robert D. Gilmore, PhD, Bacterial Diseases Branch, email: rbg9@cdc.gov

Lyme borreliosis, aka Lyme disease, continues to be a major public health concern in the USA, North America, and worldwide. A recent report by our CDC Division has estimated that there may be up to 300,000 cases of this tick transmitted illness diagnosed in this country. Understanding the biological processes of the causative agent, the spirochete *Borrelia burgdorferi*, is essential to be able to develop new strategies to combat this disease through prevention and control measures. My laboratory focuses on the pathogenesis of the Lyme disease agent utilizing molecular microbiological and immunological methodologies to study bacterial mechanisms of infection, e.g. pathogen transmission and survival at the tick/host interface. The objective is to identify *B. burgdorferi* genes that are differentially expressed during the enzootic cycle and to study the role of the encoded gene products in pathogenesis including putative protein-protein interactions that mediate survival and infection of the spirochete in the tick and mammalian hosts. Our recent successes in identifying such *B. burgdorferi* genes promises fertile ground for research in understanding the role of these gene

products in vector-host interactions, and is the basis for improving diagnostic assays, and developing new therapeutic strategies for Lyme disease.

Understanding the mechanisms of virus – vector specificity using chimeric alphaviruses.
Ann Powers, PhD, Arbovirual Diseases Branch, email: akp7@cdc.gov

Large and ongoing outbreaks of chikungunya virus (CHIKV) have caused greater than 4 million human infections around the globe in the past decade. The most closely related alphavirus, o'nyong nyong (ONNV), has caused only 2 documented but large scale outbreaks in East Africa. Although these viruses are genetically similar, they exhibit distinct ecologies and very different infection patterns of mosquito vector infection. Humans are infected with ONNV when bitten by infected Anopheles gambiae and An. funestus, while the mosquito vectors that transmit CHIKV are Aedes aegypti and Ae. albopictus. ONNV is the only alphavirus to be vectored by anopheline mosquitoes and studies have indicated that An. gambiae is highly susceptible to ONNV infection while it is refractory to CHIKV infection and that the non-structural protein 3 (nsP3) of ONNV is largely responsible for its unique ability to infect An. gambiae.

Recent work from the Alphavirus Laboratory has used chimeric viruses to study the infection patterns through artificial infectious feeds in An. gambiae and has demonstrated that ONNV nsP3 was instrumental in regulating infectivity of An. gambiae mosquitoes. Follow up studies to this publication need to focus on understanding the mechanisms of this process. By studying the virus-vector interactions of ONNV and CHIKV, we can not only shed light on the ability of these viruses to infect completely disparate vector hosts but also understand the exact mechanisms and functions of nsP3, a highly-variable protein whose properties with regard to viral pathogenesis are yet to be understood. This could lead to critical control strategies to prevent mosquitoes from becoming infected with human arboviruses.

Powers AM, Brault AC, Tesh RB, Weaver SC. 2000. Re-emergence of chikungunya and o'nyong-nyong viruses: evidence for distinct geographical lineages and distant evolutionary relationships. J Gen Virol. 81: 471–479.

Vanlandingham DL, Hong C, Klingler K, Tsetsarkin K, McElroy KL. 2005. Differential infectivities of o'nyong-nyong and chikungunya virus isolates in Anopheles gambiae and Aedes aegypti mosquitoes. Am J Trop Med Hyg. 72: 616–621.

Saxton-Shaw KD, Ledermann JP, Borland EM, Stovall JL, Mossel EC. 2013. O'nyong nyong Virus Molecular Determinants of Unique Vector Specificity Reside in Non-Structural Protein 3. PLoS Negl Trop Dis 7(1): e1931.

Myles KM, Kelly CL, Ledermann JP, Powers AM. Effects of an opal termination codon preceding the nsP4 gene sequence in the o'nyong-nyong virus genome on Anopheles gambiae infectivity. J Virol. 2006 May;80(10):4992-7.

Ecology of Mosquito Vectors and Transmission Dynamics of Arboviruses
H. M. Savage, PhD, Ecology, Entomology Activity, Arbovirus Diseases Branch, email: hms1@cdc.gov

Knowledge of the morphological and molecular identification, population structure, behavior and biology of mosquito vectors is essential to understanding the ecology and

transmission dynamics of arboviral diseases and the development of vector control strategies. Research projects that integrate field, laboratory and molecular studies to address unknown or poorly understood aspects of mosquito biology and arbovirus transmission are encouraged. Projects should focus on Culex or Aedes mosquito species that are important vectors of arboviruses.

