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Investigate, evaluate, protect

Effect of O. porcinus tick salivary gland extract on the African swine fever virus infection in domestic pig

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African swine fever is a lethal haemorrhagic swine disease with disastrous financial consequences for pig production. Ornithodoros soft ticks are able to transmit the African swine fever virus (ASFV) to pigs in farms, following the natural epidemiologic cycle of the virus. Tick saliva has been shown to modulate the host physiological and immunological responses during feeding on skin, thus affecting viral infection.

To better understand the interaction between soft tick, ASFV and pig at the bite location and the possible influence of tick saliva on pig infection by ASFV, salivary gland extract (SGE) of Ornithodoros porcinus, co-inoculated or not with ASFV, was used for intradermal auricular inoculation.

Our results showed that, after the virus triggered the disease, pigs inoculated with virus and SGE presented greater hyperthermia than pigs inoculated with virus alone. The density of Langerhans cells was modulated at the tick bite or inoculation site, either through recruitment by ASFV or inhibition by SGE. Additionally, SGE and virus induced macrophage recruitment each. This effect was enhanced when they were co-inoculated. Finally, the co-inoculation of SGE and virus delayed the early local spread of virus to the first lymph node on the inoculation side. This study has shown that the effect of SGE was powerful enough to be quantified in pig both on the systemic and local immune response.

We believe this model should be developed with infected tick and could improve knowledge of both tick vector competence and tick saliva immunomodulation.

Immunomodulating properties of *Amblyomma variegatum* saliva and role on tick-borne disease transmission

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Keywords: Amblyomma variegatum, tick saliva, immunomodulation, proteomics

The tropical bont tick, Amblyomma variegatum, is a major pest of ruminants, causing direct skin lesions, vectoring the obligate intracellular ricketsiale Ehrlichia ruminantium, the causative agent of heartwater, and being able to reactivate dermatophilosis. In general, tick salivary proteins are the result of host blood feeding adaptation and are known to contain inhibitors of blood clotting, platelet aggregation and angiogenesis, as well as vasodilators and immunomodulators. The general objective of this study was to better understand the role of the saliva in the tick interaction with the host but also in pathogen transmission or diseases activation. We therefore first analysed the immunomodulating properties of semi-fed A. variegatum female saliva on bovine peripheral blood mononuclear cells (PBMCs) in vitro. Flow cytometry and cytokine ELISAs have been used to evaluate the saliva impact on PBMCs. We focused on immunosuppressive properties by analysing both lymphocytes proliferation and monocyte-derived macrophages phenotype characterised by inhibition or induction of stimulatory and co-stimulatory molecules such as MHC-II, CD40, CD80 or CD86, and production of pro- or anti-inflammatory cytokines such as interleukin (IL)-2, IL-4, IL-6, IL-10, IL-12p40, and tumor necrosis factor (TNF)-α. Moreover, a proteomics exhaustive molecular characterisation of A. variegatum saliva was performed to cluster data set according to the evidenced immunomodulatory properties, and allowed refined characterisation of Amblyomma sialome. Bioinformatics functional analysis of tick saliva highlighted molecular determinants that could, at least in part, explain the biological effects observed on bovine PBMCs. Our results bring new insights for a better understanding of tick-ruminant interactions, and open new perspectives to develop integrative strategies to interfere with the infectious pathoimmunological process of such tick-borne infections.