

## Unraveling Tick Evasion Of Host Immunity: Evidence Of Antigenic Variation Equivalent Mechanism In Tick Saliva & its impact on tick vaccine design

<u>Albert Mulenga</u><sup>3</sup>, Tae Kim<sup>3</sup>, Lucas Tirlioni<sup>1</sup>, Antônio F. M. Pinto<sup>4,5</sup>; James Moresco<sup>5</sup>; John R. Yates III<sup>5</sup>, Zelko Radulovic<sup>3</sup>, Taylor Hollmann<sup>3</sup>, Lindsay Porter<sup>3</sup>, Mariam Bakshi<sup>3</sup>, Waithaka Mwangi<sup>3</sup>, Itabajara Vaz Jr.<sup>1, 2</sup>,

<sup>1</sup>Centro de Biotecnologia, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil. <sup>2</sup>Faculdade de Veterinária, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil. <sup>3</sup>Department of Veterinary Pathobiology, College of Veterinary Medicine, Texas A&M University, College Station, TX, USA. <sup>4</sup>Centro de Pesquisas em Biologia Molecular e Funcional, Instituto Nacional de Ciência e Tecnologia em Tuberculose (INCT-TB), Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Porto Alegre, RS, Brazil <sup>5</sup>Department of Chemical Physiology, The Scripps Research Institute, La Jolla, CA, USA.

Ticks inject hundreds of proteins in the host to evade host defenses, successfully feed and transmit disease agents. Research has shown that repeatedly infested animals can amount protective anti-tick immunity that ultimately reduce tickfeeding success. Efforts to immunize animals against tick feeding using single molecule approaches have failed replicate results in nature. This has led suggestions that tick saliva antigens may not suitable for tick vaccine development. Emerging transcriptome and tick saliva proteome data indicates that failure of tick saliva protein based vaccines could be explained by an apparent antigenic variation equivalent mechanism in tick saliva. Over the last three years our group and collaborators embarked on trying to identify Amblyomma americanum and Ixodes scapularis tick saliva proteins that are injected into animals during feeding. These data has revealed the complexity of tick feeding physiology as expected. Our data show that ticks inject unique proteins in the same class at different feeding time points. Similar to antigenic variation observed in other parasites, this could be the tick's way to protect essential tick feeding functions from host immune attack. Host immune response to tick saliva proteins injected into animals at the start of feeding will bot affect functions of unique proteins in the same class that are injected into the host by day three of feeding for example. Comparative bioinformatics has identified molecular systems that are conserved across tick species. We are using RNAi silencing, biochemical, and immunological approaches to understand role(s) of selected conserved tick molecular systems (proteases, protease inhibitors, and proteins of unknown function) in tick feeding success and physiology. A food for thought concept of how these emerging data will influence the design of future tick vaccines is discussed.

Keywords: tick, vaccine and saliva.