

Immunomodulating properties of *Amblyomma variegatum* saliva, a functional proteomics study of the molecular determinants.

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Amblyomma variegatum, the tropical bont tick, is a species of veterinary importance being considered as one of major pest of ruminants in Africa and in the Caribbean. It is associated with severe dermatophilosis and transmits the rickettsial *Ehrlichia ruminantium*, the agent of heartwater, to ruminants. Tick's saliva contains a complex mixture of bioactive molecules including proteins that modulate host responses to ensure successful blood feeding. The limited amount of saliva that can be obtained from ticks has hampered characterisation of salivary proteins using traditional protein chemistry, but recent advances in proteomics (especially mass spectrometry and bioinformatics) provide new tools to finely investigate tick sialomes. The general objective of this study was to better understand the role of *A. variegatum* saliva in tick/host/pathogen interactions. Salivation of semi-fed females was induced after detachment by injection of pilocarpin. Crude saliva proteins were pre-fractionated by SDS-PAGE and generated peptides were analysed online by nano-flow Ultimate 3000 HPLC–nanoelectrospray ionization using an Orbitrap Elite mass spectrometer. Raw data analysis was performed using the MaxQuant software and proteins identified according to UniProt Knowledgebase. Among the 336 proteins identified in *A. variegatum* saliva, a bioinformatics functional analysis of molecular determinants highlighted immunomodulators (e.g. heme lipoprotein, serpins, phospholipase A2 or ubiquitin) that could, at least in part, explain the biological effects observed on bovine immune cells *in vitro*. Our results bring new insights for a better understanding of tick-ruminant interactions at the molecular level, and pave the way towards integrative strategies to interfere with both the immunosuppressive and infectious processes in corresponding tick-borne diseases.

Keywords: *Amblyomma variegatum*, tick saliva, immunomodulation, proteomics