Savage, H.M., J.P. Ledermann, L. Yug, K.L. Burkhalter, M. Marfel and W.T. Hancock. 2015. Incrimination of Aedes (Stegomyia) hensilli Farner as an epidemic vector of chikungunya virus on Yap Island, Federated States of Micronesia, 2013. American Journal of Tropical Medicine and Hygiene 92:429-436.

Kothera, L., B. M. Nelms, W.K. Reisen, and H.M. Savage. 2013. Population genetic and admixture analyses of Culex pipiens complex (Diptera: Culicidae) populations in California, United States. American Journal of Tropical Medicine and Hygiene 89:1154-1167.

Kothera, L., M. Godsey, J.-P, Mutebi and H.M. Savage. 2010. A comparison of above ground and belowground populations of Culex pipiens (Diptera: Culicidae) mosquitoes in Chicago, Illinois, and New York City, New York, using microsatellites.
Journal of Medical Entomology 47:805-813.

Kent, R.J., S. Deus, M. Williams, and H.M. Savage. 2010. Development of a multiplexed polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) assay to identify common members of the subgenera Culex (Culex) and Culex (Phenacomyia) in Guatemala. American Journal of Tropical Medicine and Hygiene 83:285-291.

Savage, H.M., M. Anderson, E. Gordon, others. 2008. Host-seeking heights, host-seeking activity patterns, and West Nile virus infection rates for members of the Culex pipiens complex at different habitat types within the hybrid zone, Shelby County, TN, 2002 (Diptera: Culicidae). Journal of Medical Entomology 45:276-288.

Identification of the mechanisms for vertebrate host-restricted replication and mosquito interference of flaviviruses with a mosquito-restricted host range

Aaron Brault, PhD, Arboviral Diseases Branch, email: zlu5@cdc.gov

Nhumirim virus (NHUV) represents an example of a unique subset of apparently insect-specific viruses that phylogenetically affiliate with dual-host mosquito-borne flaviviruses(1). In vitro co-infection experiments have indicated that prior or concurrent infection of mosquito cells with NHUV resulted in a 10,000-fold reduction in West Nile virus (WNV) titers(2). Additionally, co-intrathoracic inoculation of Culex quinquefasciatus demonstrated significantly lower transmission rates compared to mosquitoes inoculated with WNV alone(3). These data indicate the potential that infection of Culex spp. vectors with NHUV could serve as a barrier for efficient transmissibility of flaviviruses associated with human morbidity/mortality; however, no data exists pertaining to the mechanism(s) of in vitro or in vivo superinfection exclusion (SIE). Furthermore, there is a paucity of data on the viral genetic determinants or host cellular pathways that restrict host range for flaviviruses. The phylogenetic placement of NHUV among dual host flaviviruses and a codon usage of NHUV that resembles that of flaviviruses that circulate between both vertebrate and mosquito hosts indicates the likelihood that this group of viruses has only recently lost its capacity to replicate in vertebrate cells(2, 4). As such, this affords an excellent model for dissecting both viral and host factors relevant to such a host

restrictive phenotype. The identification of the viral genetic determinants of vertebrate replication and host restriction pathways could be interrogated by assessing the vertebrate infection phenotype of NHUV/WNV chimeric viruses and by screening vertebrate cell knockdown libraries, respectively. There is a potential for SIE to alter the natural transmissibility of flaviviruses and for potential use in the derivation of novel methodologies for reducing transmission of flavivirus. As such, the study of SIE mechanism(s) is proposed be elucidated through the use of small RNA libraries, intracellular trafficking and/or exogenous expression of decoy RNAs.

1. Pauvolid-Correa A, Solberg O, Couto-Lima D, Kenney J, Serra-Freire N, Brault A, Nogueira R, Langevin S, Komar N. 2015. Nhumirim virus, a novel flavivirus isolated from mosquitoes from the Pantanal, Brazil. Arch Virol 160:21-27.
2. Kenney JL, Solberg OD, Langevin SA, Brault AC. 2014. Characterization of a novel insect-specific flavivirus from Brazil: potential for inhibition of infection of arthropod cells with medically important flaviviruses. J Gen Virol 95:2796-2808.
3. Goenaga S, Kenney JL, Duggal NK, Levis SC, Enria DA, Brault AC. 2015. Previous infection with Nhumirim virus (Flaviviridae; Flavivirus) inhibits efficient transmission of West Nile virus by Culex quinquefasciatus mosquitoes Viruses in press.
4. Blitvich B, Firth A. 2015. Insect-Specific Flaviviruses: A Systematic Review of Their Discovery, Host Range, Mode of Transmission, Superinfection Exclusion Potential and Genomic Organization. Viruses 7:1927-1959.

