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Targeting the Achilles Heel of Babesia Parasites' Mode of Survival Within Human Red Blood Cells

Choukri Ben Mamoun is an Associate Professor at Yale with a primary appointment in the Department of Internal Medicine and a secondary appointment in the Department of Microbial Pathogenesis. He received his PhD in 1996 in Molecular Microbiology in France from University of Paris XI and Institut National Agronomique Paris-Grignon. In 1996, he joined the Department of Molecular Microbiology at Washington University as a Research Fellow of the Howard Hughes Medical Institute and in 2000 became a faculty member at University of Connecticut Health Center. In 2009, he joined the faculty at the Yale School of Medicine as a Principal Investigator with a focus on the biology and therapy of the protozoan parasites that cause human malaria and babesiosis.

Dr. Ben Mamoun has authored 78 peer-reviewed papers in the field of eukaryotic pathogenesis. Among his important findings in the malaria field are: the development of selectable markers for genetic manipulation of *P. falciparum* (Mamoun et al., PNAS 1999), discovery of a novel metabolic pathway for lipid metabolism in *P. falciparum* (Pessi et al, PNAS 2004), creation of the first conditional knockouts of *P. falciparum* lacking the purine transporter or phosphoethanolamine

methyltransferase (El Bissati et al., PNAS 2006 and Witola et al., JBC 2007), discovery of lipid regulation as a critical step in *P. falciparum* sexual differentiation (Bobenchik et al., PNAS 2013). His notable findings in the babesiosis field are: Discovery of a new combination therapy consisting of atovaquone and endochin-like quinolone (ELQ-334) for radical cure of babesiosis infection in mice (Lawres et al., J. Exp. Med, 2016) and the development of a new diagnostic test for detection of B. microti active infection (Thekkiniath et al., J. Clin. Microb. 2018).

Dr. Ben Mamoun has served as a member or chair of several NIH and DOD study sections and other international organizations. He has served on the editorial board of several research journals, presented seminars and lectures both nationally and internationally and received multiple awards including the Patterson Award, the Burroughs Welcome Award and the Bill and Melinda Gates Foundation Award.

In addition to his academic program, Dr. Ben Mamoun is the founder of a biotech company, ELIV5 Therapeutics.

Conference Lecture Summary

Since the completion of the assembly and annotation of the genome of the human pathogen *Babesia microti*, my laboratory has been involved in the development of novel approaches to detect active babesia infection and discovery of more effective therapies to treat human babesiosis. In this lecture, I will present new data showing that *B. microti* uses a novel mechanism for delivery of proteins into the host, and how we exploited this information to develop a highly sensitive assay for detection of *B. microti* active infection in human and mouse blood. Furthermore, I will present our recent discovery of a new combination therapy that targets a critical step in *B. microti* metabolism during its development

within mouse and human red blood cells and results in radical cure of the disease.