Advanced Public Health Laboratory Studies on Rickettsial Diseases and their Vectors

Gregory A. Dasch, Ph.D., Rickettsial Zoonoses Branch, email: ged4@cdc.gov

The Biotechnology Applications Laboratory (BAL) of the Rickettsial Zoonoses Branch conducts both field and laboratory studies using next generation sequencing and proteomics to improve the diagnosis, prevention, control and treatment of rickettsial vector-borne diseases. Strong emphasis is placed on the most severe and/or fatal tick borne-disease in the Americas, Rocky Mountain spotted fever, caused by *Rickettsii rickettsii* and the Select Agent *Rickettsia prowazekii*. *R. rickettsii* also serves as the primary laboratory model for investigations with other *Rickettsia* agents causing human rickettsioses of varying clinical presentation caused by an ever expanding list of emerging organisms and the vectors, largely ticks, which transmit rickettsioses. Relatively little is known about the molecular mechanisms used by obligately intracellular bacteria to subvert host defense mechanisms in either humans or their arthropod vectors. The BAL laboratory is applying whole genome, transcriptomics, cellular biology, and proteomics approaches to *Rickettsia* to better understand their surface antigen diversity, pathogenic effector mechanisms, and specific host adaptations. Investigations on the physiology of tick vectors, their genomics, and their total bacterial community are also being conducted. Depending on the research interests of individual candidates, targeted research proposals are solicited including (1) molecular epidemiology/genomics of *Rickettsia*, and discovery of clinical biomarkers of rickettsial diseases; (2) dissection of vector-bacterial community-host interactions (disease ecology); (3) proteomic and metabolomics investigations of rickettsial alterations of host cell physiology; (4) cell biology, immunology and pathologic responses of vertebrate and invertebrate cells to rickettsial infections; and (5) development of

medical countermeasures (vaccines, assays, new therapies) for treating, diagnosing or preventing rickettsial diseases. While work with live *Rickettsia* must be performed in a Biosafety Level 3 laboratory, only such work with *R. prowazekii* requires Select Agent approvals. Work with animals and vectors and field studies require IACUC approval and animal training as well as field collection permits.

Bonilla, D. L.., L. A. Durden, M. E. Eremeeva, and G. A. Dasch. 2013. The biology and taxonomy of head and body lice -- Implications for louse borne disease prevention. PLOs Pathogens 9(11): e1003724.

Prusinski, M. A., J. L. White, S. J. Wong, others. 2014. Sylvatic typhus associated with flying squirrels (*Glaucomys volans*) in New York State, United States. Vector-Borne Zoon Dis. Vector Borne Zoonotic Dis. 14(4):240-244.

Williams-Newkirk, A. J., L. A. Rowe, T. R. Mixson-Hayden, and G. A. Dasch. 2014. Characterization of the bacterial communities of life stages of free living lone star ticks (*Amblyomma americanum*). PLoS One 9(7):e102130. doi: 10.1371/journal.pone.0102130.

Eremeeva, M. E., and G. A. Dasch. 2015. Challenges posed by tick-borne rickettsiae: eco-epidemiology and public health implications. Frontiers Publ Hlth 3(15):1-17.

Williams-Newkirk AJ, Burroughs M, Changayil SS, Dasch GA. 2015. The mitochondrial genome of the lone star tick (Amblyomma americanum). Ticks Tick Borne Dis. 6(6):793-801.

Ecology and Control of Ticks and Lyme disease spirochetes

Rebecca J. Eisen, PhD, and Lars Eisen, Ph.D. Ecology, Entomology Activity (EEA), Bacterial Diseases Branch, email: dyn2@cdc.gov

Lyme disease, caused by *Borrelia burgdorferi* sensu lato (Bbsl) is the most commonly reported vector-borne disease in the United States. Since the late 1990s, the number of reported cases has tripled and the primary tick vector (*Ixodes scapularis*) has continued to expand its geographical range. The primary objectives of our laboratories are to 1) Determine when and where humans are at greatest risk for exposure to ticks and Lyme disease spirochetes; 2) Improve understanding of how Lyme disease spirochetes are maintained in enzootic transmission cycles, and 3) Mitigate risk of exposure to infected ticks through improved surveillance and management strategies. Applied research projects that integrate field, laboratory, molecular or modeling studies to address these broad objectives are encouraged. Examples might include: 1) development of improved pathogen detection assays for ticks and tissues from mammalian reservoirs, 2) field studies aimed at identifying where humans are most at risk for exposure to infected ticks, 3) field and laboratory studies to elucidate how Bbsl spirochetes are maintained in enzootic transmission cycles, and 4) development and evaluation of personal protection measures against ticks (e.g., repellents, permethrin-treated clothing) or environmentally based tick/control methods (chemical and biological agents to suppress host-seeking ticks or tick host-targeted control methods).

Eisen, R.J., L. Eisen and C.B Beard. 2016. County-scale distribution of *Ixodes scapularis* and *Ixodes pacificus* (Acari: Ixodidae) in the continental United States, Journal of Medical Entomology, in press.

Eisen, R.J., L. Eisen, N.H. Ogden, and C.B. Beard. 2016. Linkages of weather and climate with *Ixodes scapularis* and *Ixodes pacificus* (Acari: Ixodidae), enzootic transmission of *Borrelia burgdorferi*, and Lyme disease in North America. 2016. Journal of Medical Entomology, in press.

Johnson, T.L., J. Bjork, D. Neitzel, F. Dorr, E. Schiffman, and R.J. Eisen*. 2016. Habitat suitability model for the distribution of black-legged ticks, *Ixodes scapularis* (Acari: Ixodidae), in Minnesota, Journal of Medical Entomology, in press.

Springer, Y.P., C.S. Jarnevich, D.T. Barnett, A.J. Monaghan, and R.J. Eisen*. 2015. Modeling the present and future distribution of the lone star tick, *Amblyomma americanum* (Ixodida: Ixodidae), in the continental United States, American Journal of Tropical Medicine and Hygiene, 93: 875-890.

Monaghan, A.J., S.M. Moore, K.M. Sampson, C.B. Beard, and R.J. Eisen*. 2015. Climate change influences on the annual onset of Lyme disease in the United States, Ticks and Tick-Borne Diseases, 6: 615-622.

Newman, E.A., L. Eisen, R.J. Eisen, N. Fedorova, J.M. Hasty, C.E. Vaughn, and R.S. Lane. 2015. *Borrelia burgdorferi* sensu lato spirochetes in wild birds in northwestern California: associations with ecological factors, bird behavior and tick infestation." PLoS One PLoS One 10(2): e0118146.

Moore, S.M., R.J. Eisen, A. Monaghan, and P. Mead. 2014. Meteorological influences on the seasonality of Lyme disease in the United States, American Journal of Tropical Medicine and Hygiene, 90: 486-496.

Eisen, R.J., J. Piesman, E. Zielinski-Gutierrez, and L. Eisen. 2012. What do we need to know about disease ecology to prevent Lyme disease in the Northeastern United States? *Journal of Medical Entomology* 49: 11-22

Q Fever: Improved therapy for *C. burnetii* infections

Gilbert J. Kersh, PhD, Rickettsial Zoonoses Branch, email: hws7@cdc.gov

Coxiella burnetii is an obligate intracellular bacterium, a category B bioterrorism agent, and the etiologic agent of Q fever. Q fever is transmitted by inhalation of the organisms usually derived from waste products of infected animals and results in an acute febrile illness characterized by fever headache, and in some cases pneumonia. In a minority of cases, a chronic infection develops which can be life-threatening and typically manifests as culture negative endocarditis. Treatment for acute Q fever is a 2-week course of the antibiotic doxycycline, whereas chronic Q fever requires 18 months of treatment with doxycycline plus hydroxychloroquine. Alternative therapies are needed due to the difficulty of compliance over such a long treatment course and the frequency with which patients are unable to tolerate these drugs. In previous work, we have established *in vitro* assays for drug efficacy that include analysis in cultured cell lines as well as liquid suspension culture. Research opportunities are available which include (i) Evaluation of the pH dependence of *C. burnetii* growth and antibiotic function; (ii) Testing of novel drug combinations for long-term treatment (iii) Evaluation of immune responses as means to eliminate *C. burnetii*; (iv) *In vivo* testing of alternative treatments in a mouse model of *C. burnetii* aerosol infection.

Studies into the pathogenesis of *Rickettsia rickettsii*, the causative agent of Rocky Mountain spotted fever

Sandor E. Karpathy, PhD and Chris Paddock, MD, MPHTM, Rickettsial Zoonoses Branch, email: evu2@cdc.gov

Rickettsia rickettsii is the most pathogenic of all known rickettsial species and continues to cause a substantial number of human cases of Rocky Mountain spotted fever (RMSF) throughout the Western Hemisphere. While the case fatality rate of RMSF has fallen dramatically with the introduction of antibiotics, early treatment is still essential as delayed

treatment leads to severe disease and mortality. Additionally, case fatality rates in Latin America are 3-5x higher than in the US, and in some countries approach 40%. Little is known about the pathogenic mechanisms involved in *R. rickettsii* infection. Recent work in our lab has shown that genetic differences exist between various strains of *R. rickettsii* that directly correlate with their geographical origins; however, it is unknown if this differentiation also represents differences in the relative virulence of the isolates. An increased understanding of the pathogenic mechanisms and regional differences in case-fatality rates of *R. rickettsii,* and the variation in virulence among different isolates, is needed to better assess the threat of human disease. Research opportunities are available to 1) investigate the relative virulence of geographically distinct isolates of *R. rickettsii* utilizing cell culture and animal models 2) investigate host cellular response to rickettsial infection, and 3) investigate rickettsial gene expression during infection in vivo and in vitro.

Karpathy SE, Dasch GA, Eremeeva ME. 2007. Molecular Typing of Isolates of *Rickettsia rickettsii* by Use of DNA Sequencing of Variable Intergenic Regions. J Clin Microbiol 45:2545-2553.

Paddock CD, Denison AM, Lash RR, Liu L, others. 2014. Phylogeography of Rickettsia rickettsii genotypes associated with fatal Rocky Mountain spotted fever. Am J Trop Med Hyg 91:589-597.

Labruna MB, Santos FC, Ogrzewalska M, others. 2014. Genetic identification of rickettsial isolates from fatal cases of Brazilian spotted fever and comparison with *Rickettsia rickettsii* isolates from the American continents. J Clin Micro 53: 3788-3791.

Alvarez-Herandez G, Murillo-Benitez C, Candia-Plata, M, Moro, M. 2015. Clinical profile and predictors of fatal Rocky Mountain spotted fever in children from Sonora, Mexico. Pediatr Infect Dis J 34:125-130.

Angerami RN, Camara M, Pacola MR, others. 2012. Features of Brazilian spotted fever in two different endemic areas in Brazil. Ticks Tick Borne Dis 3:346-348.

Dengue virus movement and invasion risk

Michael Johansson, PhD, Dengue Branch, email: eyq9@cdc.gov

Understanding the dynamic movement of dengue viruses is fundamental to our ability to implement effective prevention and control strategies. For the Southern U.S. and Hawaii, there is frequent risk of introduction. Successful introduction depends the arrival of the virus and suitable local ecology for transmission. A better understanding of both of these components can improve interventions to reduce this risk. In endemic areas, spread can introduce novel viruses leading to changing clinical and epidemiological profiles, and can hamper the effectiveness of extant interventions (e.g. vector control). To address these challenges, we have developed models utilizing multiple types of mobility, disease, and climate data to identify key components of the spread process and those components which are still poorly understood [1-5]. Fundamental questions which may be addressed include determining limiting factors for transmission in borderline areas (e.g. Southern U.S. and Hawaii), developing methods to estimate ecological suitability based on historical case data (e.g. Southern U.S. and Hawaii), developing and assessing the utility of novel mobility estimation methods (e.g. mobile phone,

GPS, or immigration data), and determining the role of local mobility in viral movement (e.g. within Puerto Rico).

1. Wesolowski, Amy; Qureshi, Taimur; Boni, Maciej F; Sundsøy, Pål Roe; Johansson, Michael A; Rasheed, Syed Basit; Engø-Monsen, Kenth; Buckee, Caroline O. Impact of human mobility on the emergence of dengue epidemics in Pakistan. *Proceedings of the National Academy of Sciences*. 112(38):11887-11892 (2015).
2. Feldstein, Leora R; Brownstein, John S; Brady, Oliver J; Hay, Simon I; Johansson, Michael A. Dengue on islands: a Bayesian approach to understanding the global ecology of dengue viruses. *Transactions of The Royal Society of Tropical Medicine and Hygiene*. 109(5):303-12 (2015).
3. Johansson, Michael A; Powers, Ann M; Pesik, Nicki; Cohen, Nicole J; Staples, J Erin. Nowcasting the spread of chikungunya virus in the Americas. *PLoS ONE*. 9(8): e104915 (2014).
4. Brady, Oliver J; Johansson, Michael A; Guerra, Carlos A; Bhatt, Samir; Golding, Nick; Pigott, David M; Delatte, Hélène; Grech, Marta G; Leisnham, Paul T; Maciel-de-Freitas, Rafael. Modelling adult Aedes aegypti and Aedes albopictus survival at different temperatures in laboratory and field settings. *Parasites & Vectors*. 6(1):351-362 (2013).
5. Johansson, Michael A; Arana-Vizcarrondo, Neysarí; Biggerstaff, Brad J; Gallagher, Nancy; Marano, Nina; Staples, J Erin. Assessing the risk of international spread of yellow fever virus: a mathematical analysis of an urban outbreak in Asuncion, 2008. *The American Journal of Tropical Medicine and Hygiene*. 86(2): 349-358 (2012).

Biology, Ecology, and Control of Tick Vectors and Vertebrate Hosts of Rickettsial Pathogens

William L. Nicholson, PhD (Disease Ecology Laboratory), email: wan6@cdc.gov and Michael L. Levin, PhD (Medical Entomology Laboratory), Pathogen Biology and Ecology Activity, Rickettsial Zoonoses Branch, email: msl3@cdc.gov.

The rickettsial diseases of humans are caused by a number of species in the genera *Anaplasma*, *Ehrlichia*, *Orientia*, *Rickettsia, Neorickettsia,* and *Neoehrlichia*. The ecologies of many rickettsial pathogens have not been elucidated, especially for many of the newly identified organisms. Natural cycles involve a complex interaction among the vector ticks, their vertebrate hosts, and the pathogens. A combination of studies utilizing fieldwork and supported by controlled laboratory experiments can provide valuable new information regarding these maintenance cycles and transmission dynamics. The ecological approach also identifies points of potential intervention to prevent or control the perpetuation of these cycles, and thus lead to reduced human exposure to these agents. Because we study many aspects of the pathogen life cycle, candidates with diverse backgrounds in entomology, wildlife biology, molecular biology, and immunology are strongly encouraged to apply. Projects can incorporate laboratory, field activities, or a combination of both. Potential project topics include: 1) field investigations to determine how enzootic cycles of transmission are maintained; 2) habitat suitability assessments to identify areas of greatest risk for tick and pathogen contact; 3) field or laboratory studies to better understand transmission dynamics in various tick-host systems; 4) laboratory investigations of the interaction of rickettsial co-infections; 5) evaluation of anti-tick and anti-pathogen vaccines; 6) vector or host competence studies; or 7) development and application of novel integrated tick control methods. Our two laboratories, unique tick vivarium, and additional branch resources provide the equipment and facilities for BSL-2/BSL-3 laboratory work, tick and animal studies, and pathogen detection using molecular, immunological, or microbiological methods.

● Prusinski, M. A., et al. 2014. Sylvatic epidemic typhus associated with flying squirrels (*Glaucomys volans*) in New York state, USA. Vector Borne Zoonotic Dis. 14 (4): 240-244.
● Pritt, B. S., et al. 2011. Emergence of a new pathogenic *Ehrlichia* species, Wisconsin and Minnesota, 2009. New Engl. J. Med. 365 (5): 422-429.
● Zemtsova, G., L. F. Killmaster, K. Y. Mumcuoglu, and M. L. Levin. 2010. Co-feeding as a route for transmission of *Rickettsia conorii israelensis* between *Rhipicephalus sanguineus*. Exp. Appl. Acarol. 52: 383-392.
● Zemtsova, G. E., et al. 2016. First report of *Rickettsia* identical to *R. slovaca* in colony-originated *D. variabilis* in the US: detection, laboratory animal model and vector competence of ticks. Vector Borne & Zoonotic Dis. 16: 77-84.
● Killmaster, L. F., et al. 2014. Detection of bacterial agents in *Amblyomma americanum* (Acari: Ixodidae) from Georgia, USA, and the use of a multiplex assay to differentiate *Ehrlichia chaffeensis* and *Ehrlichia ewingii*. J. Med. Entomol. 51:868-872.